CANNABIS AND ROAD CRASHES: A CLOSE LOOK AT THE BEST EPIDEMIOLOGICAL EVIDENCE

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CANNABIS AND ROAD CRASHES:
A CLOSE LOOK AT THE BEST EPIDEMIOLOGICAL EVIDENCE

Michael White

1 November 2017

FINAL REPORT

Report documentation and acknowledgements

TITLE: *Cannabis and road crashes: A close look at the best epidemiological evidence*

DATE: 1 November 2017

PAGES/WORDS: 142/79,818

AUTHOR: Dr Michael White

AFFILIATION AND CONTACT INFORMATION

School of Psychology, University of Adelaide, South Australia 5005, Australia
Mobile: + 61 4 0855 9710
Email: mawhite8@bigpond.com
Web: https://www.researchgate.net/profile/Michael_White24

ABSTRACT

The starting point for this review was a literature search that identified eleven epidemiological studies of the relationship between the presence of THC in a body fluid and crashing. Those studies were then scrutinised to gauge how well they dealt with a number of identified biases. It is concluded that, if cannabis *does* increase the risk of crashing, the increase is unlikely to be more than about 30%. Even the null hypothesis of no increase cannot be rejected. This review also investigated two further hypotheses about the relationship between the use of cannabis and crashing. The first is that there is a threshold concentration of THC below which there is no effect, but above which there is an effect. The second is that the use of cannabis with alcohol exacerbates the effects of alcohol on crashing. It is concluded that there is no satisfactory epidemiological evidence for either hypothesis. The review also briefly examined the literature on the results of laboratory studies of the effects of cannabis on driving-related skills, and concludes that there is nothing in that literature to challenge the null hypothesis of no effect of cannabis on crashing.

KEY WORDS

systematic review, cannabis, marijuana, THC, drug driving, roadside drug testing (RDT), road safety, impaired drivers, random breath testing (RBT), responsibility analysis, case-control methodology

DISCLAIMER

The views expressed in this report are those of the author and do not necessarily represent those of the University of Adelaide.

SOURCES OF FINANCIAL AND OTHER SUPPORT

This study has not received any financial support.

ACKNOWLEDGEMENTS

Matthew Baldock for re-introducing me to the field of drug driving; Jack McLean for making it clear that there was a job to be done; Soames Job, Mary Sheehan and Tove Hels for encouragement; Amy Berning, Ruth Pirie and Guohua Li for providing missing data; Bill Glasper, Warren Brown, David Watts, Nick Burns, Paul Hutchinson, Trevor Bailey, Ross McColl, Tony Wohlers, Eduardo Romano, Hallvard Gjerde, Ole Rogeberg and Mark Asbridge for useful feedback; the Editors of the *Journal of the Australasian College of Road Safety* and five anonymous reviewers for some useful comments; and Vicki White for generous support.

Palmer, M., Wodak, A., Douglas, B, & Stephens, L. (2016). *Can Australia respond to drugs more effectively and safely?* Weston, ACT: Australia21:

Recommendation 6: Current practices to test drivers for the presence of psychoactive substances in their blood should be rigorously reviewed with respect to efficacy and cost effectiveness. The purpose of such testing should be to ascertain whether the driver is unsafe or unfit to drive as a result of psychoactive drug use, not to ascertain whether he or she has consumed a proscribed psychoactive drug. This issue will become a particular concern as the proposed new laws governing use of medicinal cannabis come into effect.

Executive Summary

Australia is the only country to have introduced large-scale roadside drug testing programs (RDT). Victoria was the first state to do so, in 2004, for cannabis and methamphetamine. New South Wales was next to do so, and also included ecstasy. RDT for the three illegal drugs has now been introduced in all the states and territories. Victoria currently conducts about 100,000 tests per year (Noonan, 2015).

The two recognised approaches to drug policy are zero tolerance and harm reduction. RDT has ostensibly been introduced in Australia as a harm-reduction measure to improve road safety. As such, it might be expected that the evidence base for the inclusion of cannabis would be strong. The purpose of this study is to discover if that is so - which is timely given that the medical use of cannabis may soon become widespread, and the RDT protocols may need to change.

The psychoactive ingredient of cannabis is delta-9-tetrahydrocannabinol (THC). The harm done by using cannabis before driving is best measured by odds ratios (ORs) from crash studies. An OR of 1.0 for the presence of THC in the body fluids of crashed drivers would mean that the use of cannabis before driving did not increase the risk of crashing, while an OR of 3.0, for example, would mean (roughly) that the use of cannabis tripled the risk of crashing.

There is much inconsistency in the basic research literature as to the size of the cannabis-crash OR; and a number of systematic reviews and meta-analyses have reached conflicting conclusions - with the most recent meta-analysis (Rogeberg & Elvik, 2016a) exposing serious errors in two earlier meta-analyses (Asbridge, Hayden & Cartwright, 2012; Li *et al.*, 2012).

The starting point for this review was a literature search that identified eleven epidemiological studies of the relationship between the presence of THC in a body fluid and crashing. Those studies were then scrutinised to gauge how well they dealt with identified biases - most of which were over-estimation biases. It is concluded that, if cannabis *does* increase the risk of crashing, the OR is unlikely to be greater than about 1.3. Even the null hypothesis of no effect (OR = 1.0) cannot be rejected.

A meta-analysis was not conducted. A meta-analysis would inevitably have produced an over-estimated summary OR for the relationship between the prior use of cannabis and crashing, because meta-analyses do not compensate for over-estimation biases.

This review also investigated two further hypotheses about the relationship between the use of cannabis and crashing. The first is that there is a threshold concentration of THC below which there is no effect, but above which there is an effect. The second is that the use of cannabis with alcohol exacerbates the effects of alcohol on crashing. It is concluded that there is no compelling epidemiological evidence for either hypothesis.

This review also briefly examined the literature on the results of laboratory studies of the effects of cannabis on driving-related skills, and concludes that there is nothing in that literature to challenge the null hypothesis of no effect of cannabis on crashing.

If the purpose of the Australian RDT programs is to improve road safety, rather than only to possibly deter the use of illegal drugs, then cannabis should be removed from the RDT protocols. If that were not to happen, the current zero-tolerance approach, which is unjust, should be replaced by an approach that involves an above-zero cut-off that is indicative of very recent use. It is also recommended that the Victorian 'cocktail penalty' should be rescinded in the case of the co-use of cannabis and alcohol.

CONTENTS

Introduction

Background

The three psychoactive drugs currently tested for in Australian Roadside Drug Testing (RDT) programs are delta-9-tetrahydrocannabinol (THC - the active ingredient in cannabis or marijuana), N-methyl-alpha-methylphenethylamine (methamphetamine, 'meth', 'speed' or 'ice') and 3, 4, methylenedioxy-N-methamphetamine ('ecstasy'). Additional drugs are tested for in some of the Australian states. Each state has adopted a zero tolerance policy in its RDT regime.

This study was undertaken to explore the strength of the evidence supporting Australia's RDT policies in relation to cannabis.

The two recognised approaches to drug policy are zero tolerance and harm reduction. RDT has ostensibly been introduced in Australia as an evidence-based harm-reduction measure to improve road safety. As such, it might be expected that the evidence for the inclusion of cannabis would be strong. The purpose of this study is to discover if that is so, which is timely given that the medical use of cannabis may soon become widespread, and the RDT protocols will probably need to change.

THC is the psychoactive ingredient of cannabis. The harm done by using cannabis before driving is best measured by odds ratios (ORs) from crash studies. An OR of 1.0 for the presence of THC in the body fluids of crashed drivers would mean that the use of cannabis before driving did not increase the risk of crashing, while an OR of 3.0, for example, would mean (roughly) that the use of cannabis tripled the risk of crashing.

There is much inconsistency in the basic research literature as to the size of the cannabis-crash OR, and a number of systematic reviews and meta-analyses have reached conflicting conclusions - with the most recent meta-analysis (Rogeberg & Elvik, 2016a) exposing serious over-estimation biases in two earlier meta-analyses (Asbridge, Hayden & Cartwright, 2012; Li *et al.*, 2012). When Rogeberg and Elvik corrected for the biases in the earlier meta-analyses, Asbridge, Hayden and Cartwright's summary cannabis-crash OR had to be reduced from 1.9 to 1.3, while Li *et al*'s OR had to be reduced from 2.7 to 1.6. In their own meta-analysis, Rogeberg and Elvik found a summary cannabis-crash OR of 1.36 (1.2-1.6).

A brief and selective history of the introduction of RDT programs in Australia

Attitudes to the introduction of RDT in Australia can roughly be characterised as opposition or indifference from most road-safety researchers and government policy advisors in contrast with enthusiastic support from politicians.

The Australian Transport Council (ATC) was a national body that comprised the Commonwealth, state and territory ministers who had transport responsibilities. The ATC was responsible for the development of national road safety policies and strategies. Austroads is the peak organization of Australasian road transport and traffic agencies. Austroads' purpose is to support those agencies by undertaking research that underpins policy development (amongst other activities). In 1998, under the direction of the ATC, Austroads established a *Working Group on Drugs and Driving* to recommend countermeasures for drug-driving problems. The ATC hoped that the creation of the Working Group would lead to a nationally consistent approach to the development of drug-driving policy. The Woking Group mainly comprised government policy advisers, university researchers and Automobile Association representatives, all of whom were directly involved in road-safety policy development or research.

At this point, a clear distinction needs to be drawn between impairment-based and *per se* drug-driving offences. For it to be established that an impairment-based offence has been committed, the police must demonstrate, through behavioural observation, that the driver is impaired. In practice, that can be difficult and time-consuming. The driver *may* then be required to supply a

sample of oral fluid or blood for laboratory analysis, but the detection of a psychoactive drug can only be used in support of the charge of driving while impaired. In comparison, it is much easier for the police to establish that a *per se* drug-driving offence has been committed. All that is required is that the driver provide a sample of oral fluid or blood for laboratory analysis, and that the tests reveal the consumption of a proscribed drug. Under a zero-tolerance *per se* approach the mere presence of the drug is sufficient for the offence to have been committed. Under an alternative *per se* approach, the concentration of the drug above a proscribed limit must be established (as is the case for *per se* drink driving offences, where the lowest *per se* limit for most drivers is a blood alcohol concentration (BAC) of 0.05). Where *per se* drug-driving offences have been introduced, they can be enforced in random roadside drug-testing programs, which is, of course, not feasible in the case of impairment-based offences.

In 2000, the Austroads Working Group on Drugs and Driving concluded that "… a requirement for a zero blood concentration of the active ingredient of a drug is unreasonable" and that "there is no basis for defining [an above-zero] concentration of any drug that will cause unacceptable deterioration in performance in all drivers" (Potter, 2000, p. 25). The Working Group therefore recommended to the ATC "That the extent to which a driver is impaired should be the principal consideration in any drug-related driving enforcement", and "That 'roadside' drug-screening devices be considered for use only in conjunction with a structured impairment assessment (once their accuracy and reliability have been independently verified)" (Potter, 2000, p. v). In other words, the Working Group considered that the only appropriate circumstance to conduct drug-driving enforcement was where there was sound behavioral evidence that a driver was impaired (as might be obtained from crash involvement or from the results of a formal Field Sobriety Test). They considered that the introduction of zero-tolerance *per se* offences would be unjust, and that it would be implausible to attempt to introduce *per se* offences with above-zero concentration-based limits, because no particular limit for any psychoactive drug would be an unequivocal marker of impairment for all drivers. Those views are consistent with current best practice in drug-driving enforcement around the world: no country other than Australia has implemented a roadside drug-testing regime without the requirement to provide behavioral evidence of impairment.

By about mid-2002, the Victorian government had decided to introduce *per se* drug-driving legislation for *illegal* drugs, so there was no longer any hope of developing nationally harmonised impairment-based drug-driving legislation. The Convenor of the the Austroads Working Group on Drugs and Driving was Dr. Phillip Swann, who was the Manager of the Drugs, Alcohol and Fatigue Section of the Road Safety Department at VicRoads. He was assisted by Dr Jeff Potter who was the Manager of the Road User Behaviour Section of the same Department. With the Victorian Government intent on introducing *per se* drug-driving legislation, neither of the VicRoads members of the Working Group was particularly interested in the further development of nationally-consistent impairment-based legislation, and the Working Group was effectively dissolved.

The introduction of *per se* drug-driving legislation in Victoria was heralded by some of the people who were most intimately involved (including Dr Phillip Swann and Professor Olaf Drummer, who was a forensic scientist working at the Victorian Institute of Forensic Pathology) in a Catalyst TV program on 24 May 2003 (Phillips *et al*., 2003). Some of the hyperbolic claims made by the interviewees were that:

- Drugs are now responsible for more deaths on the road than alcohol
- Drivers who use cannabis, and are driving shortly after, are almost seven times more likely to be involved in a fatal crash than drug-free drivers
- Some academic studies suggest that those who consume cannabis actually overestimate the effect of the drug and therefore compensate for the impairing effect. However, many of those studies are fundamentally flawed
- Marijuana makes drivers more likely to drift across the road
- When your cannabis reading is 5 ng/ml, you are as impaired as someone with a BAC of 0.15
- If you smoke a cannabis cigarette, and also have a BAC of only 0.04 (which is under the legal limit), your risk of having an accident is 48 times higher than for someone who is free of drugs and alcohol

If these claims are close to being true, the use of cannabis before driving would create enormous road-safety risks. One aim of this study is to investigate the plausibility of such claims.

In his second reading speech on 30 October, 2003 for the bill to introduce *per se* drug driving legislation for illegal drugs, the Victorian Minister for Transport made no attempt to provide any relevant causal evidence of the road-safety risks posed by the use of illegal drugs before driving (Batchelor, 2003). That did not prevent him from concluding that "drug-driving is as much a factor in driver fatalities on Victoria's roads as drink driving" (p. 1418). He considered that the introduction of RDT would increase the fear of detection for drug-drivers and "could save many lives and serious injuries each year" (p. 1418).

The National Institute for Road Safety Research in the Netherlands (SWOV) is recognized throughout the world for its high standard of research and its scientifically founded recommendations to E.U. governments. Every three years, the International Council on Alcohol, Drugs and Traffic Safety (ICADTS) presents the 'Widmark Award' to one or more individuals who have made an outstanding contribution in the field of alcohol, drugs and road safety. During the 2016 ICADTS Conference, a Widmark Award was presented to the former SWOV researcher René Mathijssen. It was considered that his expertise was of great importance for the two large-scale European research programs into driving under the influence of alcohol and drugs: IMMORTAL (Impaired Motorists, Methods of Roadside Testing and Assessment for Licensing) and DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). It is interesting to note that, at much the same time as the Victorian Government was introducing zero-tolerance RDT for illegal drugs, Mathijssen and his colleagues were providing research-based advice to E.U. counties that "For illegal drugs, when taken alone, and with the exception of heroin, zero tolerance legislation would seem to produce a massive overkill, however, resulting in very high cost and hardly any road safety benefits" (Mathijssen & Houwing, 2005, p. 34).

The Victorian RDT program commenced in December 2004. The other Australian states and territories soon followed suit, because it was not politically feasible for any Australian jurisdiction to be seen to be 'weaker on drugs' than any other Australian jurisdiction.

Is the current study a 'systematic review'?

As described by Wikipedia, Cochrane is an independent, non-profit, non-government organization consisting of about 37,000 volunteers in about 130 countries. The organization was formed to help health professionals, patients and policy makers to make sound decisions in relation to health interventions, according to the principles of evidence-based medicine. The group collates medical research information in a systematic way, and conducts systematic reviews of randomized controlled trials of health-care interventions, which it publishes in The Cochrane Library. According to a Cochrane publication (Green *et al*., 2008):

> The key characteristics of a systematic review are: (a) a clearly stated set of objectives with an explicit, reproducible methodology; (b) a systematic literature search that attempts to identify all studies that would meet the eligibility criteria; (c) an assessment of the validity of the findings of the included studies, for example through the assessment of risk of bias; and (d) systematic presentation, and synthesis, of the characteristics and findings of the included studies.

The current study can perhaps be described as a systematic review in terms of these broad Cochrane criteria, because:

a) It has three clear objectives. (1) To discover whether there is satisfactory epidemiological evidence that the prior use of cannabis, as indicated by the presence of THC in oral fluid or blood, is associated with an increase in the risk of crashing. (2) If such a relationship exists, to discover whether there is satisfactory epidemiological evidence that there is a threshold level of THC below which cannabis has no effect and/or that there is a quantitative dose-response relationship between the concentration of THC and the risk of crashing. (3) To

discover if there is satisfactory epidemiological evidence that the prior use of cannabis with alcohol exacerbates the well-known effect of alcohol on the risk of crashing. The current study also has an explicit, reproducible methodology.

b) To be eligible for consideration in the current study, a published paper or report had to describe an epidemiological study of the role of cannabis in crashing, where the involvement of cannabis was indicated by toxicological tests for the presence of THC. However, the current study does not involve conducting a systematic literature search for articles that meet those eligibility criteria. The reason is that a number of available reviews, the most recent of which was published in early 2016, had already conducted such searches (as described in Part 2 of this report), and it is considered unnecessary to replicate that work.
c) The validity of the findings of each of the included studies is very carefully investigated, with a particular focus on identifying any biases that might be at work, and investigating how well each included study deals with the identified biases.
d) The findings are systematically presented and synthesised. Each included study is identified as either a case-control study or a responsibility study, and the results are presented separately for those two methodologies.

While the current study is certainly something *like* a systematic review, where it diverges most from a conventional systematic review is probably in its failure to conduct its own literature search.

With over four thousand systematic reviews being published each year in the field of medicine (Bastian, Glasziou & Chalmers, 2010) it has become obvious to medical researchers and practitioners that some level of standardisation is required in how the reviews are conducted and reported. One such standard is provided by the widely accepted PRISMA-P protocols (Moher *et al*., 2015; Shamseer *et al*., 2015). In terms of those protocols, the current study falls short of being a conventional systematic review in a number of respects, such as: the failure to produce and disseminate a formal description of the approach to be followed ('protocol') prior to undertaking the study and the failure to include the details of how the literature will be searched, including search items and publication timeframes.

The title of this report identifies the study as 'a *close look* at the *best* epidemiological evidence'. The italicised terms are important indicators of the main characteristics of this study. Only the 'best' epidemiological studies are included: those that identified the prior use of cannabis through the detection by toxicological analysis of THC in oral fluid or blood. That feature of the current study is not typical of systematic reviews, where the inclusion criteria are usually more relaxed. For example, previous comparable reviews have included epidemiological studies that used self-reported cannabis use or the presence of a metabolic by-product of cannabis consumption to indicate the involvement of cannabis in crashes (as described in Part 2 of this report). With only a relatively few studies included, the current study is able to have a 'close look' at the strengths and weaknesses of the included studies. That feature of the current study is also not typical of systematic reviews, where some salient features of the included studies may be identified and analysed, but the individual included studies are rarely scrutinised at a level of detail where serious idiosyncratic problems can be identified.

The question of whether or not the current study comprises a systematic review is debatable. Ultimately, the question is irrelevant. All that is being claimed is that the current study comprises a *close look* at the *best* epidemiological evidence. It should be approached as a rigorous 'close look' rather than an inadequate systematic review. It may prove to be a beautiful swan rather than an ugly duckling.

The current study does not include a meta-analysis

Cochrane defines a 'meta-analysis' as (Green *et al*., 2008):

> … The use of statistical techniques to integrate and summarize the results of studies that have been included in a systematic review. Many systematic reviews contain meta-analyses, but not all. By combining information from all relevant studies, meta-analyses can provide more precise estimates of the effects of [the independent variable] than those derived from the individual studies included within a review.

The current study does *not* incorporate a meta-analysis, because that would not be the most appropriate means of identifying a summary measure of the strength of the effect of the independent variable in this instance. The reason is that many of the research studies suffer from one or more biases, most of which tend to exaggerate the strength of the effect of a drug on crashing. A meta-analysis would not adequately compensate for over-estimation biases; it would provide an over-estimate of the 'true' strength of the cannabis-crash relationship.

The rationale for the approach taken in the current study reflects the view of Roberts and Ker (2015, p. 1536) that "Efforts by Cochrane and others to locate all trials [reported studies] have meant that many low-quality, single-centre trials, often with inaccuracies, are easily accessible. Most meta-analyses are dominated by such trials". They noted that "Inclusion of such trials results in inflated treatment effects".

Report structure

Following the Introduction, this report has twelve Parts:

- The first considers the epidemiological research methods that have been employed to explore the role of cannabis in crash causation
- The second identifies those published epidemiological studies that are of sufficient rigor to be considered further in relation to exploring the role of cannabis in crashing
- The third examines the evidence from responsibility studies that the use of cannabis increases the risk of crashing
- The fourth examines the evidence from case-control studies that the use of cannabis increases the risk of crashing
- The fifth summarizes the main findings from Parts 3 and 4
- The sixth examines the epidemiological evidence for a dose-response or threshold relationship between THC concentration and crashing
- The seventh examines the epidemiological evidence for the claim that the use of cannabis and alcohol together exacerbates the effect of alcohol on the risk of crashing
- The eighth considers the sizes of odds ratios for various crash causes other than the use of cannabis
- The ninth considers the effects of drugs on driving-related skills, with a particular focus on research involving cannabis
- In the tenth, the claim is investigated that cannabis exacerbates the detrimental effects of alcohol on driving-related skills
- In the eleventh and twelfth, the RDT policies and public information programs of Australian State governments are considered in the context of the findings
- In the eleventh, the evidence for including cannabis in the RDT protocols is examined
- In the twelfth, the evidence for the use of a zero-tolerance approach is examined

Part 1: Epidemiological research methods

Case-control and responsibility studies

The two most widely used epidemiological methods for studying the role of drugs in crash causation are case-control studies and responsibility studies. In a case-control study, the prevalence of a drug in 'cases' (such as crashed drivers) is compared with its prevalence in 'controls' (such as drivers who are randomly stopped at the same locations and same times of day that the case crashes occurred). If a drug plays a causal role in the crashes, its prevalence will normally be greater in cases than in controls. In a responsibility study, the prevalence of a drug in drivers who were responsible for the crashes is compared with its prevalence in drivers who were innocently involved in the same crashes. If a drug plays a causal role in the crashes, its prevalence will be greater in the responsible drivers than in the not responsible drivers.

Where it is not important in this report to distinguish between responsibility and case-control studies, rather than saying "the odds of being responsible for a crash" or "the odds of being involved in a crash", a simpler usage will be employed, "the odds of crashing".

Calculation of cannabis-crash odds ratios: The simplest scenario

The results for a particular drug, for example cannabis (as indicated by the detection of THC in body fluids), from a case-control study can be presented as in Table 1.1. The table describes hypothetical samples of 400 case drivers and 400 control drivers, where THC is the only drug of interest. This table would have the same structure for a responsibility study, except that the column headed 'Case Drivers' would be headed 'Drivers Responsible for the Crash', and the column headed 'Control Drivers' would be headed 'Drivers Not Responsible for the Crash'.

Table 1.1: Hypothetical results for cannabis in a case-control study

	Case Drivers	**Control Drivers**	**Total**
THC-Present	100 (a)	20 (c)	120 (a + c)
THC-Absent	300 (b)	380 (d)	680 (b + d)
Total sample	400 (a + b)	400 (c + d)	(Grand Total 800)

The information in Table 1.1 can be summarized as a single descriptive statistic: the odds ratio (OR). The OR is simply the 'odds' of THC being present (vs. absent) in the case drivers compared with (i.e., divided by) the odds of it being present (vs. absent) in the control drivers. Given that the odds themselves are ratios, the OR is a ratio of ratios. A worked example is provided:

1. Odds of THC being present (vs. absent) in the case drivers = a/b = 100/300
2. Odds of THC being present (vs. absent) in the control drivers = c/d = 20/380
3. Odds Ratio (OR) = (a/b) / (c/d) = (100/300) / (20/380) = 6.33

When an OR is calculated in this way, it is referred to as a 'counts-based OR', because it can be calculated from the raw numbers (counts) in a contingency table.

In this example, the OR of 6.33 means that the odds of THC being found in the case drivers is 6.33 times greater than the odds of it being found in the control drivers, which would be good evidence that cannabis played a role in crash causation. However, such results are essentially correlational, so any inferences about causality must be made with caution.

When an OR is reported, its 95% Confidence Interval (CI) is normally also reported. In this case, the 95% CI around the value 6.33 is from 3.8 to 10.5. Corresponding P values may also be reported. In this case, the P value is <0.0001. The formulae for the calculation of CIs and P values

are complex and are not provided here. When P values are not reported, an OR is normally considered to be statistically significant if its CI does not include the OR value of 1.00.

A drug-crash OR of 1.00 would mean that the drug was equally likely to be found in the case and control drivers, and would be evidence that the drug played no role in crash causation. A drug-crash OR of significantly less than 1.00 would mean that the drug was less likely to be found in the case drivers than in the control drivers, and would be evidence that the drug played a protective role in crash causation.

Most epidemiological studies of the relationship between the use of drugs and crashing involve drivers who are either killed or injured, because toxicological information is difficult to obtain for uninjured drivers.

Alternative definitions of the cannabis-exposure variable

Table 1.1 provided results for a case-control study where cannabis was the only drug considered. More realistically, some of the cases and controls would have used alcohol and/or other drugs, and may have done so in combination with cannabis. The first column in Table 1.2 lists all of the possible combinations of drug and alcohol use, where drugs other than cannabis and alcohol are described collectively as 'other drugs'. Subjects who have not used cannabis, alcohol or any other drug are described as 'THC, alcohol and other-drug-free' (THC&AOD-free).

Table 1.2: Defining the cannabis-exposure variable

Possible combinations of THC, alcohol and other drugs	**Categories of the cannabis-exposure variable**			
	THC-present		**THC-absent**	
	THC-only	**All-THC**	**THC&AOD-free**	**THC-free**
THC only	*	*		
Alcohol only				*
Other drugs only				*
THC & alcohol		*		
THC & other drugs		*		
Alcohol & other drugs				*
THC & alcohol & other drugs		*		
THC&AOD-free			*	*

When exposure to alcohol and/or other drugs is taken into consideration, the cannabis-exposure variable can be defined in different ways. The variable will generally comprise only two categories, which are described in Table 1.2 as 'THC-present' and 'THC-absent'. The categories must be *mutually exclusive* (such that no subject can belong to both), but they need not be *exhaustive* (inclusive of all subjects). The *general* definition of the cannabis-exposure variable is therefore, THC-present vs. THC-absent.

There are optional definitions of both categories of the cannabis-exposure variable. Amongst other possibilities, the presence of THC might be defined as the presence of THC alone (THC-only), or *any* presence of THC, whether alone or in combination with alcohol or other drugs (All-THC). Similarly, the absence of THC might also involve the absence of alcohol and all other drugs (THC&AOD-Free), or might involve the absence only of THC, whether or not alcohol and/or other drugs were present (THC-free). The two main definitions of each of the two categories of the cannabis-exposure variable are indicated by asterisks in Table 1.2. Other definitions are possible.

The two most frequently encountered *specific* definitions of the cannabis-exposure variable will now be considered. The first is: THC-only vs. THC&AOD-free (as described by the second and fourth columns in Table 1.2). No subject is included in both categories (consistent with the requirement of mutual exclusiveness); but any subject who had used alcohol only, or alcohol combined with THC, or various other drug combinations, would be excluded (such that the two categories are not exhaustive).

The second common definition of the cannabis-exposure variable is: All-THC vs. THC-free (as described by the third and fifth columns in Table 1.2). Again, no subject is included in both categories. But under this definition, all of the subjects have been included in the variable (such that the two categories are exhaustive).

Dealing with the problem of confounding

The type of drug-crash OR that was discussed in relation to Table 1.1 can be difficult to interpret unambiguously because of the problem of 'confounding'. For example, where cannabis is mainly consumed by young men, a high THC-crash OR may have nothing to do with the effect of cannabis, it may simply reflect the high crash risk of young men. Similarly, where cannabis is normally used along with alcohol, a high THC-crash OR may again have nothing to do with the effect of cannabis, it may simply reflect the high crash risk associated with the use of alcohol. In these examples, Age, Gender and Alcohol-use are confounding covariates whose effects need to be extricated from the effects of cannabis.

There are two different ways of dealing with the problem of confounding. The first, and less statistically sophisticated, is to conduct sub-group analyses. For example, by restricting the analysis to young men, and by defining the cannabis-exposure variable as THC-only vs. THC&AOD-free, the effects of cannabis on crashing would effectively be isolated from the effects Age and Gender as well as from the effects of the use of alcohol and/or other drugs. The main drawback of sub-group analyses is that they can involve the neglect of a large portion of the dataset, with a consequential loss of statistical power.

The second means of controlling for the effects of potentially confounding covariates is to apply the multivariate statistical technique known as 'multiple logistic regression', whereby the strength of the relationship between the predictor variable (the use of cannabis) and the outcome variable (involvement in a crash) is measured, and expressed as an OR, while simultaneously taking into account the effects of all identified potentially confounding covariates. While this technique may seem magical, it is actually rigorous and widely used in epidemiological research. This approach is discussed in more detail in Part 3 of this report.

Case-control and responsibility studies revisited

In concluding this section, it is probably worth emphasizing that an OR from a responsibility study must be interpreted differently from an OR from a case-control study. An OR from a responsibility study refers to the likelihood of the drivers being responsible for the crash that they were involved in, whereas an OR from a case-control study refers to the likelihood of the drivers being involved in a crash.

In some case-control studies it is possible to also conduct a responsibility sub-study. When that is done, it can be demonstrated mathematically that the responsibility study will produce a larger drug-crash ORs than the case-control study (Rogeberg & Elvik, 2016a, p. 2). That should not be surprising, given that the use of a psychoactive drug is expected to make drivers *responsible for* crashes, and not merely be *involved in* them. The reason why a drug-crash OR will be greater for a responsibility analysis than for a case-control analysis is probably best illustrated with a worked example, as provided in Attachment A.

An alternative conceptualisation of the cannabis-crash odds ratio

The information in Table 1.1 is re-presented in Table 1.3, but without any totals. The cannabis-crash odds ratio (OR) was previously defined as the odds of cannabis being present (vs. absent) in the case drivers compared with (i.e., divided by) the odds of it being present (vs. absent) in the control drivers.

In that conceptualisation, the cannabis-crash OR = (a/b) / (c/d)

That conceptualisation can be described as 'column-wise' or 'vertical' because the two separate odds (a/b and c/d) are calculated within the columns.

Table 1.3: Information required to calculate a cannabis-crash odds ratio

		Outcome	
		Case	**Control**
Exposure	**THC present**	a	c
	THC absent	b	d

An alternative conceptualisation is sometimes encountered in the epidemiological literature, wherein the cannabis-crash OR is defined as the odds of cannabis being present in the case drivers (vs. in the control drivers) compared with (i.e., divided by) the odds of cannabis being absent in the case drivers (vs. in the control drivers).

In this conceptualisation, the cannabis-crash OR = (a/c) / (b/d)

This conceptualisation can be described as 'row-wise' or 'horizontal' because the two separate odds (a/c and b/d) are calculated within the rows.

The size of the OR is the same under both conceptualisations, because:

(a/b) / (c/d) = (a/c) / (b/d) = (a x d) / (b x c)

In this report, the calculations will always be described according to the column-wise conceptualisation.

Part 2: Identification of epidemiological studies to review

How the studies were identified for possible inclusion

It was not necessary in the present study to search the literature for all the potentially relevant pre-2012 articles on the relationship between the use of cannabis and crashing, because such searches had already been undertaken as part of four different reviews: Asbridge, Hayden and Cartwright (2012); Elvik (2013); Hartman and Huestis (2013); Li, Brady, DiMaggio, Lusardi, Tzong and Li (2012).

While Elvik's (2013) review explored the effects of all types of psychoactive drugs on crashing, the other three reviews restricted their attention to the effects of cannabis.

Elvik (2013) included twenty-nine studies of the effects of cannabis on crashing; Asbridge, Hayden and Cartwright (2012) included nine; Hartman and Huestis (2013) included ten; and Li *et al*. (2012) included nine. Beyond the apparent failure by some reviewers to discover some relevant articles, there were a number of reasons for the differences in the numbers of included studies. Some of the reviewers adopted rejection criteria that limited the scope of their literature searches. For example, Asbridge, Hayden and Cartwright included only one study of the many available that employed self-reports to measure the use of drugs (preferring studies with toxicological evidence for drug use). And Li *et al*. did not include any articles published before 1990; nor did they include any responsibility studies. Elvik's coverage of the literature was the most comprehensive. However, his count of twenty-nine studies was increased by triple-counting one study and double-counting two others (see below).

The four reviews acknowledged the variable quality of the included studies (Asbridge, Hayden & Cartwright, 2012, pp. 2-3; Elvik, 2013, pp. 258-259; Hartman & Huestis, 2013, p. 489; Li *et al*. 2012, p. 66). In particular, Elvik considered that the ways of determining the use of drugs varied considerably in quality, with self-reported drug use being considerably less reliable than the laboratory analysis of body fluids. Hartman and Huestis agreed that "Self-reported prevalence estimates are often underestimated, owing to the sensitivity of illicit drug-related information". Similarly, Asbridge *et al*. (2014, p. 402) noted that, while the general consumption of alcohol is legal, the consumption of cannabis is not, and so "… respondents may feel uncomfortable, either morally or through fear of legal action, in admitting cannabis consumption – despite assurances of anonymity and confidentiality".

As a major aim of the present study is to review the best available epidemiological evidence for the role of cannabis in crashing, the studies that employ self-reports to determine drug use will not be further considered. The implications are that the present study will not consider: one of the nine studies included by Asbridge, Hayden and Cartwright (2012); twelve of the twenty-nine studies included by Elvik (2013); four of the ten studies included by Hartman and Huestis (2013); and five of the nine studies included by Li *et al*. (2012). The remaining studies (all of which involved the laboratory analysis of body fluids for drugs) are listed in Table 2.1, where they are identified by the name of the first author, the publication date and the country from where the data was obtained. The coverage of the research studies in the four reviews is indicated by asterisks. Three of the four reviews incorporated meta-analyses. The review that did not was by Hartman and Huestis.

It was not necessary in the present study to search the literature for all the potentially relevant articles on the relationship between the use of cannabis and crashing that were published between 2011 and 2015, because such a search was undertaken as part of a recent review by Rogeberg and Elvik (2016a), whose strategy for identifying all relevant studies for their meta-analysis had two stages. The first was simply to include studies that had been included in any of the three previously published meta-analyses (Asbridge, Hayden & Cartwright, 2012; Li *et al*., 2012; and Elvik, 2013). In the second stage, "Studies published since 2011 were identified using a structured search in Google Scholar and the Web of Science. The database was supplemented by reviews of the authors' personal research libraries" (pp. 1350-1351). Table 2.1 lists the eight studies identified by Rogeberg and Elvik for the years 2011 to 2015.

The author and some colleagues have paid close attention to the publication of possibly relevant studies since 2015. Five such studies have been identified (Lacey *et al*., 2016; Chihuri, Li & Chen, 2017; Romano *et al*., 2017a; and Li, Chihuri & Brady, 2017; Romano, Voas & Camp, 2017b).

Table 2.1: Coverage of published studies in five epidemiological reviews

First Author & Publication Year	Country	Responsibility (R) or Case-Control (C)	Cannabis Indicator: (THC or Other)	Redundant?	Asbridge *et al*. (2012)	Elvik (2013)	Hartman & Huestis (2013)	Li *et al*. (2012)	Rogeberg & Elvik (2016a)
Terhune, 1982	U.S.	R	THC		*	*			
Williams, 1985	U.S.	R	THC			*			
Terhune, 1992	U.S.	R	THC		*	*			
Drummer, 1994	Australia	R	Other	Yes		*			
Longo, 2000	Australia	R	THC		*	*			
Swann, 2000	Australia	R	THC	Yes		*			
Lowenstein, 2001	U.S.	R	Other			*			
Dussault, 2002	Canada	R/C	Other	Yes		*			
Mura, 2003	France	C	THC		*	*		*	
Brault, 2004	Canada	R/C	Other			*		*	
Drummer, 2004	Australia	R	THC		*	*	*		
Movig, 2004	Netherlands	C	Other	Yes		*	*	*	
Assum, 2005	Norway	C	Other			*			
Laumon, 2005	France	R	THC		*	*	*		
Mathijssen, 2005	Netherlands	C	Other		*	*			
Soderstrom, 2005	U.S.	R	Other		*				
Bedard, 2007	U.S.	R	Other	Yes	*		*		
Woratanarat, 2009	Thailand	C	Other			*	*	*	
Gjerde, 2011	Norway	C	THC	Yes		*	*		
Hels, 2011	6 E.U. Countries	C	THC	Yes					*
Kuypers, 2012	Belgium	C	THC	Yes					*
Gjerde, 2013	Norway	C	THC						*
Hels, 2013	6 E.U. Countries	C	THC						
Li, 2013	U.S.	C	Other	Yes					*
Romano, 2014	U.S.	C	Other	Yes					*
Poulsen, 2014	New Zealand	R	THC						*
DuBois, 2015	U.S.	R	Other						*
Lacey, 2016	U.S.	C	THC						*
Chihuri, 2017	U.S.	C	Other						
Romano, 2017a	U.S.	C	Other						
Li, 2017	U.S.	R	Other						
Romano, 2017b	U.S.	R	Other						

In 2015, the U.S. National Highway Transport Safety Administration (NHTSA) released a 'Research Note' by Compton and Berning which announced that a rigorous government-funded case-control study of the effects of drugs and alcohol on the risk of crashing had been completed, and that its findings would soon be released as an NHTSA report. The report, with Lacey as the first author, was released in late-2016. So, the study that was referred to by Rogeberg and Elvik (2016a) as 'Compton and Berning (2015)' is referred to here as 'Lacey *et al*. (2016)'.

Exclusion of redundant studies

As noted above, the studies included by Elvik (2013) involved some redundancies. The partial datasets that were analyzed by Drummer (1994) and Swann (2000) were included in a complete dataset that was analyzed by Drummer *et al*. (2004). Similarly, a partial dataset that was analyzed by Dussault *et al*. (2002) was included in the dataset that was analyzed by Brault *et al*. (2004); and the partial dataset that was analyzed by Movig *et al*. (2004) was included in the dataset analyzed by Mathijssen and Houwing (2005). The redundant studies are identified in Table 2.1. They will not be further considered.

In 2013 Gjerde *et al*. published a case-control study with 508 cases, 204 of whom had previously been included in a 2011 publication by the same research group. The latter study was published after the four earlier reviews. The earlier study, included in two of the earlier reviews, will not be further considered.

In 2015 Dubois *et al*. published a variant of a responsibility study that was based on data from the U.S. Fatality Analysis Reporting System (FARS) for the years 1991 to 2008. That study was similar to an earlier study by the same research group (Bedard, Dubois & Weaver, 2007) that was based on the subset of FARS data for the years 1993 to 2000. The latter study was published after the four earlier reviews. The earlier FARS study, which was included in two of the four reviews, will not be further considered. The earlier study was omitted from Elvik's (2013) comprehensive meta-analysis on the grounds that it "did not use accident involvement as a dependent variable" (p. 258). However, as it was a variant of a responsibility study, Elvik could legitimately have included it. Rogeberg and Elvik (2016a) did include it.

In 2013, Hels *et al*. published a journal article that was based entirely on results that had been published two years earlier in a DRUID report (Hels *et al*., 2011). In the current review, the focus is on the later journal article. (Some components of the DRUID research program are discussed in a different context in Part 9 of this report).

In 2017, Chihuri, Li and Chen published a study that was a replication and extension of an earlier study by Li, Brady and Chen (2013). Both studies drew their cases from the FARS database. The two studies differed in that, while the first investigated the effect of all drugs, the second restricted its attention to the effects of cannabis. The first study will not be further considered in the main Parts of this report.

In 2017, Romano *et al*. published a study that was a replication and refinement of an earlier study by the same authors (Romano *et al*., 2014). Both studies drew their cases from the FARS database. The two studies differed in that, while the first investigated the effect of all drugs, the second restricted its attention to the effects of cannabis. The first study will not be further considered in the main Parts of this report

Exclusion of studies that did not always determine the presence of THC

The prior use of cannabis can be measured through the toxicological detection of THC in oral fluid or blood but not in urine, or through the detection of other cannabinoids, some of which are metabolites of THC, in blood, urine or oral fluid. Some of the other cannabinoids can be detected for days or weeks after using cannabis, which is much longer than the detection window for THC. It follows that the non-THC cannabinoids are detectable for much longer than any possible impairing effects of cannabis.

All five reviews acknowledged that the studies that measured the use of cannabis through the detection of THC were of superior quality to those that measured the use of cannabis through the detection of other cannabinoids (Asbridge, Hayden & Cartwright, 2012, p. 3; Elvik, 2013, p. 254; Hartman & Huestis, 2013, p. 479; Li *et al*. 2012, p. 70; Rogeberg & Elvik, 2016a, p. 1353). Given that most of the drivers who are detected with non-THC cannabinoids in a body fluid are not likely to be impaired by cannabis, any study that used non-THC cannabinoids to measure the prior use of cannabis would effectively be studying the crash risk of the types of people who use

cannabis, rather than the crash risk that may be attributable to the psychoactive effects of cannabis itself. In other words, a study that detected non-THC cannabinoids would be exploring something like the *personality* of cannabis users.

Given that the aim of this study is to explore psychotropic drug effects rather than personality traits, studies that measured the use of cannabis other than always through the toxicological detection of THC will not be considered in the following parts of this report. The excluded studies are identified by 'Other' in the 'Cannabis Indicator' column in Table 2.1.

Because the excluded studies would have classified many effectively drug-free subjects as being affected by cannabis, their results would be expected to under-estimate any real psychoactive effect of cannabis crashing. The cannabis-crash ORs might therefore be expected to be lower in the excluded studies.

A radically different possibility for how the cannabis-crash ORs might be expected to differ between the included and excluded studies is implicit in the findings of a population-based case-control study by Blows *et al*. (2005). That study is not considered anywhere in this review because the definitions of the cannabis variables involved self-reported use. Nevertheless, the study was considered rigorous enough to be included in the reviews by: Asbridge, Hayden & Cartwright (2012); Li, Brady, DiMaggio, Lusardi, Tzong & Li (2012); Elvik (2013); Hartman & Huestis (2013); and Rogeberg & Elvik (2016). Blows *et al*. distinguished between the 'acute' use of cannabis soon before the crash, and the 'habitual' use of cannabis as a lifestyle choice. They found that the acute use of cannabis was not related to the risk of crashing, but that the habitual use (controlling for acute use) was strongly related. It was as though the types of people who use cannabis are prone to crashing, but become safer soon after using cannabis. If the acute use of cannabis is actually having a protective effect against crashing, it might be expected that the rejected studies (where there is evidence only of habitual use) would have higher cannabis-crash ORs than the included studies (where there is plausible evidence for some acute use).

Whatever the expectations as to the differences between studies that do and do not use toxicological evidence of the presence of THC to indicate the use of cannabis, it would seem appropriate to separately consider the two types of studies.

Summary of the main findings of the excluded studies

The rejection of studies from a review can raise suspicions of selective reporting ('cherry-picking'). While it is not intended that each of the rejected studies be subjected to a 'close look', it is appropriate for their main findings to be briefly noted in this part of the report. Table 2.2 provides the main findings for the twelve rejected studies (Drummer, 1994; Lowenstein & Koziol-McLain, 2001; Brault *et al*., 2004; Assum, 2005; Mathijssen & Houwing, 2005: Soderstrom *et al*., 2005; Woratanarat *et al*., 2009; DuBois *et al*., 2015; Chihuri, Li & Chen, 2017; Romano *et al*., 2017a; and Li, Chihuri & Brady, 2017; Romano, Voas & Camp, 2017b). Despite being described as 'redundant' in Table 2.1, Drummer (1994) is included, because it analyzed the effects of a non-THC cannabinoid, while the later study (Drummer *et al.*, 2004) analyzed the effects of only THC.

Some of the rejected studies identified the prior use of cannabis through the toxicological detection of Non-THC Cannabinoids Only (identified in the fourth column of Table 2.2 as 'NTCO'), while others identified prior use through the detection of *either* THC *or* non-THC cannabinoids (identified as 'Either'). Some of the studies that were classified as 'Either' relied on the collation of toxicological information from different laboratories, some which did not routinely test for THC. Case-control studies might also be classified as 'Either' if they involved the analyses of different body fluids for cases and controls.

Two of the twelve cannabis-crash ORs in Table 2.2 are less than 1.00. A further seven are greater than 1.00, but not significantly so. Only three of the excluded studies (DuBois *et al*., 2015; Chihuri, Li & Chen, 2017; Li, Chihuri & Brady, 2017) have cannabis-crash ORs that are significantly greater than 1.00. All three drew their cases from the U.S. Fatality Analysis Reporting System (FARS) database.

Table 2.2: Main findings of the excluded studies

Study	Responsibility (R) or Case-Control (C)	Crash Severity	Non-THC Cannabinoids Only vs THC or NTC (Either)	Used FARS data?	N Cannabis drivers contributing to the OR	Counts-based OR for Cannabis-Only	MLR-based OR for Cannabis-Only
Drummer, 1994	R	Fatal	NTCO		43	0.6 (0.3-1.2)	
Lowenstein, 2001	R	Injury	Either		34	1.1 (0.5-2.4)	
Brault, 2004	C/R	Fatal	NTCO		~50	1.2 (0.5-2.9)	
Assum, 2005	C	Fat / Inj	Either		3	2.4 (0.2-26.8)	
Mathijssen, 2005	C	Injury	Either		~154	1.5 (0.6-3.3)	
Soderstrom, 2005	R	Injury	NTCO		~185	1.2 (0.8-1.6)	
Woratanarat, 2009	C	Injury	NTCO		24	0.8 (0.3-2.4)	
Dubois, 2015	R	Fatal	Either	Yes	3,387		1.2 (1.1-1.3)
Chihuri, 2017	C	Fatal	Either	Yes	694		1.5 (1.2-2.0)
Romano, 2017a	C	Fatal	Either	Yes	~382		1.3 (0.9-1.8)*
Li, 2017	R	Fatal	Either	Yes	2,409		1.5 (1.3-1.7)
Romano, 2017b	R	Fatal	Either	Yes	101	1.3 (0.9-2.0)*	

*The cannabis-positive variable includes drivers who are also positive to other drugs

Comments on some of the excluded studies

Lowenstein and Koziol-McLain (2001) included 34 drivers who tested positive for cannabis, as initially identified through the presence of non-psychoactive cannabinoids in the urine. The results for that group are given in Table 2.2. In follow-up toxicological analyses an undisclosed number (ten or fewer) of those drivers tested positive for THC. For that sub-group, described by the authors as being positive for 'acute marijuana use', the cannabis-crash OR was 0.7 (0.1-3.3). It was decided to reject the study from further consideration in this study rather than to include it with an unknown number of THC-positive drivers. If it had been included in the main part of this study, it would have been associated with a THC-crash OR of 0.7 (0.1-3.3).

Brault *et al*. (2004) reported the final results of the 'Quebec Drug Study', which comprised a responsibility study nested within a case-control study. They reported a cannabis-crash MLR-based OR of 1.6 (1.1-2.4) for the case-control study. However, they correctly observed that "The relatively small numbers of participants in the roadside survey [the control drivers] who provided urine samples could lead to an over-estimation of risks" (p. 7). In fact, without going into details, their case-control study probably suffered from most of the over-estimation biases identified in Part 4 of this report. On the other hand, there is no evidence that their responsibility study (OR = 1.2; 0.5-2.9) suffered from any over-estimation biases. It is therefore appropriate to provide the results of the responsibility analysis in Table 2.2.

The crashed case drivers in Assum's (2005) study were tested for THC. It is not clear if the control subjects were tested for THC or non-THC cannabinoids. The evidentiary value of Assum's study with respect to the absolute value of the cannabis-crash OR is very low, because there were only three cannabis-positive subjects altogether (one case driver and two controls). The non-significant OR of 2.4 (0.2-26.8) is therefore virtually meaningless (as indicated by its very wide 95% confidence interval).

Altogether, seven of the redundant or excluded studies drew their cases from the FARS database (Li, Brady & Chen, 2013; Romano *et al*., 2014; Dubois *et al*., 2015; Chihuri, Li & Chen, 2017; Romano *et al*., 2017a; and Li, Chihuri & Brady, 2017; Romano, Voas & Camp, 2017b). While these

studies are not further considered in the main parts of this report, it is difficult to ignore them, so they are considered together in Appendix E, where the effects of a number selection biases are discussed. The discussion in Appendix E will show that none of the FARS-based studies provides any convincing evidence that the use of cannabis increases the risk of crashing.

This part of the report has presented a brief overview of the studies that were rejected from further consideration because they used the presence of non-THC cannabinoids, with or without THC, rather than the presence of THC alone, to indicate the prior use of cannabis. The information presented here is consistent with the possibility that the prior use of cannabis does not increase the risk of crashing. That conclusion is not surprising given that most of the drivers detected with non-THC cannabinoids in a body fluid would probably not have been impaired, or otherwise affected, by cannabis at the time of their crash.

Is this review biased?

A paper summarizing some of the main findings from this review was submitted for publication in an appropriate journal, and was rejected. One of the main reasons was that an anonymous reviewer considered the paper to be biased:

> [This review] picks a number of papers which the author deems as "best" and highlights their limitations in a non-systematic fashion, with a greater emphasis on the flaws of those that support the role of cannabis in crashes. As a result, the paper in my view is of little scientific value ... While I am not going to go through each study "reviewed" or mentioned in this paper, I will focus on the most recent meta-analysis (Rogeberg & Elvik, 2016) to demonstrate how the author "cherry-picks" limitations and strengths to suit his conclusions. […]. The point that I am trying to make is that the author … picked some studies and then proceeded to highlight the limitations of those that show significant increased risk in crashes as a result of cannabis use, and chose to ignore the limitations of those that do not.

It will be up to the reader to decide if this report is biased. There are many types of bias. The author certainly did not 'cherry-pick' the literature to find studies that fitted with pre-conceptions about the benign nature of cannabis. The previous sections of this part of the report clearly show that rigorous procedures were used to select studies for close examination.

However, the author does plead guilty to having a 'null-hypothesis bias'. In his book on the *History of Freedom of Thought* (1913, p. 20), Bury argued that the burden of proof does *not* lie with the sceptic (or, 'rejecter'); it lies with the claim-maker:

> Some people speak as if we were not justified in rejecting a theological doctrine unless we can prove it false. But the burden of proof does not lie upon the rejecter... If you were told that in a certain planet revolving around Sirius there is a race of donkeys who speak the English language …, you could not disprove the statement; but would it, on that account, have any claim to be believed? Some minds would be prepared to accept it, if it were reiterated often enough, through the potent force of suggestion.

Admittedly, the claim that cannabis causes road crashes is not as outlandish as the claim that there are extra-terrestrial donkeys, but the principle still holds as to where the burden of proof lies. The same general principle is widely accepted by scientists. It is exemplified in Popper's (1934) view that one of the main duties of a scientist is to attempt to falsify claims that causal relationships have been proven.

It would nevertheless be disingenuous to adopt a pro-null-hypothesis stance if it were not for a further fact. When considering the variety of biases affecting the outcomes of the included studies, it was found that almost all of the plausible and relevant biases acted against the null hypothesis. So, the author makes no excuses for subjecting the studies that reject the null hypothesis to a greater level of scrutiny than those that retain the null hypothesis.

Some brief comments on the retained studies

The retained studies all define the cannabis variable in terms of toxicological evidence for the presence of THC in blood or oral fluid. It is not claimed here that all of the drivers with detectable levels of THC were affected by the drug at the time of the crash. That matter is further considered in Part 12 of this report. However, it is claimed that the ORs under consideration are relevant to the enforcement regime in Australia, where it is an offence to drive with any detectable level of THC in a body fluid.

The eleven retained studies are listed in Tables 2.4 and 2.5. Seven responsibility studies are listed in Table 2.4, and four case-control studies in Table 2.5. These tables show the ways that the subjects have been sampled, and the types of body fluids (sometimes called 'matrices') that have been used for the detection and quantification of alcohol and drugs.

In epidemiological studies it is important for the case and control drivers to be drawn from the same population. In responsibility studies (Table 2.4), the responsible ('case') and not-responsible ('control') drivers are necessarily drawn from much the same population of crashed drivers. However, in case-control studies (Table 2.5), the case drivers are involved in crashes, while the control drivers are not – which may mean that different populations are being sampled.

Table 2.4: Responsibility studies of the relationship between cannabis and crashing

Author	Subjects	Matrix
Terhune, 1982	Driver Injured	Blood
Williams, 1985	Driver Fatality	Blood
Terhune, 1992	Driver Fatality	Blood
Longo, 2000	Driver Injured	Blood
Drummer, 2004	Driver Fatality	Blood
Laumon, 2005	Driver Fatality or Injured	Blood
Poulsen, 2014	Driver Fatality	Blood

Table 2.5: Case-control studies of the relationship between cannabis and crashing

Author	Case subjects	Case matrix	Control subjects	Control matrix
Mura, 2003	Driver in Serious Crash	Blood	Emergency Unit Patient	Blood
Gjerde, 2013	Driver Fatality	Blood	Driver On-road	Oral Fluid
Hels, 2013	Driver Injury	Blood	Driver On-road	Blood / Oral Fluid
Lacey, 2016	Driver Crashed	Oral Fluid	Driver On-road	Oral Fluid

In a responsibility study, the body fluid to be analyzed would be expected to be the same for the responsible and not-responsible drivers, as for all of the studies in Table 2.4. However, that is not necessarily the situation in case-control studies. Table 2.5 shows that the body fluids were the same for the cases and controls in two of the four studies, but different in the other two. The implications of that fact are not considered to be important, and are not explored in this study.

The seven selected responsibility studies will be examined in Part 3 of this report, and the four case-control studies in Part 4.

Part 3: Evidence from responsibility studies that cannabis increases crash risk

Assignment of responsibility

Table 3.1 provides some information on the assignment of responsibility in the seven selected responsibility studies.

Table 3.1: Assignment of responsibility

Author	Crash Severity	Fate of Contributory Drivers	% Contributory Excluded	% Responsible
Terhune, 1982	Injury	Not Responsible	0.0%	42.6%
Williams, 1985	Fatal	Responsible	0.0%	88.0%
Terhune, 1992	Fatal	Divided	0.0%	79.9%
Longo, 2000	Injury	Excluded	6.2%	58.4%
Drummer, 2004	Fatal	Excluded	5.5%	84.1%
Laumon, 2005	Fatal	Responsible	0.0%	63.0%
Poulsen, 2014	Fatal	Excluded	3.0%	83.4%

Williams *et al*. (1985) used information from police accident reports to directly create a dichotomous variable, in which responsible and 'probably responsible' drivers were classified as 'responsible' and the remainder as 'not responsible'. Effectively, this method has assigned drivers who are partly responsible ('contributory') to the 'responsible' category.

For all other studies, the level of responsibility for the crash was first scored quantitatively (from fully responsible to fully not responsible) and then a dichotomous variable was created. This two-step method requires a decision to be made about drivers who are contributory. In 1982, Terhune classified all of the contributory drivers as 'not responsible', on the grounds that "The preferable comparisons are with the proportions of drivers judged fully culpable, because there is least ambiguity with those data" (p. 86). However, in 1992, Terhune *et al*. subdivided the contributory drivers and classified those who were more contributory as 'responsible', and those who were less contributory as 'not responsible'.

In the remaining four studies, the level of responsibility for the crash was quantified using a method devised by Robertson and Drummer (1994). This method normally involves the exclusion from further analyses of those drivers who were neither clearly responsible nor clearly not responsible. Such drivers were excluded in three of the four studies, but were somehow retained by Laumon *et al*. (2005). The fate of the contributory drivers in the assignment of responsibility is summarized in Table 3.1. Where the contributory drivers are excluded, the percentages excluded are quite small, ranging from 3.0% to 6.2%.

Table 3.1 also shows the percentages of responsible drivers in the final samples (after excluding contributory cases where relevant). As might be expected, the smallest percentages (42.6% and 58.4%) are found where the drivers are involved in injury crashes rather than fatal crashes. The 42.6% for Terhune (1982) is particularly small, because he assigned all of the contributory drivers to the 'not responsible' category. Williams *et al*. (1985) restricted their study to young male drivers who were killed, so it is not surprising that they had the highest frequency of responsibility (88.0%) - especially given that their method of allocating responsibility probably favored the 'responsible' category. Poulsen, Moar and Pirie (2014) describe their study as a replication of Drummer *et al*. (2004), so it is not surprising that the percentages of responsible drivers are similar in the two studies (83.4% and 84.1%). The sample used by Laumon *et al*.

(2005) originally comprised 6766 responsible and 3982 not-responsible drivers, giving an original responsibility percentage of 63.0% (as in Table 3.1). However, they then rejected about a quarter of the not-responsible drivers before conducting their final analyses, which increased the final responsibility percentage to 69.2%. That matter is further discussed below.

The problem of non-independent assessments

The most obvious threat to the legitimacy of a responsibility study is that the assessment of responsibility could be influenced by the knowledge of toxicological results. If a person assessing the level of responsibility knew, for example, that a crashed driver had a low BAC, that knowledge would be expected to bias the assessment in favour of the driver being responsible. The converse also holds true. It follows that any lack of independence between the responsibility and toxicological assessments would probably lead to an exaggeration of the drug-crash OR.

All of the responsibility studies included in this report have acknowledged the potential problem of non-independent assessments, and all have reacted appropriately by ensuring, as far as possible, that the responsibility and toxicological assessments were conducted independently. However, it is unlikely that total independence was ever achieved. It is unknown if police comments such as "smelt of alcohol", or "had a glazed expression" were always deleted from the crash reports. Even where no such comments were available to the assessors, it seems likely that the crash descriptions might have given some hints as to the likelihood of the prior use of drugs or alcohol. For example, a comment such as "The car was weaving before colliding with the cyclist" might reasonably be taken to imply that the driver was affected by alcohol or drugs.

The responsibility bias

One type of selection bias can occur when drivers are selected for drug testing on the grounds that they are likely to have been responsible for the crash they were involved in. For example, where it is the duty of the police to determine which drivers will be tested for drugs and alcohol, their prosecution-motivated focus will be on drivers who are considered to be both responsible for the crash and likely to be impaired by drugs and/or alcohol. Because the targeted drug testing is motivated by the need to discover why the responsible drivers caused their crashes, it will introduce a selection bias for the presence of drugs in the responsible drivers. The over-representation of drugs in the responsible drivers will increase drug-crash ORs for both case-control studies (where the majority of case drivers are responsible for their crashes) and responsibility studies.

The evolution and methodological rigour of responsibility analyses

The research design that is described in this report as a 'responsibility analysis' evolved from a design that was first described by Thorpe in 1964 (and further developed by Haight in 1970 and Koornstra in 1973) in which patterns of causal factors were compared across single- and multi-vehicle crashes, but without assigning responsibility for the multi-vehicle crashes to any of the individual drivers involved. Thorpe assumed that all of the drivers in single-vehicle crashes, and 50% of the drivers in multi-vehicle crashes, were responsible (culpable) for their crashes. That research design, which was described by Haight (1973) as 'induced exposure', was never widely employed, and has never been used to explore the effects of illegal drugs on the risk of crashing.

The research design that is described in this report as a 'responsibility analysis' was first used by Carr in a study that was published in 1969. As did Thorpe in 1964, Carr assumed that all of the drivers in single-vehicle crashes, and 50% of the drivers in two-vehicle crashes, were responsible for their crashes. However, unlike Thorpe, Carr assigned the status of 'responsible' or 'not-responsible' to all of the drivers involved in two-vehicle crashes. His technique of using the not-responsible drivers in two-vehicle crashes as a control group for the responsible 'case' drivers in both single- and two-vehicle crashes was described by Haight (1973) as 'quasi-induced

exposure'. That term is used interchangeably with 'responsibility analysis' in the subsequent literature.

The legitimacy of a responsibility analysis rests on the assumption that the non-responsible drivers in multi-vehicle crashes provide a legitimate (i.e., representative) a control group for the responsible 'case' drivers in the same set of *multi-vehicle crashes*. That assumption has been shown to hold true in a number of studies (Lyles, Stamatiadis & Lighthizer, 1991; Stamatiadis & Deacon, 1997; Lardelli-Claret *et al*., 2006; Jiang & Lyles, 2010; and Curry, Pfeiffer & Elliott, 2016).

A major concern of many of the researchers who have employed responsibility analyses has been the legitimacy of using the non-responsible drivers in multi-vehicle crashes as a control group for the responsible 'case' drivers in *single-vehicle crashes*. To avoid any possible problems, Carr (1969) conducted separate analyses of single- and two-vehicle crashes. In later responsibility studies, Perneger and Smith (1991) and Lyles, Stamatiadis and Lighthizer (1991) avoided possible problems by restricting their analyses to two-vehicle crashes. More recently, two studies have clearly demonstrated the inappropriateness of using the non-responsible drivers in multi-vehicle crashes as a control group for the responsible drivers in single-vehicle crashes. Stamatiadis and Deacon (1997) and Lardelli-Claret *et al*. (2006) investigated whether or not the non-responsible drivers in multi-vehicle crashes were representative in important ways of the drivers involved in single-vehicle crashes, and concluded that they were not. It is clearly inappropriate to blur the distinction between single- and multi-vehicle crashes, and to analyse the two types of crashes together. Nevertheless, that has been done in all seven of the studies discussed in this part of the report. The main problem arising from the failure to separate the two types of crashes is identified as the 'mismatch problem' in the following section.

The mismatch problem

Single- and multi-vehicle crashes are different in many respects. Most obviously, drivers will have a very high level of responsibility for single-vehicle crashes (either 100%, or near to 100%, depending on how 'responsibility' is defined in the study), while the level of driver responsibility for multi-vehicle crashes might reasonably be expected to be about 50%. Compared with multi-vehicle crashes, single-vehicle crashes are more likely to involve male drivers and the use of alcohol, and to occur in rural areas, at night (Voas *et al*., 2013b). Given the mismatch between single- and multi-vehicle crashes, they should not be treated as a single population in a responsibility study, as discussed in the previous section. As observed by Terhune in 1983 "Since the non-responsible drivers are predominantly in the multi-vehicle crashes, they may not represent well the exposure of drivers in single-vehicle crashes" (p. 245). Unfortunately, Terhune is probably the only author involved in a responsibility study of the role of illegal drugs in crashes to have been overtly concerned about the 'mismatch problem'. All of the responsibility studies reviewed in this Part of the report included flawed 'mismatch' analyses of combined single- and multi-vehicle crashes.

It is relevant to consider how the measurement of a drug-crash OR might be biased by the mismatch. Voas *et al*. (2013b, p. 2) have considered the mismatch in relation to possible biases in the measurement of alcohol-crash ORs:

> Responsibility analysis produces a control group only for multi-vehicle crash drivers. It does not produce a control group for single-vehicle crash drivers. Those drivers must be compared against the innocent drivers in multi-vehicle crashes. Since the BACs of drivers in single-vehicle crashes have been shown to be higher than those in multi-vehicle crashes, using the control group created by the not-responsible multi-vehicle crash drivers may overestimate the relative risk of BAC in crashes.

The same argument is relevant to the measurement of cannabis-crash ORs: The prevalence of THC-positive drivers may be greater at the locations, times and other circumstances of single-vehicle crashes than at the locations, times and other circumstances of multi-vehicle crashes. If so, the control sample of non-responsible drivers drawn from multi-vehicle crashes would have

fewer THC-positive drivers than the 'true controls' for the drivers involved in single-vehicle crashes would have. That would exaggerate the cannabis-crash OR for the single-vehicle crashes. And if there is no distinction in the analyses between single- and multi-vehicle crashes, the overall cannabis-crash OR will be exaggerated.

So, where a responsibility analysis includes both single-vehicle and multi-vehicle crashes (as is the usual practice in the studies reviewed in this report), the size of the cannabis-crash OR might be overestimated. The potential problem can only be a real problem (exaggerating the cannabis-crash OR) where the prevalence of cannabis is greater in single- than in multi-vehicle crashes. That relationship is widely acknowledged to hold true for alcohol. However, it may not always hold true for cannabis.

The nature of the mismatch problem is probably best illustrated with a worked example, as provided in Attachment B.

The most obvious solution to the mismatch problem is to exclude the single-vehicle crashes from the responsibility analysis, as discussed in the previous section. The use of the sub-group of multi-vehicle crashes would eliminate the mismatch problem for both counts-based and MLR-based analyses. In presenting the findings of a responsibility study that included both single-vehicle and multi-vehicle crashes, it would therefore be informative to compare the drug-crash ORs for all crashes combined (the usual, but questionable, way of calculating an OR) with the ORs for only multi-vehicle crashes (the best way of calculating an OR).

In the case of MLR-based analyses, there is another potential solution to the mismatch problem, which is to include drivers from both single- and multi-vehicle crashes in the analysis, and to statistically control for the distinction between single- and multi-vehicle crashes through the inclusion of a predictor variable (covariate) that codes for the distinction. However, that approach might not be appropriate where radically different sub-populations of single- and multi-vehicle crashes are involved.

Not all of the seven selected responsibility studies have acknowledged the mismatch problem. Those that did, have responded to it in different ways, as indicated in the discussion below.

ORs for the responsibility studies: Counts-based analyses

There are two main approaches to the calculation of a cannabis-crash OR. The first has been discussed above in relation to Table 1.1. That approach, known as a 'counts-based analysis', delivers a 'counts-based OR'. The OR calculations can be done by hand using data from 2x2 contingency tables. As noted above, the second way that an OR can be calculated is through a multivariate analysis (multiple logistic regression), and will be discussed later.

As indicated in the discussions relating to Tables 1.1 and 1.2, there are many ways of producing counts-based ORs for the relationship between cannabis and crashing, because there are potentially many definitions of the cannabis-exposure variable. However, the simplest way uses only a sub-set of the data. Subjects are included only if they have THC-only or if they are THC&AOD-free. It follows that they are excluded if they have: alcohol only; other drugs only; alcohol combined with other drugs; or THC combined with alcohol and/or other drugs. A counts-based OR is not adjusted for the possible confounding effects of any personal or crash-related covariates. However, as noted above, the potential confounding effects of alcohol and/or other drugs are effectively eliminated by excluding all subjects who tested positive for those substances.

Counts data for THC-only vs. THC&AOD-free subjects were obtained for all seven studies. In the case of Laumon *et al*. (2005) the data were obtained indirectly through the journal website relating to a review article by Rogeberg and Elvik (2016a). For the other six studies, the data were available in the original articles. The counts data, along with the counts-based ORs and 95% confidence intervals are provided in Table 3.2.

It is evident from Table 3.2 that the set of seven ORs has a wide range (from 0.46 to 3.16). Three are less than 1.00 (but not significantly so), while four are greater than 1.00 (with two significantly so). It is unlikely that such a wide range of ORs could result from random variation. It is more likely that there are systematic differences between the studies such that some ORs are more valid than others.

Table 3.2: ORs for THC derived from counts data for seven responsibility studies

Study	Responsible THC-Only	Responsible THC&AOD-Free	Not Responsible THC-Only	Not Responsible THC&AOD-Free	Total Subjects	OR for THC-Only	95% CI
Terhune, 1982	9	94	8	179	290	**2.14**	0.8-5.7
Williams, 1985	10	55	9	23	97	**0.46**	0.2-1.3
Terhune, 1992	11	541	8	258	818	**0.66**	0.3-1.6
Longo, 2000	21	996	23	891	1931	**0.82**	0.5-1.5
Drummer, 2004	51	(1214)	5	(376)	1646	**3.16**	1.3-8.0
Laumon, 2005	319	4386	131	3585	8421	**1.99**	1.6-2.5
Poulsen, 2014	74	403	18	128	623	**1.31**	0.8-2.3

One of the articles did not report all of the relevant information. Drummer *et al*. (2004) used crash and laboratory data for the ten-year period from 1990 to 1999. However, the laboratory analysis of bloods to determine the presence and concentration of THC was undertaken only in the last three years or so of that period. The data here in Table 3.2 comes from Drummer *et al*'s Table 2, where the bracketed information for the THC&AOD-free subjects comes from the full 10-year period, while the information for the THC-only subjects comes from the last few years. So, in their Table 2, Drummer *et al*. provided incompatible information for the THC-only and THC&AOD-free subjects.

ORs for the responsibility studies: MLR-based analyses

There are advantages and disadvantages of counts-based analyses. One advantage is, that by using a sub-set of data that excludes all cases who are potentially affected by alcohol or other drugs, cannabis is the only drug that can possibly be contributing to the risk of being responsible for the crash. One disadvantage, as noted previously, is that the use of a bivariate analysis fails to take into account the effects of potentially confounding covariates such as Age and Gender. If, for example, young men are much more likely than other groups to use cannabis *and* to cause the crashes they are involved in, the larger counts-based ORs in Table 3.2 might simply be reflecting a 'young man' effect rather than a cannabis effect. A more accurate picture should therefore emerge from a multivariate analysis, which can extricate the young-man effect from the THC effect, and give more valid, and probably lower, OR for THC.

The type of multivariate analysis that is most commonly used to analyze the results of responsibility studies and case-control studies is a multiple logistic regression (MLR). This type of analysis can estimate the effect of a dichotomous predictor variable (such as the presence vs. absence of THC) on a dichotomous outcome variable (such being responsible or otherwise for the crash) while simultaneously taking into account the effects of potentially confounding covariates such as Age, Gender and BAC. As for counts-based analyses, the effect of the cannabis-exposure variable in a MLR is expressed as an OR. 95% confidence intervals can also be calculated.

Only four of the seven responsibility studies employed an MLR to explore the effects of THC on responsibility for crashing. The results are presented in Table 3.3.

Table 3.3 also provides information on the numbers of subjects involved and the main covariates that were statistically controlled for. Where 'contributory' subjects have been removed from the analysis (as identified in Table 3.1) the total number of subjects given in the second column does not include them.

Table 3.3: ORs for THC derived from multiple logistic regressions for the responsibility studies

Author	Total N	N THC-Only	N All-THC	MLR Performed?	Covariates Controlled for *	THC-Present	THC-Absent	OR for THC	95% CI
Terhune, 1982	497	17	47	No	n/a	n/a	n/a	n/a	n/a
Williams, 1985	440	19	162	Yes	A, AL	u/k	u/k	**NS**	u/k
Terhune, 1992	1882	19	109	No	n/a	n/a	n/a	n/a	n/a
Longo, 2000	2279	44	61	No	n/a	n/a	n/a	n/a	n/a
Drummer, 2004	(3210)	56	~120	Yes	A, G, C	THC-Only	THC&AOD-Free	**2.70**	1.0-7.0
Laumon, 2005	9772	450	759	Yes	A, AL, D, V, T	All-THC	THC-Free	**1.78**	1.4-2.3
Poulsen, 2014	1015	92	265	Yes	A, G, AL, D, C	All-THC	THC-Free	**1.29**	0.7-2.3

* (A = Age; G = Gender; AL = Alcohol (BAC); D = Presence of Drugs other than alcohol or cannabis; C = Crash Type [single- vs. multi-vehicle crash]; V = Vehicle type; T = Time of crash)

As for the counts-based analyses, the MLRs require a clear definition of the THC-present and THC-absent categories of the cannabis-exposure variable. In the counts-based analyses reported in Table 3.2, the categories were always THC-only and THC&AOD-free. As a consequence, many subjects were excluded. One reason for conducting a MLR is to avoid the waste of subjects. It follows that the categories of the cannabis exposure variable in an MLR should be exhaustive. The most obvious way to achieve that is to use All-THC as an indicator of the presence of THC, and THC-Free as an indicator of the absence of THC. It may seem problematic that both the All-THC and the THC-free categories will usually include some drivers who have used alcohol and/or other drugs. However, that should not be a problem because MLRs explore the effects of a predictor variable in combination with potentially confounding covariates in such a way that the effects of the confounders can be extricated from the effect of the predictor variable.

Only one of the four MLRs in Table 3.3 (Laumon *et al*., 2005) produced a significant OR for THC (where significance is defined by a 95% confidence interval that excludes the value 1.0).

It is worth noting that, in the absence of statistical adjustments for the effects of *all* confounders, drug-crash ORs are likely to be exaggerated. As pointed out by Elvik (2013) in the context of his meta-analysis of drug-crash effects "Many of the studies reviewed in this paper did not control very well for confounding factors. It is likely that the estimates of risk in these studies are influenced by residual confounding, i.e., they show an increase in risk which is attributable to a set of correlated risk factors, not just the single risk factor of drug use" (p. 265). It follows that evidence in favour of the *absence* of a drug-crash effect (a drug-crash OR of 1.0 or less) is more substantial than evidence in favour of its *presence* (a drug crash OR of more than 1.0).

The seven responsibility studies will now be considered individually. Given that all of the biases identified above would tend to exaggerate cannabis-crash ORs, studies with cannabis-crash ORs of less than 1.00 are considered unlikely to be exhibiting the effects of any bias, and are therefore not scrutinized for the effects of any bias.

Comments on the results of each responsibility study

Terhune (1982) provided information from which a counts-based OR for THC of 2.14 (0.8-5.7) could be calculated (Table 3.2). He did not provide an MLR-based OR for THC (see Table 3.3).

As noted previously, Terhune (1982) acknowledged the relevance of the mismatch problem. He went so far as to speculate that "… culpability ratings do little more than reflect the number of single-vehicle accidents within a substance [drug] group" (p. 97). As discussed above, a *potential* mismatch problem can only become a *real* problem (of possibly exaggerating the size of a drug-crash OR) where the prevalence of the drug in question is greater for single- than for multi-vehicle crashes. As that was not the case for THC in Terhune's 1982 study (see p. 154), the potential consequences of the mismatch problem cannot be realized. So, the counts-based OR of 2.14 (0.8-5.7) for all crashes would probably not have been reduced if the analysis had been restricted to multi-vehicle crashes.

Over-estimation biases pertaining to unadjusted counts-based ORs have already been discussed. It follows that Terhune's (1982) non-significant counts-based OR of 2.14, based on only 17 THC-positive subjects, fails to provide good evidence that cannabis plays a causal role in crashing.

Williams *et al*. (1985) provided information from which a counts-based OR of 0.46 (0.2-1.3) could be calculated (Table 3.2). They did not provide any of the details of their MLR. They simply reported that the OR for THC was 'not significant' (Table 3.3), which is not surprising, given that their counts-based OR was well below 1.00. Their non-significant counts-based OR, based on only 19 THC-positive subjects, provides some evidence that cannabis plays no causal role in crashing.

Terhune *et al*. (1992) provided information from which a counts-based OR of 0.66 (0.3-1.6) could be calculated (Table 3.2). They did not provide an MLR-based OR for THC (Table 3.3). The non-significant counts-based OR, based on only 19 THC-positive subjects, provides weak evidence that cannabis plays no causal role in crashing.

Longo *et al*. (2000) reported a counts-based OR for THC of 0.82 (0.5-1.5) (Table 3.2). They did not provide an MLR-based OR for THC (Table 3.3). Their non-significant counts-based OR, based on 44 THC-positive subjects, provides moderately good evidence that cannabis plays no causal role in crashing.

Drummer *et al*. (2004) provided information from which a statistically significant counts-based OR for THC of 3.16 (1.3-8.0) could be calculated (Table 3.2). That value is presumably increased by the over-estimation biases that pertain to unadjusted counts-based ORs.

Drummer *et al*. (2004, Table 4) reported a marginally non-significant MLR-based OR for THC of 2.70 (1.0-7.0) (Table 3.3). As expected, the MLR-based OR was smaller than the counts-based OR.

All of the information on crashes and toxicology that was used by Drummer *et al*. (2004) came from three Australian states over the 10-year period from 1990 to 1999. While some *patchy* testing for THC was done in the earlier years of the decade, *routine state-wide* testing was only done in the last two years, as indicated by the darkly shaded cells in Table 3.4 (Potter, 2000, pp. 12-17). However, THC results were *routinely* available from *some parts* New South Wales from 1995 to 1997 as indicated by the lightly shaded cells.

Drummer *et al*. (2004) considered that only the routinely collected information was sufficiently reliable to be used in the calculation of the MLR-based OR for THC (2.70; 1.0-7.0). In calculating their OR, they compared information for the THC-only drivers from the last two or so years of the decade (corresponding to all of the shaded cells in Table 3.4) with information for the THC&AOD-free control drivers from the full ten years. The size of the ten-year sample is given here, bracketed, in the second column of Table 3.3. The comparison of odds from different timeframes in the calculation of a single OR is a serious analytical error that throws the validity of THC-crash OR into doubt.

Table 3.4: The shading identifies the years between 1990 and 1999 during which THC testing was routinely conducted on road-crash fatalities within three Australian states

State	90	91	92	93	94	95	96	97	98	99
Victoria										
Western Australia										
New South Wales										

Drummer *et al*'s (2004) THC-crash OR of 2.70 (1.0-7.0) was for the sub-sample of THC-only vs. THC&AOD-free drivers. However, it might have been more appropriate to conduct the MLR analysis on All-THC vs. THC-free, and thereby not exclude the many drivers who tested positive for alcohol and/or other drugs.

It is common practice in a paper on an epidemiological study to describe the sampling procedures in some detail, so that the reader might be able to come to some understanding of the likelihood of the influence of various potential selection biases. Drummer *et al*. (2004) provide very little useful information on their sampling procedures, such that it is difficult for the reader to determine the extent to which the driver fatalities might have been under-sampled. On page 241 they say that: "In each state, a central forensic laboratory performed a full toxicological investigation on all driver fatalities irrespective of type or cause". Later in the paper (p. 246), they confirm that: "Each jurisdiction had policies of conducting toxicology irrespective of the type of motor vehicle crash, and investigated all such cases through a centralised coronial system". It might seem from those two statements that a sample of body fluid was taken from every driver killed in Victoria, New South Wales and Western Australia over the full study period (from 1990 to 1999), and that each sample was subjected to a full set of toxicological analyses for alcohol and other potentially impairing drugs. However, that apparently straightforward interpretation is wrong. A clue to the correct interpretation lies in a statement that relates to the data provided from Western Australia: "Drivers were identified on the basis of records obtained *from the toxicology section* of the Chemistry Centre" (p. 241). From that and other information (see below) it can be concluded that the correct interpretation of the two quoted statements is that: *If toxicological testing was undertaken*, then a *full set of tests* was conducted for alcohol and drugs. No real information that is relevant to the extent of under-sampling is provided in the Drummer *et al*. paper. That is a serious omission, as it makes it impossible to evaluate the role of selection biases, such as the 'responsibility bias' described above.

The publication of Drummer *et al*. (2004) was preceded by the publication of a number of interim reports that are not readily available in the public domain. One of those reports (Drummer, 1994) provides some information in Table 1 on the extent of under-sampling in New South Wales for the period from January 1990 to March 1993, and in Victoria for the period January 1990 to September 1993. No information is available on the extent of toxicological under-sampling in Western Australia, because all of the cases were sampled from the toxicology section of the Chemistry Centre. In New South Wales, only 262 (38.5%) of the 680 recorded driver fatalities were included in the study. Of those excluded, 175 (25.7% of the 680) were excluded because of missing toxicology. In Victoria only 490 (57.9%) of the 847 recorded driver fatalities were included in the study. Of those excluded, 248 (29.3% of the 847) were excluded because of missing toxicology. Drummer (1994) noted that driver fatalities began to be routinely tested in Victoria from late-1991, but he gave no information on possible improvements to the coverage of the testing regime in New South Wales. And there is no relevant information for Western Australia. It is evident that there was a considerable level of under-sampling of driver fatalities in the earlier years of the Drummer *et al*. (2004) study, which most probably continued to some extent through the full ten-year period. It is therefore likely that the responsibility bias artificially increased the drug-crash ORs.

As noted above, the over-estimation of an OR due to the mismatch problem can only be realized where the prevalence of the drug in question is greater for single- than for multi-vehicle crashes. In a 2003 paper, Drummer *et al*. describe the main features of the sample of drivers that were to be used in their 2004 responsibility study. In Table 3 of their 2003 paper, they show that there is a higher prevalence of cannabis for single-vehicle (15.9%) than for multi-vehicle crashes

(11.1%). Unfortunately, those results are for all detections of 'cannabis' as indicated by the detection of either THC or an inactive cannabis metabolite. Although no comparable results are provided for THC alone, any such results would be expected to follow the pattern for cannabis. So, the mismatch problem *is* a real problem for their responsibility analysis. Their MLR-based OR was adjusted for the effects of age and gender. It did not need to be adjusted for the effects of alcohol and/or other drugs as the sub-sample analyzed was alcohol- and other-drug-free. Drummer *et al*. (2004) made no explicit reference to the mismatch problem. However, they were presumably aware of it, because their MLR-based OR for THC was also adjusted for the effect of 'Type of Accident', a variable that coded for the distinction between single- and multi-vehicle crashes. It seems likely that if Drummer *et al*. had responded to the mismatch problem more appropriately by conducting a multi-vehicle-only analysis, then their non-significant OR for THC of 2.70 (1.0-7.0) would have been reduced.

It is concluded that Drummer *et al*'s (2004) findings are of questionable validity and are probably over-estimated because of the responsibility bias. In any case, because of their marginal statistical significance, they would provide only weak evidence that the use of cannabis increases the risk of crashing.

Laumon *et al*. (2005) provided information to Rogeberg and Elvik (2016a) from which a statistically significant counts-based OR for THC of 1.99 (1.6-2.5) could be calculated (Table 3.2). They reported the results of a conventional MLR analysis where the (exhaustive) cannabis exposure variable was All-THC vs. THC-free, from which a statistically significant OR of 1.78 (1.4-2.3) was obtained (Table 3.3). As expected, the OR from the MLR was slightly smaller than from the counts-based analysis. Of the seven selected responsibility studies, Laumon *et al*'s had by far the largest number of THC-positive cases (759, see Table 3.3), and therefore had the greatest potential to provide a valid estimate of the size of the OR for THC.

In the six other responsibility studies, small numbers of crashed drivers were excluded from the analyses for one justifiable reason or another (such as the inability to draw sufficient blood for laboratory drug analysis). However, in Laumon *et al*'s (2005) study, 9,653 (47.3%) of the 20,401 eligible drivers involved in the fatal crashes were excluded. Drivers were excluded if they had not had "full tests for drugs and alcohol" (p. 1). Where it is the responsibility of the police to determine which drivers will be tested for drugs and alcohol (as was the case in this study), their prosecution-motivated focus will be on drivers who are considered to be both responsible for the crash and likely to be impaired by drugs and/or alcohol. Strong selection biases in the direction of exaggerating the size of drug-crash ORs are therefore expected. Laumon *et al*. gave insufficient credence to the likelihood that selection biases were involved in their study.

Laumon *et al*. (2005), in a second phase of subject exclusion, rejected about a quarter of the not-responsible drivers (976 out of 3982) before conducting their analyses. A not-responsible driver was rejected if he or she was the only fatality in the crash. The reasons for doing so are not clear, but they somehow relate to the fact that the not-responsible sole-fatalities are more likely to test positive for cannabis. Laumon *et al*. seem to be motivated by a perceived need for the not-responsible 'control' drivers to be representative of the French driving population. They say that, in particular, they want "the prevalence of cannabis observed [in the not-responsible drivers to be] an acceptable estimation for the driving population" (p. 4). There seems to be a misunderstanding here of the purpose of the not-responsible 'control' group. They are not supposed to comprise a total-driver-population-representative sample; they are supposed to be representative of the crash circumstances. That methodological issue is discussed more fully in the next part of this report. The rejection of a large group of not-responsible drivers who are likely to test positive for cannabis is expected to exaggerate the OR for THC.

Laumon *et al*. (2005) made no explicit reference to the mismatch problem. As a first step, it is relevant to discover if the prevalence of cannabis is greater for single-vehicle than for multi-vehicle crashes. Despite providing detailed information on many features of the crashed drivers and the crash circumstances, Laumon *et al*. did not provide any information on crash types.

However, their database was independently analyzed some years later by Lenguerrand *et al*. (2008). From information in their Table 1 it can be calculated that THC is twice as prevalent for

drivers in single-vehicle crashes (12.8%) as for drivers in two-vehicle crashes where responsibility can clearly be assigned to one of the two drivers (6.2%). So, it is very plausible that the prevalence of cannabis was greater under the broad environmental and demographic circumstances of single-vehicle crashes. Laumon *et al*'s MLR-based OR for THC of 1.78 (1.4-2.3) was adjusted for the effects of age, gender, the use of alcohol, the use of other drugs, vehicle type and the time of day that the crash occurred (Table 3.3). However, the OR was not adjusted for the type of crash (single- versus multi-vehicle). Their two reasons for not doing so were because the type of crash was "the result of the crash" (p. 3) and because, to include a covariate for crash type would "lead to over-adjustment" (p. 3). Neither of those justifications is convincing. It is concluded that Laumon *et al*. have not responded adequately to the mismatch problem. In particular, they did not provide separate results for multi-vehicle crashes.

Three different sources of probable bias have been identified in the Laumon *et al*. (2005) study (a responsibility bias; a mismatch bias; and a selection bias arising from the misguided attempt to make the non-responsible 'control' group representative of the total driving population) - all of which would be expected to exaggerate the size of the cannabis-crash OR. It is concluded that their findings do not comprise satisfactory evidence that cannabis plays any causal role in crashing. However, it seems appropriate to note that a study that is not fit for the purpose of obtaining a valid *absolute* measure of a drug-crash OR may nevertheless be fit for other purposes, such as determining the prevalence of psychoactive drugs in crashed drivers, or even for providing *relative* estimates of the size of ORs for different psychoactive substances.

In 2008, Lenguerrand *et al*. conducted some further analyses of Laumon *et al's* (2005) data. One of their analyses is of particular interest. They discarded all of the single-vehicle crashes and many of the multi-vehicle crashes from the analysis, and retained only those two-vehicle crashes where one driver was entirely responsible for the crash and the other was entirely not responsible. That method, which is sometimes referred to as involving only 'clean crashes', eliminates the possible role of the mismatch bias, because single-vehicle crashes are not included. From their clean-crash MLR analysis Lenguerrand *et al*. obtained a cannabis-crash OR of 1.70 (1.1-2.8). That value is similar to the value of 1.78 (1.4-2.3) from the more conventional MLR analysis as reported in Table 3.3. Given the closeness of these two values, and the fact that the clean-crash analysis did not suffer from the mismatch bias, it would seem that the mismatch bias was not very influential in the original Laumon *et al*. study.

In 2008, Biecheler *et al*. clarified some of the methodological complexity of Laumon *et al*'s (2005) approach. And in 2011, Gadegbeku, Amoros and Laumon provided additional analyses of the original data. No further reference is made to either of those articles in this review.

Poulsen, Moar and Pirie (2014) undertook a responsibility study in New Zealand that was designed to replicate Drummer *et al's* (2004) Australian study. In their Table 4, they reported a non-significant counts-based OR for THC of 1.31 (0.8-2.3). They also employed a conventional MLR analysis where the cannabis exposure variable was All-THC vs. THC-free. They reported three separate ORs for three different THC concentrations, without providing an overall result. The overall OR of 1.29 (0.7-2.3) reported here in Table 3.3 was provided to the author by Ruth Pirie.

Poulsen, Moar and Pirie (2014) did not make any explicit reference to the mismatch problem, nor did they provide a separate responsibility analysis for the multi-vehicle crashes in their paper. However, on request, Ruth Pirie conducted the multi-vehicle analysis, and provided an MLR-based OR for THC of 1.33 (0.7-2.4). The fact that the overall OR of 1.29 (0.7-2.3) was not greater than the multi-vehicle OR of 1.33 (0.7-2.4) is evidence that the results of the study were not biased by the mismatch problem.

Poulsen, Moar and Pirie's (2014) findings are consistent with the possibility that the use of cannabis does not increase the risk of crashing. It is worth noting that this replication study, based on many more THC-positive subjects than Drummer *et al*'s study (265 vs. 56; see Table 3.3), indicates that Drummer *et al*'s OR for THC of 2.7 (1.0-7.0) is an over-estimate.

Part 4: Evidence from case-control studies that THC increases crash risk

Selection of cases and controls

As noted previously, case-control studies of the effects of alcohol and drugs on crashing require the cases and controls to be selected from the same population. The most methodologically sound way of doing that is to match one or two control drivers at the roadside with each crashed case driver with respect to the type of vehicle involved in the crash, the road location of the crash, the direction of travel of the crashed driver, the time of day and day of week when the crash occurred and any other factor known to be related to crash risk such as driver age and gender. Only one of the four studies (Lacey *et al*., 2016) selected control drivers by matching on some of the most relevant variables (see Table 4.1).

Table 4.1: The selection of cases and controls in four case-control studies

Author	Selection of Cases	% Refusal / Rejection	N Cases	Selection of Controls	% Refusal / Rejection	N Controls
Mura, 2003	At emergency units	u/k	900	At emergency units	u/k	900
Gjerde, 2013	Fatally injured drivers	48%	508	Random at roadside	5.8%	9,261
Hels, 2013	At emergency units	0% - 5.4%	1,760	Random at roadside	5% - 52%	12,040
Lacey, 2016	Crash-involved drivers	17.8%	3,095	2:1 matched at roadside	6.3%	6,190

A potential problem with case-control studies relates to their vulnerability to selection biases. In all four case-control studies, it is likely that many of the otherwise-eligible crashed case drivers were not tested for alcohol or drugs, as shown in Table 4.1. In three of the studies (Mura *et al*., 2003; Gjerde *et al*., 2013; Hels *et al*., 2013) the cases were hospitalized crash victims. Where the police or coronial officers have some discretion as to which crash victims should be tested for alcohol and/or drugs, they are more likely to require that testing be done for drivers who are judged to be impaired, such that the presence of alcohol and drugs is over-represented in the case drivers, and the drug-crash ORs are consequently exaggerated. In the study by Gjerde *et al*., testing for drugs was at the discretion of the police. As the researchers explained (p. 143), "Factors giving incorrectly high ORs were that [blood] samples were probably not taken from killed drivers if the police did not regard the probability of finding alcohol or drugs as high". Hels *et al*. made a similar observation (p. 349) that "... there may have been sampling bias, with patients more likely to be positive for psychoactive substances included more readily. If this were the case, it would result in an overestimation of risk".

Selection biases can also pertain to the controls. For example, randomly apprehended control drivers will be more likely to refuse to have samples taken of their blood or oral fluid if they have recently been using alcohol or illegal drugs. As a consequence, the presence of alcohol and drugs will be under-represented in the control drivers, which will again have the effect of exaggerating drug-crash ORs. Table 4.1 provides rejection/refusal rates for the cases and controls in the four case-control studies, which give some indication of the potential for selection biases.

In the fourth of the four case-control studies (Lacey *et al*., 2016), the cases were crashed drivers who were mostly tested for alcohol and drugs at the site of the crash (some were tested in hospital or at the morgue), while the controls were randomly selected drivers who were tested at the roadside at the same crash sites. All who were tested at the crash sites had the right to refuse to be involved in the study. It is likely that many refusals were motivated by the desire not to be found to have recently used alcohol or drugs. About 11% more cases than controls refused to be involved (see Tables 4.1 and 4.5). As a consequence, it is likely that there was a relative under-

representation of alcohol and drugs in the cases, and a subsequent underestimation of the drug-crash ORs. This is the only study where it is likely that drug-crash ORs were underestimated.

In two of the case-control studies that were conducted in the E.U. (Gjerde *et al*., 2013 and Hels *et al*., 2013) the controls were selected to be representative of the *general* driving population rather than of the *crashed* driver population with respect to both driver demographics and traffic volumes. Given that the crashed drivers are more likely to be young males, and that the crashes are more likely to occur at night, the controls will be more benign than if they had been selected to be representative of the crashed-driver population. This inappropriate choice of controls, if not remedied by post-hoc adjustments, will exaggerate alcohol- and drug-crash ORs. Rothman (2012, p. 102) has emphasized this point in his textbook on *Epidemiology: An Introduction*, where he says that "The case definition implicitly defines the source population for cases from which the controls should be drawn. It is this source population for the cases that the controls should represent, not the entire … population". He also notes that some textbooks have provided the misleading advice that controls should be [driver-] population-representative.

A worked example may help to explain this problem. Consider a hypothetical case-control study in which 10% of the case drivers, who have been seriously injured in road crashes, have positive toxicology for cannabis. In the first scenario, suppose that 10% of the 'crash-representative' control drivers also have positive toxicology for cannabis. These drivers have not been involved in a crash, but have been sampled at the roadside such that they are 1:1 matched with the cases with respect to these factors: day of week; time of day; crash location; and rough demographic profile. They are likely to be young males, driving at night or on weekends, and possibly in high-speed zones. The comparison of these controls with the cases would give a cannabis-crash OR of 1.00, implying that the prior use of cannabis plays no causal role in the crashes. In the second scenario, consider that 5% of the 'driver-population-representative' control drivers have positive toxicology for cannabis. These drivers are representative of all driver demographics, locations, day of week, time of day etc., and will therefore include many mothers and fathers driving their children to and from school, and many CBD workers commuting slowly to and from work in peak-hour traffic. The comparison of these controls with the cases would give a cannabis-crash OR of 2.00, implying that the prior use of cannabis doubles the risk of crashing. Even if these scenarios are extreme, they illustrate the point that the use of 'driver-population-representative' controls will result in exaggerated drug-crash ORs.

Calculation of ORs for the case-control studies: Counts-based analyses

As for the responsibility analyses discussed in the previous part of this report, counts data are analyzed here for subjects who had used THC-only or who were THC&AOD-free. Mura *et al*. (2003) provided some counts data - but not for the appropriately selected subjects. Their results are discussed separately below (see Table 4.3). Appropriate counts data were readily available for Gjerde *et al*. (2013, Table 4) and Hels *et al*. (2013, Table 8). Appropriate counts data were also available in Appendix Q Table 7 of Lacey *et al*'s (2016) report. The counts data for the three studies, along with the ORs and 95% confidence intervals are provided in Table 4.2.

Table 4.2: ORs for THC from counts data for three case-control studies

Study	Cases THC-Only	Cases THC&AOD-Free	Controls THC-Only	Controls THC&AOD-Free	Total N for Counts Data Analysis	OR for THC	95% CI
Gjerde, 2013	7	298	48	9054	9407	**4.43**	2.0-9.9
Hels, 2013	24	1177	138	11073	12412	**1.64**	1.1-2.5
Lacey, 2016	164	2487	301	5171	8411	**1.13**	0.9-1.4

It can be seen from Table 4.2 that all three ORs are greater than 1.00 - with two significantly so. The ORs have a wide range: from 1.21 to 4.43. As for the responsibility studies, it is unlikely this range could result from random variation; it is more likely that there are systematic differences between the studies, such that some are unlikely to provide valid ORs.

It is conventional to report overall findings before sub-group findings. However, Mura *et al*. (2003) failed to do so in their paper: they reported only the ORs for THC for the younger age groups (less than 27 years old). The results reported here in Table 4.3 for all age groups are derived from information extracted from their Table 1 and Figure 2. Even then, information for the full sample could not be found for the appropriate way of describing counts data: THC-only vs. THC&AOD-free. The information in Table 4.3 is for All-THC vs. THC-free (as would more typically be subjected to a MLR). A statistically significant OR of 1.88 (1.3-2.7) was found for THC.

Table 4.3: OR for THC derived from counts data for Mura et al. (2003)

Study	Cases All-THC	Cases THC-Free	Controls All-THC	Controls THC-Free	Total N for Counts Data Analysis	OR for THC	95% CI
Mura, 2003	88	812	49	851	1800	**1.88**	1.3-2.7

As mentioned previously, the unadjusted ORs for the four case-control studies (Tables 4.2 and 4.3) are expected to be overestimates, as they do not compensate for the various personal and other risk factors that pertain to the use of cannabis.

Calculation of ORs for the case-control studies: MLR-based analyses

Three of the four case-control studies employed MLR analyses to further explore the effects of THC on the risk of crashing. As is common for epidemiological studies published before 2004, Mura *et al*. (2003) did not conduct an MLR. The results for the three MLRs are presented in Table 4.4, along with information on the numbers of subjects involved and the identity of the covariates that were statistically controlled for.

It is interesting to note that none of the three MLRs employed the exhaustive definition of the cannabis exposure variable: All-THC vs. THC-free. Two of the analyses defined the cannabis-exposure variable as THC-only vs. THC&AOD-free (as would normally be subjected to a counts-based analysis). Lacey *et al*. (2016) defined it as All-THC vs. THC&Drug-free.

Table 4.4: ORs for THC derived from multiple logistic regressions for four case-control studies

Author	N Cases THC-Only	N Cases All-THC	N Controls THC-Only	N Controls All-THC	MLR Performed?	Covariates Controlled for *	THC-Present	THC-Absent	OR for THC	95% CI
Mura, 2003	n/a	88	n/a	49	N	n/a	n/a	n/a	n/a	n/a
Gjerde, 2013	7	31	48	54	Y	A, G, T, W, R	THC-Only	THC&AOD-Free	**1.90**	0.8-4.6
Hels, 2013	24	u/k	138	u/k	Y	A, G, Ct	THC-Only	THC&AOD-Free	**1.91**	1.2-3.2
Lacey, 2016	164	234	301	379	Y	A, G, E, AL, Al	All-THC	THC&Drug-Free	**1.00**	0.8-1.2

* (A = Age; G = Gender; E = Ethnicity; AL = Alcohol; T = Time of day; W = Day of week; R = Road Type; Ct = Country)

Two of the three studies (Gjerde *et al*., 2013 and Hels *et al*., 2013) reported adjusted ORs for THC that were greater than 1.00, but only one (Hels *et al*., 2013) reported an OR that was significantly greater than 1.00.

From their MLR, Gjerde *et al*. (2013) obtained a non-significant OR for THC of 1.90 (0.8-4.6). As expected, the value of 1.90 is smaller than the value of 4.43 (2.0-9.9) from the comparable counts-based analysis (Table 4.2), demonstrating that the statistical control of confounding personal and crash-related variables can substantially reduce the value of an OR. There was no need to control for the presence of alcohol or other drugs in this MLR, as the definition of the cannabis-exposure variable as THC-only v. THC&AOD-free excluded all subjects in whom alcohol and/or other drugs were detected. These results indicate that cannabis may have substantially increased the risk of crashing.

Hels *et al*. (2013) found a statistically significant OR of 1.91 (1.2-3.2) for THC-only vs. THC&AOD-free when statistically controlling for the effects of age, gender and country. Again, there was no need to control for the presence of alcohol or other drugs in this MLR. Strangely, the statistical control of confounding personal variables seems to have *increased* the value of the OR from its counts-based value of 1.64 (1.1-2.5) (see Table 4.2). These results for Hels *et al*. are similar to those for Mura *et al*. (2003) and Gjerde *et al*. (2013), and indicate that cannabis may have substantially increased the risk of crashing.

Compton and Berning (2015) described Lacey *et al's* (2016) NHTSA case-control study as "… the largest and most comprehensive study to address alcohol and drug crash risk in the US", noting that the study "employed a rigorous design involving a precise matching of cases and controls" (p. 3). The study involved 3,095 crash-involved case drivers (across all levels of crash severity) and 6,190 control drivers. Many of the crashes were at a low level of severity, with only a third of them involving injuries and 15 being fatal. The OR for cannabis (THC), when statistically adjusted for the effects of various demographic and crash-related covariates, including BAC, was exactly 1.00 (0.8-1.2). As expected, the value of 1.00 is slightly smaller than the value of 1.13 (0.9-1.4) from the counts-based analysis (Table 4.2). These results indicate that cannabis did not increase the risk of crashing.

In comparing the evidential strength of the four case-control studies, it is worth noting that Lacey *et al.* (2016) included 234 THC-present cases, in contrast with 88 for Mura *et al*. (2003), 7 for Gjerde *et al*. (2013) and 24 for Hels *et al*. (2013).

Comments on the results of each case-control study

The case and control subjects in **Mura *et al's* (2003)** French study were all recruited from the emergency units of a number of hospitals. The cases were injured car drivers. The controls were patients at the same emergency units who attended for non-traumatic reasons. The researchers provide no information on what types of permissions were required for the hospitals to take blood or urine samples for laboratory analysis. Nor did they provide any information on refusal rates. It is conceivable that the injured case drivers were required by law to provide blood, while the uninjured control patients were not. If so, strong selection biases might be operating for the controls. In any case, the use of uninjured hospital patients as controls is far from optimal. For example, patients planning to attend emergency units for non-traumatic reasons may very well refrain from their normal consumption of alcohol or other drugs before attending. Additionally, Mura *et al*. report that "… those admitted for voluntary or accidental intoxication (including alcohol) were excluded" (p. 80). By reducing the measured prevalence of drugs in the control group, the drug-crash ORs would be exaggerated. A further serious deficiency of Mura *et al's* research design is that it failed to control for the likely contaminating effects of the co-presence of alcohol with the THC. It is concluded that Mura *et al*'s counts-based OR for THC of 1.88 (1.3-2.7) is of little evidential value in determining the true value of the OR for the relationship between the use of cannabis and crashing.

The cases in **Gjerde *et al*'s (2013)** Norwegian study were fatally injured car and van drivers. The police had the authority to order that samples of their blood be taken for analysis. Nevertheless, they did not require samples to be taken from 39% of the drivers. It is a fairly safe assumption that they only wanted samples to be taken if they considered that the drivers were likely to have used alcohol or drugs. The controls comprised drivers from a random roadside survey in Norway that was not originally designed for the purpose of the case-control study. The control drivers were required by the police to stop at the roadside and participate in an alcohol breath test. With the permission of the police, the drivers were then approached by a member of the research team and asked to voluntarily and anonymously provide a sample of oral fluid for alcohol and drug testing. The refusal rate was 5.8%. The researchers acknowledged that the refusers were more likely than the compliant drivers to have used alcohol or drugs, thus reducing the prevalence of alcohol and drugs in the control group. There was a further factor that reduced the prevalence of alcohol (and therefore probably also drugs, because of poly-drug use) in the control group: the police denied access by the research team to about 25% of the clearly intoxicated control drivers, who instead were immediately taken to a police station for evidential testing (Gjerde *et al*., 2011, p. 1199). It is likely that the size of the ORs for alcohol and drugs in this study were substantially increased by the strong selection biases operating on both the cases and controls. For example, Gjerde *et al*. (Table 5) reported a very high MLR-based OR of 124.6 (69.1-224.9) for alcohol alone. By reference to comparable results from other studies (Tables 7.6 and 8.3), it can be seen that this value is exceptionally high. It is concluded that Gjerde *et al*'s study is incapable of providing realistic *absolute* OR values for any drug or drug combination. Their non-significant MLR-based OR for THC of 1.90 (0.8-4.6) is therefore of little evidential value in determining the true value of the OR for the relationship between the use of cannabis and crashing. The researchers themselves acknowledge that their study produced "incorrectly high ORs" (Gjerde *et al*., 2013, p. 143).

The case and control drivers in the Gjerde *et al*. (2013) study were not matched on any person-related or crash-related variables. The researchers argued that the lack of matching on crash-related variables (such as road locations and times of day) could be remedied by including appropriate control variables for location and time in the MLR. It is possible that the inadequacies in the original research design were not fully remedied by the post-hoc statistical adjustments.

As an aside, it is worth noting that the researchers have apparently discovered a statistical artefact that tends to exaggerate the size of the ORs that are obtained where base rates of impaired driving are very low, as is the case in Norway and Finland (Gjerde, Bogstrand & Lillsunde, 2014). Nevertheless, it is still probable, as they acknowledge, that their cannabis-crash OR is over-estimated.

Hels *et al*. (2013) reported the findings of a collaborative study that was part of the E.U.-wide DRUID program of research on drug-driving. The Norwegian component of the overall study was reported separately by Gjerde *et al*. (2013), and was discussed above. The results reported by Hels *et al*. are from six countries: Belgium, Denmark, Finland, Italy, Lithuania and the Netherlands. However, the data from Finland and Italy were not included in the OR calculations, so the numbers reported here are for the four remaining countries. The cases in the Hels *et al*. study were 1,760 car or van drivers who were seriously injured in road crashes and treated at hospitals, where their blood was taken for alcohol and drug testing. The controls were drivers recruited in roadside surveys. The voluntary and anonymous surveys were designed to be "representative of all traffic on all roads at all times" (p. 348). The surveyed drivers were therefore *not* selected to be representative of the crashed drivers in age or gender, nor were the survey times of day selected to be representative of when the crashes occurred. The 12,040 controls were required by police to stop at the roadside and participate in an alcohol breath test. They were then asked by members of research teams to provide samples of oral fluid or blood for alcohol and drug testing. There were different refusal rates in the different countries: 5% in Denmark and The Netherlands; 24% in Lithuania; and 52% in Belgium. While Hels *et al*. provide some arguments that all of the complexities of this multi-country study have been taken into account in the calculation of realistic ORs, it seems likely that some of the shortcomings of this study would be similar to those discussed above in relation to the Gjerde *et al*. study.

It is likely that the Hels *et al*. (2013) study has also produced "incorrectly high ORs". The research team seems to acknowledge that in saying "The non-respondents in the control sample are likely to be positive for psychoactive substances, whereas in the case sample the hospital staff may be more likely to include patients believed to be positive. Thus, the non-respondents in both the control and case samples may have led in the same direction – to an over-estimation of risk" (p. 354). In the light of these reservations, it would be appropriate to consider that the true value of the OR for THC is well below the reported value of 1.91. It is concluded that Hels *et al's* MLR-based OR for THC of 1.91 (1.2-2.3) is of little evidential value in determining the true value of the OR for the relationship between the use of cannabis and crashing.

The 3,095 cases in **Lacey *et al's* (2016)** study were crash-involved drivers. The 6190 controls were selected in the optimal way, using 1:2 case to control matching for the main crash characteristics of location, day of week, time of day, and direction of travel of the crashed car. Participation in the study was voluntary and anonymous. Quantitative analyses of alcohol were based on breath samples, while laboratory tests for the presence of drugs were based on samples of oral fluid and/or blood.

To this point in the report, studies that have not found a significant cannabis-crash OR have been less thoroughly scrutinised than those that have found ORs that are significantly above 1.00. The reason for that admittedly uneven-handed approach has been that all of the biases discovered to this point have been over-estimation biases, such that there has been little need to scrutinise studies with ORs of 1.00 or below. However, there is the possibility that Lacey *et al's* (2016) cannabis-crash OR of 1.00 has been under-estimated, so it deserves some scrutiny.

In Lacey *et al's* (2016) study, information was obtained from the cases and controls in a number of stages, with breath-testing for alcohol occurring before oral-fluid and/or blood testing for drugs. All drivers were informed that they could opt out at any stage. From Figure 6 and Table 9 in their report, the opt-out rates in Table 4.5 can be calculated.

Table 4.5: Opt-out rates for drivers in Lacey et al's (2016) case-control study

Stage of recruitment	Number	% of eligible	Total % loss from eligible N	Incremental % loss at each stage
Crash-involved cases				
Total eligible case drivers	3,887	100.00%	-	-
Breath sample taken for alcohol analysis	3,467	89.19%	10.81%	10.81%
Oral fluid and/or blood sample taken for drugs	3,196	82.22%	17.78%	6.97%
Final sample size after 1:2 case-control matching	3,095			
Roadside Controls				
Total eligible control drivers	7,397	100.00%	-	-
Breath sample taken for alcohol analysis	7,078	95.69%	4.31%	4.31%
Oral fluid and/or blood sample taken for drugs	6,935	93.75%	6.25%	1.94%
Final sample size after 1:2 case-control matching	6,190			

Overall, 17.78% of case drivers opted out of the study before the drug-testing stage, in comparison with 6.25% for the control drivers. There is therefore an 11.53% (17.78% - 6.25%) greater non-participation rate for the case drivers than for the control drivers - which could potentially introduce a selection bias in the direction of reducing the cannabis-crash OR, assuming that some of those who opted out were deliberately avoiding the drug tests because of their recent use of cannabis.

The percentage of control drivers who gave breath samples for alcohol analysis, but who did not go on to give oral-fluid and/or blood samples for drug testing is 1.94%, which is considerably less than the corresponding percentage of 6.97% for the case drivers. It is therefore unclear why Lacey *et al*. (2016) stated on p. 39 that "There were many *control* drivers who did not give oral fluid but gave breath samples. These drivers were included in the analyses for alcohol crash risk but not for drug crash risk. Therefore, the sample size for alcohol analyses sometimes was larger than for other analyses". Perhaps there was an editing error whereby 'control drivers' was used instead of 'case drivers'.

There are some factors that could mean that the 11.53% difference in participation rates has little or nothing to do with differences in the level of avoidance of drug-testing. For example, one of the reasons for the high number of drop-outs amongst the cases as compared with the controls could be that the cases were overwhelmed by their involvement in the crash, and did not want to face the additional burden of being involved in a lengthy (up to 20 minutes) survey.

However, Lacey *et al*. (2016, pp. 44-46) have provided evidence against the likelihood of any such avenue of exoneration. They conducted a sub-study wherein they offered $100 to case and control drivers who had initially refused to participate to change their minds and continue their involvement in the study. Most of their conversion attempts were declined, with fewer cases than controls being converted. However, some interesting information was obtained from those who did convert. The converted cases were more likely than the converted controls to test positive to alcohol and illegal drugs. Those findings strongly indicate that some of the cases, in particular, were reluctant to be involved with the study because of their prior use of alcohol and/or illegal drugs.

In conclusion, it seems likely that, despite being derived from the most rigorous case-control study reviewed in this report, Lacey *et al's* (2016) cannabis-crash OR of 1.00 (0.8-1.20) suffered to some extent from an under-estimation bias. That likelihood is strengthened by the fact that Lacey *et al*. failed to replicate the substantial cannabis-crash ORs that have been consistently reported for illegal drugs other than cannabis (Elvik, 2013).

The exact extent of the underestimation of the cannabis-crash OR is difficult to estimate. In their Summary (p. 65) Lacey *et al*. note, in support of the accuracy of their drug-crash ORs, that their alcohol-crash ORs are comparable with those found in other rigorous studies, which fact, they argue, implies that their drug-crash ORs must also be fairly accurate. In their own words: "The alcohol-based risk curves were very similar to those reported in NHTSA's previous case-control study (Blomberg *et al*., 2009). Replicating the results for alcohol and crash risk adds further assurance of the strong methodology of this study's design and dataset". While that argument has some merit, it does not exclude the possibility that their cannabis-crash OR was somewhat under-estimated.

Lacey *et al's* (2016) Discussion is only two pages long. Methodological problems are usually addressed in Discussions, but Lacey *et al*. failed to consider the likely role of selection biases in theirs. They should have been more sceptical about their finding that drugs, including cannabis, did not increase the risk of crashing. It is concluded that the Lacey *et al's* drug-crash ORs have most probably been under-estimated to some extent. However, given the realistic alcohol-crash results, it is unlikely that the cannabis-crash OR of 1.00 (0.8-1.2) was greatly under-estimated.

It is concluded that Lacey *et al's* (2016) non-significant MLR-based OR for THC of 1.00 (0.8-1.2) does not provide convincing evidence that cannabis has no effect on the risk of crashing. However, their finding is compatible with cannabis having only a small effect.

Part 5: Summary of the main findings from Parts 3 and 4

Selecting a single cannabis-crash OR from each study

The cannabis-crash ORs from Parts 3 and 4 are provided in Table 5.1. Only one OR is given for each of the eleven studies. Where a study provided both a counts-based and an MLR-based OR, the MLR-based OR is presented, as it is taken to be a more valid estimate of the true OR. Where the OR is based on counts data, the cannabis-using subjects are usually (with Mura *et al.,* 2003 being the exception) defined as having used cannabis but no other drug or alcohol (THC-only). But where the OR is based on an MLR, the cannabis-using subjects are equally likely to be defined as having used only cannabis (THC-only) or having used alcohol and/or other drugs along with cannabis (All-THC).

Table 5.1: Summary of ORs for cannabis and crashing

Study	Responsibility or Case-Control Study	Counts-Based or MLR-Based	N Subjects THC-Only	N Subjects All-THC	OR (95% CI)	OR Significant or Not-Significant
Terhune, 1982	R	Counts	17		2.14 (0.8-5.7)	N.S.
Williams, 1985	R	Counts	19		0.46 (0.2-1.3)	N.S.
Terhune, 1992	R	Counts	19		0.66 (0.3-1.6)	N.S.
Longo, 2000	R	Counts	44		0.82 (0.5-1.5)	N.S.
Mura, 2003	C	Counts		137	1.88 (1.3-2.7)	Sig
Drummer, 2004	R	MLR	56		2.70 (1.0-7.0)	N.S.
Laumon, 2005	R	MLR		759	1.78 (1.4-2.3)	Sig
Gjerde, 2013	C	MLR	55		1.90 (0.8-4.6)	N.S.
Hels, 2013	C	MLR	162		1.91 (1.2-3.2)	Sig
Poulsen, 2014	R	MLR		265	1.29 (0.7-2.3)	N.S.
Lacey, 2016	C	MLR		613	1.00 (0.8-1.2)	N.S.

From Table 5.1 it can be seen that four of the eleven cannabis-crash ORs are 1.00 or less, and therefore indicate that cannabis does not play a role in crash causation. Furthermore, four of the seven that are greater than 1.00 are not significantly greater. That leaves only three of the eleven ORs that are significantly greater than 1.00.

The question of interest is whether or not the information provided in Table 5.1, when taken as a whole, comprises evidence that the prior use of cannabis plays a causal role in road crashes. To answer that question it is first necessary to consider the overall effects of all the biases that have been identified in Parts 3 and 4 of this report. However, before doing so, it seems appropriate to restate an important caveat.

The biases identified in Parts 3 and 4 of this report, and summarized in this part, are relevant only to the *absolute* sizes of the cannabis-crash ORs. They are not necessarily relevant to the *relative* sizes of those ORs or to other important issues that the studies might address, such as the nature of alcohol-drug interaction effects. So, a study that is identified as being flawed in this part of the report could still be rigorous in many respects.

Taking the quality of the studies into account

Table 5.2 describes the biases that are likely to be exaggerating the size of the cannabis-crash OR for each of the seven responsibility studies that were discussed in Part 3. It is considered unlikely that any of the three studies with ORs that are not greater than 1.00 (Williams *et al*., 1985; Terhune *et al*., 1992; Longo *et al*., 2000) suffer from the effects of any biases, as all of the identified biases tend to over-estimate the 'null-hypothesis OR' of 1.00. The single counts-based OR that is greater than 1.00 (Terhune, 1982) is likely to be exaggerated by the lack of statistical control for confounding variables ('confounder bias'). The four ORs that are greater than 1.00 (Terhune, 1982; Drummer *et al*., 2004; Laumon *et al*., 2005; Poulsen. Moar & Pirie, 2014) are all likely to be exaggerated to an unknown extent by the problem of non-independent assessments. One of those ORs had been identified in Part 3 as being likely to be exaggerated by the mismatch problem (Laumon *et al*., 2005). The same study is also likely to have suffered from strong selection biases. Drummer *et al*. (2004) most probably suffered from a particular type of selection bias, the responsibility bias.

Table 5.2: Summary of biases exaggerating the cannabis-crash ORs in the responsibility studies

Study	Counts-Based or MLR-Based	N Subjects THC-Only	N Subjects All-THC	OR for THC	OR > 1.00?	Confounder Bias?	Bias from Non-Independent Assessments?	Mismatch Bias?	Selection Bias?
Terhune, 1982	Counts	17		2.14		Yes	Possibly	No	No
Williams, 1985	Counts	19		0.46	No	No	No	No	No
Terhune, 1992	Counts	19		0.66	No	No	No	No	No
Longo, 2000	Counts	44		0.82	No	No	No	No	No
Drummer, 2004	MLR	56		2.70		No	Possibly	No	Yes
Laumon, 2005	MLR		759	1.78		No	Possibly	Yes	Strong
Poulsen, 2014	MLR		265	1.29		No	Possibly	No	No

Table 5.3 describes the biases that are likely to be affecting the size of the cannabis-crash OR for each of the four case-control studies that were discussed in Part 4. The study with an OR equal to 1.00 (Lacey *et al*., 2016) may suffer from an under-estimation bias. The single counts-based OR that is greater than 1.00 (Mura *et al*., 2003) is likely to be exaggerated by the lack of statistical control for confounding variables. Three of the four studies are likely to have suffered from strong over-estimation biases (Mura *et al*., 2003; Gjerde *et al*., 2013; Hels *et al*., 2013).

Table 5.3: Summary of biases exaggerating the cannabis-crash ORs in the case-control studies

Study	Counts-Based or MLR-Based	N Subjects THC-Only	N Subjects All-THC	OR for THC	OR > 1.00?	Confounder Bias?	Selection Biases?
Mura, 2003	Counts		137	1.88		Yes	Strong
Gjerde, 2013	MLR	55		1.90		No	Strong
Hels, 2013	MLR	162		1.91		No	Strong
Lacey, 2016	MLR		613	1.00	No	No	Yes

The prevalence of such biases should perhaps not be surprising. In their textbook on *Modern Epidemiology*, Rothman, Greenland and Lash (2008, p. 112) observed that "Because it need not be

extremely expensive or time-consuming to conduct a case-control study, many studies have been conducted by naïve investigators who do not understand or implement the basic principles of valid case-control design". In a similar vein, Schulz and Grimes (2002, p. 431) commented that "Case-control studies tend to be more susceptible to biases than other analytical, epidemiological designs". Studies conducted within the DRUID framework (including Gjerde *et al*., 2013 and Hels *et al*., 2013) were specifically critiqued by Houwing *et al*. (2013), who concluded that they all suffered from selection biases that would have exaggerated the drug-crash ORs obtained.

Table 5.4 provides a Total Bias Score for each of the eleven studies. Individual biases that are indicated by a 'Yes' in Tables 5.2 and 5.3 are given a score of 1, while those that are described as 'Strong' are given a score of 2. Biases that are indicated by a 'Possibly' in Table 5.2 are given a score of zero, because of the lack of firm evidence for the existence of that bias.

Table 5.4: Summary of ORs for cannabis and crashing, with evaluations of study quality

Study	Responsibility or Case-Control Study	Counts-Based or MLR-Based	N THC Drivers	OR (95% CI)	OR Significant or Not-Significant	Total Bias Score	Sample Size	Total Demerit Points
Terhune, 1982	R	Counts	17	2.14 (0.8-5.7)	N.S.	1	Small	2
Williams, 1985	R	Counts	19	0.46 (0.2-1.3)	N.S.	0	Small	1
Terhune, 1992	R	Counts	19	0.66 (0.3-1.6)	N.S.	0	Small	1
Longo, 2000	R	Counts	44	0.82 (0.5-1.5)	N.S.	0	Medium	0
Mura, 2003	C	Counts	137	1.88 (1.3-2.7)	Sig	3	Large	3
Drummer, 2004	R	MLR	56	2.70 (1.0-7.0)	N.S.	1	Medium	1
Laumon, 2005	R	MLR	759	1.78 (1.4-2.3)	Sig	3	Large	3
Gjerde, 2013	C	MLR	55	1.90 (0.8-4.6)	N.S.	2	Medium	2
Hels, 2013	C	MLR	162	1.91 (1.2-3.2)	Sig	2	Large	2
Poulsen, 2014	R	MLR	265	1.29 (0.7-2.3)	N.S.	0	Large	0
Lacey, 2016	C	MLR	613	1.00 (0.8-1.2)	N.S.	1	Large	1

Another important indicator of the credibility of a study is the number of THC-positive drivers that the cannabis-crash OR is based on. Those numbers are somewhat arbitrarily described as 'Small' (< 40), 'Medium' (> 40 and < 100) and 'Large' (> 100) in Table 5.4. Studies with Small sample sizes are given a single 'Demerit Point', which is added to the Total Bias Score to produce the Total Demerit Points in Table 5.4.

The 'Better' studies are defined as those with a Total Demerit Points of 0 or 1, while the 'Worse' studies are those with a Total Demerit Points of 2 or 3. From Table 5.5, it can be seen that the un-weighted mean cannabis-crash OR for the six Better studies (1.16) is considerably less than for the five Worse studies (1.92). It seems that the more rigorous studies provide lower estimates of the cannabis-crash OR.

Table 5.5: Mean cannabis-crash ORs by study quality

Total Demerit Points	N Studies	Mean OR
Better (0 or 1)	6	1.16
Better without Drummer (2004)	5	0.85
Worse (2 or 3)	5	1.92

The study by **Drummer *et al*. (2004)** is an exception. Although classified as a Better study, it has the highest cannabis-crash OR of all the studies (2.70; 1.0-7.0). When Drummer *et al*. is removed from the Better studies, their un-weighted mean OR is reduced from 1.16 to 0.85.

There are three problematic features of the Drummer *et al*. (2004) study that were not taken into account in the calculation of its Total Demerit Points.

The first has already been discussed. It relates to the fact that the laboratory evidence on the presence of THC was collected only in the last two or so years of the 10-year study period (see Table 3.4). The THC-crash OR calculations involved comparing the responsibility findings from a THC-positive group selected from one timeframe (the last two or so years of the 10-year period) with those from an alcohol-and-drug-free group selected from a very different timeframe (the full 10-year period). The analysis should have been restricted to the last two or so years of the 10-year period. The comparison of results from very different timeframes is not a satisfactory statistical procedure. However, it is not obvious what effect the faulty analysis might have had on the size of the THC-crash OR.

The second is that the data were provided by three different jurisdictions, and within those jurisdictions it was provided under different managerial regimes at different times. There room to doubt that the many collaborators were all strictly adhering to the data-collection protocols, such as the total independence of the laboratory and culpability assessments.

The third reason to be cautious about the Drummer *et al*. (2004) results was noted by Potter (2000, p. 17). His concerns (which were shared by Baldock, 2007/08, p. 808) were that:

> There is an apparent inconsistency between the newer data [mostly 1997-1998] and the older [1990-1996]: in the newer data, a substantial proportion of the total cannabis user group was THC-positive, and culpable. If the same were true for the older data set, an elevated odds ratio for the total cannabis user group should have been evident. [But it was not]. It is unlikely that the underlying risk associated with driving while THC-positive has changed in the last few years. It is possible that the proportion of cannabis users who drive while THC-positive has increased sharply. Alternatively, the apparent incidence of culpable THC-positive drivers in either data set could be a statistical aberration.

In other words, Potter (in a report that was endorsed by the Austroads Working Group on Drugs and Driving) was suggesting that the finding of a substantial cannabis-crash OR by Drummer *et al*. (2004) was unexpected in the light of their earlier, and more benign, results, and could be the result of some sort of aberration.

It is also relevant to note, as mentioned previously, that Poulsen, Moar and Pirie (2014) designed a New Zealand study to replicate Drummer *et al*'s Australian study, but failed to reproduce Drummer *et al's* high cannabis-crash OR of 2.70 (1.0-7.0). Using many more THC-positive drivers than Drummer *et al*. (265 vs. 56), Poulsen, Moar and Pirie found a much smaller, and non-significant, OR of 1.29 (0.7-2.3). The failure to replicate the findings of a study is a strong indication that the original findings are not valid.

Conclusions

It is not immediately obvious how some broad conclusions might be reached from the information in Tables 5.4 and 5.5, given that the summarized studies are of such variable quality (for the purpose of establishing absolute OR values). A typical solution would be to conduct a meta-analysis of the cannabis-crash results from the eleven studies. However, that approach is inappropriate in this instance. Given that most of the identified biases act to exaggerate the cannabis-crash OR, a meta-analysis would simply produce a summary over-estimate of the true OR. This matter is discussed in more detail at the end of this part of the report.

It seems clear from the information in Tables 5.4 and 5.5 that there is no good evidence that the true value of the cannabis-crash OR is greater than 1.00. However, if it is greater than 1.00, the evidence in Tables 5.4 and 5.5 indicate it unlikely to be *much* greater. It is unclear how an upper limit to the value might be determined. The most rigorous meta-analysis conducted to date (Rogeberg & Elvik, 2016a) provided a summary cannabis-crash OR of 1.36 (1.2-1.6). Given that that estimate is from a meta-analysis and is therefore likely to be an *over*-estimate, it seems fair to conclude that the true value of the cannabis-crash OR is unlikely to be greater than 1.30.

Comparison of results for responsibility studies and case-control studies

It was noted in Part 1 of this report (see also Attachment A) that, all things being equal, responsibility studies should produce higher drug-crash ORs than case-control studies. Table 5.6 provides the un-weighted mean cannabis-crash ORs for the studies listed in Table 5.4, broken down by the two types of study. It can be seen that, contrary to expectation, the case-control studies have the higher mean OR.

Table 5.6: Mean cannabis-crash ORs for responsibility and case-control studies

Study Type	N Studies	Mean OR
Responsibility	7	1.41
Case-control	4	1.67

From their meta-analysis, Asbridge, Hayden and Cartwright (2012, p. 8) also found a higher mean cannabis-crash OR for case-control studies (2.79; 1.2-6.3) than for responsibility studies (1.65; 1.1-2.5).

If sufficient information is available in a case-control study on the causal roles of the drivers involved in the crashes, it is possible to nest a responsibility study within the case-control study. The best evidence that case-control analyses typically provide higher drug-crash ORs than responsibility analyses would come from a nested study. That was not done for any of the four case-control studies that were included in this review. However, it was done for one of the six case-control studies that were excluded: Brault *et al*. (2004). Table 5.7 provides case-control- and responsibility-based drug-crash ORs from Brault *et al.* for both alcohol and cannabis. It is evident that the case-control analyses produce the higher ORs for both types of drug.

Table 5.7: ORs for cannabis and alcohol from a responsibility study nested in a case-control study

Source	Alcohol or Cannabis	Case-Control or Responsibility	OR (95% CI)
Brault *et al*. (2004)	Alcohol alone Equal or Above BAC 0.02	Case-control	10.8 (8.3-14.1) Unadjusted
		Responsibility	7.6 (2.9-19.7) Unadjusted
	Cannabis alone	Case-control	2.0 (1.4-2.9) Unadjusted
		Responsibility	1.2 (0.5-2.9) Unadjusted

While most of the differences explored here are not statistically significant, the findings are consistent, which raises the question of why, contrary to a mathematically-based expectation, the case-control studies typically produce the higher cannabis-crash ORs. The answer seems clear from the evidence provided in Part 4 of this report (see also Baldock, 2007/8). It is that most of the case-control studies that have been published in this area suffer from strong selection biases that exaggerate their drug-crash ORs, while the responsibility studies are relatively unbiased.

Some critiques of three meta-analyses

It was noted in Part 2 of this report that four meta-analyses investigating the relationship between the prior use of cannabis and involvement in road crashes had been published since 2011: Asbridge, Hayden and Cartwright (2012); Li *et al*. (2012); Elvik (2013); and Rogeberg and Elvik (2016a). Given that Rogeberg and Elvik's meta-analysis was an extension and refinement of the cannabis-related parts of Elvik's earlier meta-analysis, the earlier study will not be considered further. Some salient features of the three meta-analyses are reported in Table 5.8.

From the perspective of this study, there is one respect in which two of the three meta-analyses (Li *et al*., 2012; and Rogeberg & Elvik, 2016a) are considered deficient: their toxicological definition of the cannabis variable is over-inclusive. By allowing the presence in body fluids of non-psychoactive cannabinoids to indicate the recent use of cannabis, they included drivers who could have used cannabis many days or weeks prior to the toxicological testing. Although Asbridge, Hayden and Cartwright's (2012) toxicological definition of the cannabis variable was in terms of the presence of psychoactive cannabinoids, they erred with respect to their inclusion of the study by Bedard, Dubois and Weaver (2007) who used driver fatalities from the FARS database that includes drivers with non-psychoactive cannabinoids (see Attachment E), and Mathijssen and Houwing (2005) who also included some drivers with non-psychoactive cannabinoids.

Table 5.8: Salient features of three cannabis-crash meta-analyses

	Asbridge *et al*. (2012)	**Li *et al*. (2012)**	**Rogeberg & Elvik (2016a)**
Definition of the cannabis variable	Toxicological detection of psychoactive cannabinoids; and self-reported use of cannabis (but for only one study)	Toxicological detection of various cannabinoids; and self-reported use of cannabis	Toxicological detection of various cannabinoids; and self-reported use of cannabis (but for only one study)
Rejection criteria		Responsibility studies or studies published before 1990	
Number of ORs incorporated into the summary OR	9	9	28
Counts-based or MLR-based ORs?	Counts-based ('unadjusted')	Counts-based ('unadjusted')	MLR-based ('adjusted') where available
Reported Summary OR	1.92 (1.4-2.7)	2.66 (2.1-3.4)	Method A: 1.36 (1.2-1.6) Method B: 1.22 (1.1-1.4)
Summary OR as 'corrected' by Rogeberg & Elvik	1.25 (1.0-1.6)	1.55 (1.1-2.2)	
The 'purity' of responsibility vs. case-control			Case-control analyses are more basic, or 'purer'

It is also considered inappropriate to define the cannabis variable in terms of self-reports of cannabis use, as was done in all three meta-analyses, because such reports are unreliable. In contrast, the current review incorporated only those studies that defined the cannabis variable in terms of the toxicological detection of THC in blood or oral fluid, thereby attempting to provide the best possible indicator of the recent use of cannabis.

Rogeberg and Elvik (2016a) described the drivers in the studies they reviewed as being afflicted by 'acute cannabis intoxication'. That description was clearly wrong, as Gjerde and Morland (2016) pointed out. In response to the criticism, Rogeberg and Elvik (2016b) acknowledged their lack of toxicological expertise, and the inaccuracy of their description. Certainly, some of the drivers in whom various cannabinoids were detected would have been to some extent 'under the influence of cannabis', while most were probably not. That situation would have been improved

if Rogeberg and Elvik had restricted the studies they covered to those that defined the cannabis variable in terms of the toxicological detection of THC.

Before leaving this discussion of the appropriate definition of the cannabis variable (for the purpose of including a study in a review), it should be noted that Gjerde and Morland (2016) advised that the best definition would not be in terms of the mere detection of THC in a body fluid, but would be in terms of the detection of relatively high concentrations of THC, which, they argued, would indicate very recent use of cannabis and therefore the likelihood of 'acute cannabis intoxication'. However, that advice is based on the supposition that a dose-response relationship exists between THC concentration and the risk of crashing, which is shown to be unproven in Part 6 of this report.

One of the main purposes of this review is to provide evidence that could be relevant to the further development of drug-driving policy in Australia, where it is an offence to drive with any detectable amount of THC in a body fluid, which corresponds with the definition of the cannabis variable used in this review.

One point of criticism of Li *et al's* (2012) study is quite minor, but deserves to be mentioned. It is considered that their rejection criteria are arbitrary, and consequently that they have failed to incorporate some relevant research findings. It is difficult to find any plausible justification for rejecting responsibility studies or studies published before 1990.

As noted previously, Rogeberg and Elvik (2016a) considered that there was a serious methodological flaw in the meta-analyses of both Asbridge Hayden & Cartwright (2012) and Li *et al.* (2012) (see below), as well as some simple mistakes in the meta-analyses, the cumulative effects of which were to exaggerate the summary ORs for the strength of the relationship between the use of cannabis and crashing. When Rogeberg and Elvik re-calculated the summary ORs, correcting for the methodological flaw and mistakes, Asbridge, Hayden and Cartwright's original summary OR of 1.92 (1.4-2.7) was reduced to a value of 1.25 (1.0-1.6), and Li *et al*'s summary OR of 2.66 (2.1-3.4) was reduced to 1.55 (1.1-2.2) (see Rogeberg & Elvik's Figure 4). The corrected, reduced values were of roughly the same size as Rogeberg and Elvik's own estimate of 1.36 (1.2-1.6).

The methodological flaw that Rogeberg and Elvik (2016a) noticed in the other two meta-analyses was that they used counts-based (unadjusted) cannabis-crash ORs where MLR-based (adjusted) values were available. For example, both of the meta-analyses used an unadjusted cannabis-crash OR of 7.16 (2.8-18.5) from Blows *et al*. (2005) where an adjusted value of 0.80 (0.2-3.3) was available. That large difference contributed to the over-estimated summary cannabis-crash ORs in both meta-analyses. By basing their ORs on raw counts data, the two meta-analyses were unable to make adjustments for demographic confounders such as age and gender. Although Asbridge Hayden and Cartwright (2012) made some attempt to control for the combined use of alcohol and cannabis by restricting their analyses to alcohol-free drivers (although failing in the case of Blows *et al*.), Li *et al*. (2012) made no such attempt. The use of unadjusted ORs where adjusted values are available (as was the case for a majority of the studies incorporated into the two meta-analyses) is a serious methodological flaw. In the preface to the second edition of his *Introduction to Epidemiology* (2012), Rothman says "I believe that the problem of confounding exemplifies why we need to understand epidemiologic principles lest we fall victim to fallacious inferences". By virtually ignoring the problem of confounding, Asbridge, Hayden & Cartwright and Li *et al*. have allowed themselves to 'fall victim to fallacious inferences'.

It is likely that Asbridge Hayden and Cartwright (2012) and Li *et al.* (2012) chose to base their summary cannabis-crash ORs on raw counts data so that their findings would be transparent, such that the reader could check the calculations from the raw data provided (which, of course, could not be done for MLR-based ORs). However admirable the motives, the results were lamentable. In 2017 (as part of an exchange of Letters to the Editor between Li, DiMaggio & Brady, and Rogeberg & Elvik), Li and his colleagues tried to clarify their stance in saying "We made clear that our estimated summary odds ratio was based on empirical data and was not adjusted for any confounding factors. Albeit imperfect, our approach reflected accurately the state of evidence as supported by the epidemiological literature". That attempt to make a silk

purse of a sow's ear would have to be one of the most bizarre statements in the drug-driving literature. No credible epidemiologist could argue that an unadjusted OR, contaminated by the effects of confounders, "accurately reflected the state of the evidence as supported by the epidemiological literature".

When correcting for the methodological flaw and the mistakes in the other two meta-analyses, Rogeberg and Elvik (2016a) also made adjustments that reduced the value of an OR from a responsibility study to the value it would have had if it had been from a case-control study (all other things being equal), on the dubious grounds that a case-control study is a more basic or 'purer' form of epidemiological investigation. Given that Li *et al*. (2012) did not include any responsibility studies in their meta-analysis, the 'responsibility adjustments' did not affect their summary cannabis-crash OR. However, for Asbridge Hayden and Cartwright (2012), six of the nine included studies were responsibility studies, so their summary cannabis-crash OR was reduced, albeit by a very small margin (see Rogeberg & Elvik's Figure 4). From the perspective of the current review, the responsibility adjustments were overly intrusive and unnecessary.

Why the use of a meta-analysis in this study would be inappropriate

It was argued in the Introduction to this report that a meta-analysis of the results from the eleven included studies would have provided an inappropriately high summary OR for the relationship between the use of cannabis and crashing. That argument is supported here with reference to a single study as integrated into a single meta-analysis: the study was by Gjerde *et al*. (2013), and it was integrated into the meta-analysis by Rogeberg and Elvik (2016a).

Gjerde *et al*. (2013) reported an adjusted OR of 1.90 (0.8-4.6) for the effect of cannabis on crashing in Norway (see Table 5.4). Rogeberg and Elvik (2016a) incorporated the value of 1.90 into their meta-analysis, even though Gjerde *et al*. (p. 143) had acknowledged that their methodology had produced ORs that were "incorrectly high" (for reasons that are described in some detail in Part 4 of this report). While meta-analyses provide different *weights* for the incorporated ORs that reflect the numbers of case and control subjects that the ORs are based on (sometimes using what is known as the 'inverse variance' procedure), they do not normally adjust the *sizes* of the incorporated ORs. So, an overestimated OR from a single study will inevitably contribute an overestimation bias to the summary OR. Rogeberg and Elvik provided a summary OR of 1.36 (1.2-1.6) for the relationship between cannabis and crashing that were derived from slightly different analytic procedures. This OR was inevitably biased upwards by including the cannabis-crash OR of 1.90 from Gjerde *et al*.

In their reference text on *Modern Epidemiology*, Rothman, Greenland and Lash (2008, p. 682) concur with the view expressed here in saying that "Meta-analytic methods do not provide a means for directly evaluating the bias of the individual studies considered in a review".

Translation of meta-analysis findings into government policy and practice

Given that most of the biases identified in this review for the eleven selected studies are overestimation biases, the use of a meta-analysis in this study would simply have produced an overestimated summary cannabis-crash OR. A meta-analysis was therefore not employed. Meta-analyses are formulaic and, if used uncritically, can drain the thoughtfulness out of science.

Meta-analyses can play a major role in translating research results into government policy and practice. So, it is unfortunate when the meta-analyses are misleading. For example, when providing advice to the UK government that cannabis should be a classed as a proscribed drug under the new *per se* drug-driving legislation, Wolff *et al*. (2013, p 67) noted that Asbridge, Hayden and Cartwright (2012) had concluded that the prior use of cannabis approximately doubles the risk of crashing. As it happened, cannabis was then included as a proscribed drug. That is an unfortunate example of a seriously flawed meta-analysis possibly playing a role in determining the shape of government practice.

More broadly, Rogeberg and Elvik (2016b, p. 1497) have noted that the two meta-analyses by Asbridge, Hayden and Cartwright (2012) and Li *et al*. (2012) have been collectively cited more than 300 times according to Google Scholar. Despite their serious inadequacies, the two meta-analyses are presumably having a widespread influence on how other researchers, and probably also policy developers, are evaluating the dangers of driving after having used cannabis.

For example, in 1994 Wayne Hall and his colleagues published a broad review of *The health and psychological effects of cannabis use*, which was conducted under the umbrella of the National Drug Strategy, and had been commissioned by the Australian National Taskforce on Cannabis. In a second edition of the 1994 review, Hall *et al*. (2001, p. 34) observed that "It is unclear whether cannabis use increases the risk of being involved in motor vehicle accidents". Hall revisited his 1994 review twenty years later in an article titled *What has research over the past two decades revealed about the adverse health effects of recreational cannabis use?* in which he concluded that "In the past decade, better-designed epidemiological studies have found that cannabis users who drive while intoxicated approximately double their risk of a car crash" (Hall, 2014, p. 21). His evidence for that conclusion came from two individual epidemiological studies (selected for no obvious reason from the many published by then), two meta-analyses (Asbridge, Hayden & Cartwright, 2012 and Li *et al*., 2012) and one systematic review (Hartman & Huestis, 2013). It is likely that Hall's conversion to the opinion that cannabis doubles the risk of crashing was influenced by the two misleading meta-analyses.

Another example is provided in a wide-ranging review of *The health effects of cannabis and cannabinoids* that was conducted by the U.S. National Academies of Sciences, Engineering and Medicine (2017, pp. 228-230), where it was concluded that "There is substantial evidence of a statistical association between cannabis use and increased risk of motor vehicle crashes". That conclusion was based "six systematic reviews of fair or good quality that summarised the association between driving under the influence of cannabis and motor vehicle crashes". Two of those systematic reviews were by Asbridge, Hayden and Cartwright (2012) and by Li *et al*. (2012). However, one of the reviews was by Rogeberg and Elvik (2016a), which they appropriately described as "the most comprehensive" of the six, and which may have influenced them against reaching a more extreme conclusion about the dangers of cannabis on the roads.

Part 6: The possibility of dose-response or threshold relationships

Hill (1965) proposed ten criteria for inferring that a relationship between two variables is causal rather than accidental. Hill's criteria are still widely cited in epidemiological publications, despite the fact that none of them provides conclusive proof of causality (Rothman, Greenland & Lash, 2008, pp. 25-31). One of the criteria that is very indicative of causality was described by Hill as a "biological gradient", but in the context of this report is better described as a 'dose-response' relationship. A large volume of research, starting with Robert Borkenstein's Grand Rapids case-control study in 1964, has clearly demonstrated that a dose-response relationship exists between drivers' BACs and their risk of crashing. This part of the report investigates the possibility that such a relationship also exists for cannabis. If the relationship were found to exist, it would add weight to the claim that the use of cannabis plays a causal role in crashing.

A threshold effect is similar to a dose-response effect, except that it involves the absence of a drug effect below a threshold concentration. A drug-crash relationship could involve both a threshold effect at a lower dose and a dose-response effect at higher doses. The cut-off levels of THC that are used to define THC-concentration groups are measured in terms of nanograms of THC per milliliter of body fluid (ng/mL, where a nanogram is one thousandth of one millionth of a gram).

A study that found a non-significant simple effect might nevertheless find a significant supra-threshold effect, especially if the sub-threshold results had been obscuring (diluting) a real relationship. Similarly, a study that found a non-significant simple effect might find a significant dose-response effect (such as a linear trend effect).

Seven of the eleven studies examined in Parts 3 and 4 of this report investigated the possibility of a dose-response and/or threshold effect of the use of cannabis on crashing. In three of the four studies where the possibility of an effect was not considered, the main effect of THC on crashing was not statistically significant, so the researchers presumably thought that it would be pointless to carry their investigations further. The evidence for dose-response or threshold effects is roughly summarized in Table 6.1. Only two of the eleven research groups claimed to have demonstrated the existence of a dose-response or threshold effect.

Table 6.1: Evidence for dose-response relationships between THC concentration and crashing

Study	OR (95% CI) for THC and Crashing	N THC Subjects	OR Significant or Not-Significant?	Dose Relationship Examined?	Cut-Off Level of THC	Dose Relationship Claimed?
Terhune, 1982	2.14 (0.8-5.7)	17	N.S.	Y	2 ng/mL	N
Williams, 1985	0.46 (0.2-1.3)	19	N.S.	Y	Continuous	N
Terhune, 1992	0.66 (0.3-1.6)	19	N.S.	N	n/a	N
Longo, 2000	0.82 (0.5-1.5)	44	N.S.	Y	1.1 and 2.1 ng/mL	N
Mura, 2003	1.88 (1.3-2.7)	137	Sig	Y	2.0 ng/mL	N
Drummer, 2004	2.70 (1.0-7.0)	56	N.S.	Y	5.0 ng/mL	Y
Laumon, 2005	1.78 (1.4-2.3)	759	Sig	Y	See Table 6.2	Y
Gjerde, 2013	1.90 (0.8-4.6)	55	N.S.	N	n/a	N
Hels, 2013	1.91 (1.2-3.2)	162	Sig	N	n/a	N
Poulsen, 2014	1.29 (0.7-2.3)	265	N.S.	Y	See Table 6.3	N
Lacey, 2016	1.00 (0.8-1.2)	613	N.S.	N	n/a	N

Terhune (1982) did not find a statistically significant simple effect of THC on crash responsibility. Nevertheless, he divided the 17 drivers into lower (N = 8) and higher (N = 9) THC concentration groups and calculated culpability rates for both. Although the higher concentration group had a higher level of culpability, neither group had a culpability rate that was significantly higher than that for drug-free drivers (Table 16). So, Terhune failed to demonstrate a dose-response or threshold effect.

Williams et al (1985) did not find a statistically significant simple effect of THC on crash responsibility. Nevertheless, they investigated the possibility of a relationship between the concentration of THC and crash responsibility for the 19 THC-positive drivers. They did not find any such relationship.

Terhune *et al*. (1992) did not find a statistically significant simple effect of THC on crash responsibility for their 19 THC-positive drivers. They did not attempt to demonstrate a dose-response or threshold effect.

Longo *et al*. (2000) did not find a statistically significant simple effect of THC on crash responsibility. Nevertheless, they divided the 44 drivers into lower (N = 7), middle (N = 19) and higher (N = 18) THC-concentration groups and calculated a culpability rate for each group. They reported higher culpability rates at the higher concentrations. Nevertheless, they found that "There was no significant difference in the culpability of drivers across the THC concentrations for THC alone, and there was no significant linear relationship" (p. 627 and Table 5). So, Longo *et al*. did not find a statistically significant dose-response or threshold effect.

Mura *et al*. (2003) found a statistically significant simple effect of THC on crash responsibility for the full sample (which included 137 THC-positive subjects). However, they were mostly interested in subjects who were less than 27 years old (which included a few more than 70 THC-positive subjects). They investigated the possibility of a dose-response or threshold effect only for the younger subjects, who were divided into two THC-concentration groups. They found an OR of 2.5 for the lower-concentration group, and a slightly higher OR of 2.7 for the higher-concentration group. They reported that "No significant difference in ORs was observed between the studied groups" (p. 83), and commented that "We were not surprised by this finding because several previous studies have shown that THC concentrations in blood were not directly related to a specific degree of driving impairment" (p. 83). So, Mura *et al*. did not find a dose-response or threshold effect.

Drummer *et al*. (2004) did not find a statistically significant simple effect of THC on culpability (although the OR of 2.7 was close to being significant with a 95% CI of 1.0 to 7.0). Nevertheless, they divided the 56 THC-positive drivers (unevenly) into lower (N = 7) and higher (N = 49) THC-concentration groups. They did not provide an OR for the lower-concentration group. Their OR of 6.6 (1.5-28.0) for the higher-concentration group (p. 244; Table 4) was interpreted as evidence that the relationship between the concentration of THC and culpability comprised a "biological gradient" (p. 254). That was a poor choice of words, as their evidence was relevant only to the possible existence of a *threshold* effect and not to a *dose-response* effect. They speculated that only the higher levels of THC (above 5 ng/ml) were indicative of the recent use of cannabis, and therefore that it was only the higher levels of THC that had an effect on culpability.

The volatility of the measured size of the OR in relation to the number of THC-positive drivers in the sample deserves some attention. According to Drummer *et al*. (p. 245) "The estimated association of culpability with THC in concentrations of at least 5 ng/ml was much greater than the association of all identifiable concentrations of THC (OR 6.6 versus 1.9)". So, by omitting 7 of the 56 THC-positive drivers from the analysis, the OR has more than tripled. This volatility could be taken to indicate that the reported findings might have been different if the cut-off concentration of THC had been other than exactly 5 ng/ml. As an aside, it is not clear where the OR of 1.9 came from, as the value reported in their Table 4 is 2.7 (1.0-7.0). The 1.9 is most probably an error. The fact that the value of 6.6 is an unrealistically high OR for the relationship between the 'recent use' of cannabis and culpability raises further questions about the validity of the purported threshold effect. It is concluded that Drummer *et al*'s evidence for a threshold effect is not strong.

Poulsen, Moar and Pirie (2014) (as described more fully below) designed their responsibility study as a replication of Drummer *et al*'s (2004) study. They used many more THC-positive drivers than Drummer *et al*., but failed to replicate the threshold effect. That fact adds a further doubt about the strength of Drummer *et al*'s evidence for a threshold effect.

From an MLR analysis, **Laumon *et al*. (2005)** reported a statistically significant overall effect of the use of cannabis on responsibility for crashing. In their investigation of a possible dose-response effect, they divided the 759 THC-positive drivers into four THC-concentration groups, and obtained adjusted ORs for each group. The main results from their Table 3 are reproduced here in Table 6.2.

Table 6.2: Adjusted ORs for driver responsibility by THC concentration from Laumon et al. (2005)

THC Concentration (ng/mL)	N THC-positive Drivers	OR (95% CI) for THC and Crash Responsibility
Negative	9013	1.00
< 1.0	78	1.57 (0.84-2.95)
1 to 2	298	1.54 (1.09-2.18)
3 to 4	143	2.13 (1.22-3.73)
= or > 5	240	2.12 (1.32-3.38)
All levels	**759**	**1.78 (1.40-2.25)**

Although the two higher concentration groups have slightly higher levels of culpability than the two lower concentration groups, there is a considerable amount of overlap between the 95% confidence intervals of all four groups. The overlapping of CIs is conventionally interpreted as meaning that the means are not significantly different. Given the high level of overlap that is evident in Table 6.2, it has to be concluded that there is no plausible evidence for a dose-response relationship between THC-concentration and crash responsibility. It is concluded that Laumon et al. have failed to demonstrate a dose-response effect. That conclusion contradicts the claim in their Abstract that "A significant dose effect was identified" (p. 1). That misleading claim was inappropriately based on *unadjusted* ORs.

This is not the first time that Laumon *et al*. (2005) have been criticized for defective reporting. In a BMJ Commentary, titled *Presentation of the results is misleading*, Franjo Grotenhermen (14 December 2005) observed that Laumon *et al*. had inappropriately presented unadjusted 'significant' ORs instead of adjusted non-significant ORs:

> Results have been cited in the popular media stating that cannabis users face a three times greater risk of being responsible for a fatal crash. But the results do not support this conclusion. The presentation of the results in the Abstract is somewhat misleading, which may have caused this misinterpretation. The figures for the unadjusted ORs suggest a more than threefold risk increase for all THC-positive drivers …. However, closer review of the results shows that two other factors contributed to the higher accident risk, i.e., alcohol consumption and the younger age of the THC-positive drivers.

Gjerde *et al*. (2013) did not find a statistically significant simple effect of THC on the risk of crashing for their 55 THC-positive drivers. They did not attempt to demonstrate a dose-response or threshold effect.

Hels *et al*. (2013) found a statistically significant simple effect of THC on the risk of crashing for their 162 THC-positive drivers, which they described as "a slightly elevated risk" (p. 351). They did not attempt to demonstrate a dose-response or threshold effect.

Poulsen, Moar and Pirie (2014) did not find a statistically significant simple effect of THC on the risk of being responsible for a crash for their 265 THC-positive drivers. Nevertheless, because their study was a replication of Drummer *et al*'s 2004 study, where a threshold effect was purportedly found (see above), Poulsen Moar and Pirie attempted to replicate the threshold (or dose-response) effect. To make their analysis directly comparable with that of Drummer *et al*., they considered only those drivers who had used cannabis alone (THC-only). They divided the 96 THC-positive drivers (evenly) into three THC-concentration groups and obtained unadjusted ORs for each group. The main results from their Table 4 are reproduced here in Table 6.3.

Table 6.3: Unadjusted ORs for driver responsibility at different THC concentrations from Poulsen, Moar and Pirie (2014)

THC Concentration (ng/ml)	N THC-positive Drivers	OR (95% CI) for THC and Crash Responsibility
Negative	531	1.00
< 2	32	3.08 (0.9-10.3)
2 to 5	34	0.92 (0.4 -2.1)
> 5	30	1.00 (0.4-2.4)
All levels	**96**	**1.31 (0.8-2.3)**

None of the three unadjusted ORs is statistically significant. And it is worth noting that the ORs for the two higher concentration groups (0.92 and 1.00) are considerably smaller than for the lowest concentration group (3.08). These results clearly fail to demonstrate a threshold or dose-response effect of THC on the odds of being responsible for a crash. Using a greater number of THC-positive drivers than Drummer *et al*. (2004) (96 vs. 56), Poulsen, Moar and Pirie (2014) have failed to replicate Drummer *et al*'s purported threshold effect.

Lacey *et al.* (2016) did not find a statistically significant simple effect of THC on the risk of crashing for their 613 THC-positive drivers. They did not attempt to demonstrate a dose-response or threshold effect.

To summarize: Claims that dose-response or threshold THC effects had been discovered were made in only two of the eleven studies. The claim by Laumon *et al*. (2005) was clearly false; and the claim by Drummer *et al*. (2004) was of questionable merit, and unable to be replicated by Poulsen, Moar and Pirie (2014). It is concluded that there is no compelling evidence from the eleven epidemiological studies for the existence of dose-response or threshold THC effects.

Part 7: Does cannabis exacerbate the effect of alcohol?

Definition of an 'exacerbation effect'

This part of the report investigates the possibility that the recent combined use of alcohol and cannabis exacerbates the effect of alcohol on crashing. The statistical issues involved when considering the joint effects of two predictor variables can be complex. Furthermore, the terminology used to describe such effects can be confusing (Bolt & Day, 1979). For that reason, the terms 'interaction effect' and 'synergistic effect' are not used in this report. Joint effects are often assumed to be either additive or multiplicative (VanderWeele & Knol, 2014). That is *not* the approach adopted here, where the question asked is whether the use of cannabis makes *any* difference to the effect of alcohol on crashing. For example, if the OR for cannabis alone was 2.50 and the OR for alcohol alone was 6.00, then an OR of 7.00 for their joint effect (if significantly greater than the OR of 6.00 for alcohol alone) would count as evidence for an 'exacerbation effect' of cannabis on alcohol, despite the fact that the OR of 7.00 is lower than for an additive effect (7.50: OR1+OR2-1.00), and much lower than for a multiplicative effect (15.00). An exacerbation effect is possible even where there is no demonstrable individual effect of cannabis on crashing.

Two ways of demonstrating an exacerbation effect

There are two alternative statistical procedures for investigating the possibility that the use of cannabis with alcohol exacerbates the effect of alcohol on crashing. They will be illustrated with a worked example that uses the information in Table 7.1. But first, a two features of that information will be made evident.

Table 7.1. Crash responsibility and drug usage for a worked example

Group	Responsible	Not-Responsible	Total
THC-Only	100 (r)	100 (s)	200
Other drug combinations	180	90	270
THC&BAC-Only	120 (a)	10 (b)	130
BAC-Only	800 (p)	200 (q)	1000
THC&AOD-Free	900 (x)	900 (y)	1800
Total Drivers	**2100**	**1300**	**3400**

The first is that the data for THC-only in Table 7.1 are consistent with cannabis alone playing no direct role in crash causation. The OR for THC-only is: (r/x)/ (s/y) = (100/900)/ (100/900) = 1.00 (0.7-1.3).

The second is that the data for Alcohol-only in the table are consistent with alcohol alone playing a strong direct role in crash causation. The OR for BAC-only is: (p/x)/ (q/y) = (800/900)/ (200/900) = 4.00 (3.3-4.8).

Perhaps the most obvious way of investigating a possible exacerbation effect is to compare an OR for the combined use of cannabis and alcohol without any other drugs (THC&BAC-only vs. THC&AOD-free) with an OR for alcohol alone (BAC-only vs. THC&AOD-free). Finding an OR for the combined use that was significantly greater than the OR for alcohol alone (as indicated by non-overlapping 95% confidence intervals) would be good *prima facie* evidence that cannabis had exacerbated the effect of alcohol. That approach involves the calculation and comparison of two ORs.

Step 1 of the two-step procedure <u>THC&BAC-Only vs. THC&AOD-Free:</u>

Step 1 OR = (a/ x)/ (b/y) = (120/900)/ (10/900) = 12.00 (6.3-23.0)

Step 2 of the two-step procedure (as above) BAC-0nly vs. THC&AOD-Free:

Step 2 OR = (p/x)/ (q/y) = (800/900)/ (200/900) = 4.00 (3.3-4.8)

From the two-step procedure, it can be observed that the OR of 12.00 for the use of cannabis and alcohol together without any other drugs is three times as great at the OR of 4.00 for the use of alcohol alone. It can also be observed that the two 95% CIs do not overlap, indicating that the difference is statistically significant. That is good *prima facie* evidence that the use of cannabis has exacerbated the effect of alcohol.

However, the two steps can be reduced to one. The single-step procedure involves the direct comparison of the odds for responsible drivers of having THC&BAC-only vs. BAC-only with comparable odds for the not-responsible drivers. If the single OR is significantly greater than 1.00, it might be concluded that cannabis has exacerbated the effect of alcohol.

Single-Step procedure: THC&BAC-Only vs. BAC-Only:

Single-Step ('Exacerbation') OR = (a/p)/ (b/q) = (120/800)/ (10/200) = 3.00 (1.5-5.8)

From the single-step procedure it can be observed that the odds of the joint use of cannabis and alcohol without any other drugs being related to crash responsibility are three times greater than the odds of alcohol alone being related to crash responsibility. It can also be observed that the 95% CI does not include the value 1.0, which indicates that the difference is statistically significant. Again, that is good *prima facie* evidence that the use of cannabis has exacerbated the effect of alcohol.

It is worth noting that here is a simple mathematical relationship between the single-step and the two-step procedures, such that:

Single-Step ('Exacerbation') OR = (Step 1 OR) / (Step 2 OR)
That is: 3.00 = 12.00/4.00.

The term 'exacerbation OR' will be used from this point in the report to describe the OR that is derived from the single-step procedure.

It would seem that an analysis of the data in Table 7.1 has provided excellent evidence of an exacerbation effect. However, that conclusion would be premature, as discussed below.

The exacerbation effect and the high-BAC artefact

Williams *et al*. (1985, p. 19) noted that drugs are "typically found in combination with high blood alcohol concentrations". The truth of that claim has implications for the type of evidence that is required to demonstrate that cannabis exacerbates the effect of alcohol on crashing.

As discussed above, there are two different ways of using ORs to demonstrate an exacerbation effect. However, the mere demonstration of a statistically significant 'exacerbation effect' by the simple application of one of those approaches might not be sufficient evidence for a *real* exacerbation effect, given the possible confounding role of the 'high-BAC artefact'.

The nature of the high-BAC artefact will be demonstrated with a worked example that starts with the data in Table 7.1 and the ORs that were calculated above. In Table 7.2 the overall results for the role of alcohol are broken down for five BAC groups. The grouped BAC data is consistent with published research on fatally injured drivers (see Attachment C): the highest BAC group has the most drivers (35% for BAC > 0.20); and the ORs increase sharply as the BAC increases, with a very high OR (24.0) for the highest BAC group.

A high-BAC-artefact scenario is presented in which cannabis has no direct effect on crashing (The cannabis-crash OR = 1.0), *nor an indirect effect* through the exacerbation of the alcohol effect (despite the fact that the 'exacerbation OR' of 3.00 (1.5-5.8) is statistically significant).

Table 7.2: Information for four groups of subjects on crash responsibility for a worked example

Group	Total		Responsible	Not-Resp	OR
THC-Only	**200**		**100**	**100**	**1.00 (0.7-1.3)**
THC&BAC-Only	**130**		**120**	**10**	**12.00 (6.3-23.0)**
THC&BAC-Only	As for the scenario discussed below				**11.00 (8.2-14.7)**
BAC-Only	**1000**	**100%**	**800**	**200**	**4.00 (3.3-4.8)**
<0.05	190	19%	95	95	1.00 (0.7-1.3)
0.05-0.10	150	15%	100	50	2.00 (1.4-2.8)
0.10-0.15	150	15%	119	31	3.84 (2.6-5.8)
0.15-0.20	160	16%	150	10	15.00 (7.9-28.6)
>0.20	350	35%	336	14	24.00 (14.0-41.3)
THC&AOD-Free	**1800**		**900**	**900**	**1.00**

Scenario: If cannabis had no direct or indirect effects on crashing, but was used only by the 66% (15% + 16% + 35%) of drivers who were in the three highest BAC groups (with BACs equal to or greater than 0.10), then the OR for the combined use of cannabis and alcohol (THC&BAC-Only) would simply reflect the overall OR for those three BAC levels, which can be calculated to be 11.0 (8.2-14.7). Given that the OR of 11.0 for the combined use is much higher than for the use of alcohol alone (4.0; 3.3-4.8), and given that the two 95% confidence intervals do not overlap, it would be concluded that cannabis had exacerbated the effect of alcohol.

A mean BAC can be calculated for whole BAC-Only sample (N = 1000), using a mid-range BAC to represent the drivers in each of the four lower BAC groups, and a value of 0.275 for the highest BAC group. Mean BACs can similarly be calculated for the THC&BAC-Only group under the scenario. The results are given in Table 7.3.

Table 7.3: Mean BACs for the BAC-Only sample, and under the two scenarios

Group	Composition	BAC Range	N	% Full Sample	Mean BAC
Full Sample	BAC-Only	<0.05 to >0.20	1000	100%	0.159
Scenario	THC&BAC-Only	>0.10	660	66%	0.217

It can be seen from Table 7.3 that, under the scenario, the mean BAC of a THC&BAC-Only sample (0.217) does not have to be much higher than for the Alcohol-Only sample (0.159) to create a situation where the high-BAC artefact can provide a satisfactory explanation for the exacerbation effect. There are obviously many other possible scenarios where the more frequent use of cannabis by the heavier drinkers could lead to the false conclusion that cannabis had exacerbated the effect of alcohol on crashing.

The potential problem posed by the high-BAC artefact is easily remedied. All that is required is that the one-step procedure for demonstrating the exacerbation effect be subjected to an MLR-based analysis where the driver's BAC is included as a covariate.

Another way to address the potential problem would be to provide separate exacerbation analyses broken down by BAC levels (such as the five levels given in Table 7.2). If there was a real exacerbation effect it would be demonstrated by finding statistically significant exacerbation ORs

for all or some of the BAC-level subgroups. If there were no real exacerbation effect, but only the operation of the high-BAC artefact, the exacerbation ORs for each BAC-level subgroup should not be statistically-significantly different from 1.0. In other words, there would be no evidence of an exacerbation effect for any BAC-level subgroup.

Survey evidence supports the likelihood of the high-BAC artefact

The artefactual explanation for the exacerbation effect is founded on a strong relationship between the use of cannabis and *heavy* drinking. In the US, a large-scale population-representative National Alcohol Survey (NAS) has been conducted roughly every five years since 1965. Two studies have used NAS data to investigate the relationship between the use of cannabis and alcohol (Midanik, Tam & Weisner, 2007; Subbaraman & Kerr, 2015). Both studies distinguished between three categories of drinkers: those who used only alcohol; those who used both alcohol and cannabis, but never together; and those who 'sometimes or usually' used alcohol and cannabis 'simultaneously'. Using data from the 2000 NAS (N = 4,630 drinkers), Midanik, Tam and Weisner (Table 2) found that simultaneous users of alcohol and cannabis had five or more drinks a day much more frequently (76 days per year) than users of alcohol only (16 days per year). Using data from the 2005 and 2010 NASs (N = 8,626 drinkers), Subbaraman and Kerr replicated Midanik, Tam and Weisner's results for the frequency of heavy drinking, and went on to investigate the levels of drinking in typical drinking sessions (Table 1). They found that that simultaneous users of alcohol and cannabis had *three times as many* drinks in a typical drinking session as users of alcohol only, when drinking either in bars, or at parties, or at home. That extraordinary difference in drinking levels makes the high-BAC artefact very plausible.

Detailed examination of the evidence for an exacerbation effect in the eleven studies

Each study is now examined to see if there is any sustainable evidence for an exacerbation effect.

Terhune (1982) did not find a statistically significant effect of THC on crash responsibility. From information in his Table 15, an OR of 4.50 (2.6-7.9) can be calculated for alcohol alone. From information in his Table 15 and on page 92, an OR of 1.59 (0.6-3.8) can be calculated for the combination of alcohol and cannabis without any other drugs. The combined effect of the two drugs is considerably less than the individual effect of alcohol. Analyses of Terhune's data have clearly failed to demonstrate that cannabis exacerbates the effect of alcohol.

Williams *et al*. (1985) did not find a statistically significant effect of THC on crash responsibility. From information in their Table 7, an OR of 5.02 (2.2-11.3) can be calculated for alcohol alone. From further information in Table 7, an OR of 8.78 (2.9-26.8) can be calculated for the combination of alcohol and cannabis without any other drugs. Although the combined effect of the two drugs is very slightly greater than the effect of alcohol alone, the 95% CIs are mostly overlapping, so the difference between the ORs is not close to being statistically significant. Analyses of Williams *et al*'s data have failed to demonstrate that cannabis exacerbates the effect of alcohol.

Terhune *et al*. (1992) did not find a statistically significant effect of THC on crash responsibility. From information in their Table 5.14, an OR of 4.83 (3.6-6.5) can be calculated for alcohol alone. From further information in Table 5.14, an OR of 8.35 (2.0-35.0) can be calculated for the combination of alcohol and cannabis without any other drugs. Although the combined effect of the two drugs is considerably greater than the individual effect of alcohol, the difference between the estimates is not statistically significant. Analyses of Terhune *et al*'s data have failed to demonstrate that cannabis exacerbates the effect of alcohol.

Longo *et al*. (2000) did not find a statistically significant effect of THC on crash responsibility. From information in their Table 1, an OR of 8.05 (5.3-12.3) can be calculated for alcohol alone, and an OR of 5.37 (1.2-24.0) for the combination of alcohol and cannabis without any other drugs. Because the combined effect of the two drugs is less than the effect of alcohol alone, Longo *et al*. have clearly not shown that cannabis exacerbates the effect of alcohol.

Mura *et al*. (2003) found a statistically significant effect of THC on crash responsibility for the full sample, and for the sub-sample of subjects who were less than 27 years old. They were mostly interested in the younger subjects. For that sub-sample, in their Table 2, they reported an OR of 3.8 (2.1-6.8) for alcohol alone, and an OR of 4.6 (2.0-10.7) for the combination of alcohol and cannabis without any other drugs. Although the combined effect of the two drugs is very slightly greater than the individual effect of alcohol, the 95% CIs are mostly overlapping, so the difference between the ORs is not close to being statistically significant. Mura *et al*. have failed to demonstrate that cannabis exacerbates the effect of alcohol.

Drummer *et al*. (2004) did not find a statistically significant effect of THC alone on culpability (although their effect was close to significance). In their Table 4, they reported an MLR-based exacerbation OR of 2.9 (1.1-7.7) for THC&BAC-Only vs. BAC-Only, where the BAC cut-off was 0.01. They interpreted this statistically significant result as evidence that "THC does enhance the impairment caused by alcohol" (p. 244). In other words, they claimed to have demonstrated an exacerbation effect.

The information necessary to calculate *counts-based* exacerbation OR was not provided by Drummer *et al*. (2004). They failed to report an OR for alcohol alone (at a BAC cut-off of 0.01) or to provide the raw data from which the OR could be calculated. They also failed to report an OR for the combination of alcohol (at a BAC cut-off of 0.01) and THC without any other drugs, or to provide the raw data from which that OR could be calculated. However, much of the missing information can be found in a 2001 conference paper by Drummer, Chu and Gerostamoulos. That information was based on "about 3,400 fatal crashes" (p. 1). Given that the final results (Drummer *et al*., 2003 & 2004) were based on exactly 3,398 fatal crashes, it can be assumed that the conference paper was based on the complete final dataset.

Table 7.4 provides the raw data from which a counts-based exacerbation OR can be calculated for Drummer *et al*. (2004). The count of 43 comes from Table 4 in Drummer *et al*., while the remaining counts come from Table 1 in Drummer, Chu and Gerostamoulos (2001).

Table 7.4: Data used to calculate a counts-based exacerbation OR for Drummer et al. (2004)

	Responsible	**Not-Resp**	**Total**
Alcohol (> 0.01 g %) & THC - Only	42	1	43
Alcohol (> 0.01 g %) Only	720	39	759

As an aside, it should be noted that Drummer, Chu and Gerostamoulos (2001) and Drummer *et al*. (2004) were inconsistent in how they described their BAC cut-offs. In the text describing their Table 1, Drummer, Chu and Gerostamoulos identified the cut off as 0.01, but in the table itself the cut-off is given as 0.05. Conversely, in the text describing their Table 4, Drummer *et al*. identified the cut off as 0.05, but in the table itself the cut-off is given as 0.01. A close scrutiny of all the relevant published information clearly shows that the cut-off used in both cases was 0.01.

The counts-based exacerbation OR that was calculated from the information in Table 7.4 is 2.28 (0.3-17.0). That statistically non-significant finding contrasts with Drummer *et al*'s (2004) statistically significant MLR-based exacerbation OR of 2.9 (1.1-7.7). It would normally be expected that an MLR-based OR would be smaller than a counts-based OR, because the MLR re-allocates some of the drug-effect variance to the other covariates such as age and gender. The failure of the counts-based OR to replicate the significant outcome of the MLR-based OR questions the validity of Drummer *et al*'s MLR-based analysis.

A 'timeframe problem' that affects some of Drummer *et al*'s (2004) analyses was identified in Part 3 of this report. The same problem exists here. The information for alcohol combined with THC comes from only the last two or so years of the ten-year study period (see Table 3.4), while the information for alcohol alone comes from the full ten-year period. For the first eight or so years, the dichotomous variable that coded for the presence of Alcohol-plus-THC in the MLR was

coding Alcohol-alone for those drivers in whom THC was actually present. As noted previously, the comparison of odds from different timeframes in the calculation of a single OR is a serious analytical error that throws the validity of Drummer *et al*'s findings into doubt.

Although Drummer *et al*. (2004) did not explicitly address the possibility that their exacerbation effect was biased by the high-BAC artefact, they did statistically control for "alcohol level (in five strata)" (p. 243), which should have been an adequate means of countering the potential artefact.

The fact that Poulsen, Moar and Pirie (2014) designed their responsibility study as a replication of Drummer *et al*'s (2004) study, but failed to replicate the exacerbation effect (as discussed below) adds further support to the conclusion that Drummer *et al*'s reported exacerbation effect is an aberration.

From an MLR analysis, **Laumon *et al*. (2005,** Table 3) reported a statistically significant OR (1.78; 1.4-2.3) for effect of cannabis on the risk of crashing. They also found a large and statistically significant OR (8.51; 7.2-10.1) for the effect of alcohol. They then looked for evidence of a 'potentiation' effect (pp. 3 & 5):

> We estimated the adjusted joint effect corresponding to blood concentrations of both THC and alcohol, present at any dose, to be 14.0 (8.0-24.7), which was very close to the value obtained from the product of the adjusted individual effects (1.78 x 8.51 = 15.1). We were not able to highlight any interaction: consumption of both cannabis and alcohol would only multiply the risks related to the consumption of either cannabis or alcohol alone, without specific potentiation of the effects of one by the other.

Laumon et al. (2005) identified a 'potentiation' effect with a supra-multiplicative interaction effect. When they failed to find that effect, they concluded that they had failed to demonstrate a potentiation effect. From the approach taken in this review, their evidentiary bar was set too high (as noted in the introductory comments above), making the demonstration of a potentiation (i.e., exacerbation) effect almost impossible to achieve.

From the perspective of this review, the fact that Laumon *et al*. (2005) obtained an MLR-based OR for the combined use of alcohol and cannabis (14.0; 8.0-24.7) that was higher than for the use of alcohol adjusted for the use of cannabis (8.5; 7.2-10.1) is *prima facie* evidence for an exacerbation effect. However, the fact that there was some overlap between the 95% CIs for the two ORs shows that the possible effect did not achieve statistical significance (in terms of the rule-of-thumb test for significance used in this report). Although there was no explicit consideration of the role of the high-BAC artefact, it was probably inadvertently dealt with through the multivariate analysis.

There is a further consideration. Laumon *et al's* (2005) study design was a complex variant of a responsibility analysis, where many non-responsible controls were rejected in such a way as to reduce the representation of THC amongst the controls, as described on page 2 of their paper. The evidential value of their study with respect to the absolute values of any ORs for THC-positive drivers is seriously compromised by those manipulations. It is concluded that Laumon *et al*. have failed to demonstrate an exacerbation effect (a conclusion they would agree with, but arguably for the wrong reasons).

Gjerde *et al*. (2013) did not find a statistically significant effect of THC on the risk of crashing. In their Table 5, they reported a very high MLR-based OR of 124.6 (69.1-224.9) for alcohol alone. As noted previously, that value indicates that their study could not provide credible *absolute* drug-crash OR values. They did not attempt to demonstrate that cannabis exacerbates the effect of alcohol on the risk of crashing. However, from information provided in their paper, and given here in Table 7.6, a counts-based exacerbation OR of 0.83 (0.2-4.3) can be calculated for the exacerbation effect. Clearly, that finding is not consistent with an exacerbation effect.

Hels *et al*. (2013) found a statistically significant effect of THC on the risk of crashing, which they described as "a slightly elevated risk" (p. 351). In their Table 8, they reported a high MLR-based OR of 9.79 (8.2-11.7) for alcohol alone. They did not investigate the possibility of an exacerbation effect for cannabis. And, as indicated in Table 7.6, they did not provide the information from which an exacerbation OR could be calculated.

Poulsen, Moar and Pirie (2014, Table 4) did not find a statistically significant MLR-based OR for the effect of THC alone on the risk of being responsible for a crash. They did find a high OR of 13.7 (4.3-43.8) for alcohol alone, and a lower OR of 6.9 (3.0-16.0) for the combination of cannabis and alcohol without any other drugs. It is interesting to note that the OR for the combination of cannabis and alcohol was lower than for alcohol alone. Cannabis was therefore not exacerbating the effect of alcohol.

As noted above, Poulsen, Moar and Pirie (2014) designed their study as a replication of Drummer *et al*'s (2004) study. Using a greater number of THC&BAC-only drivers than Drummer *et al*. (142 vs. 43), they failed to replicate Drummer *et al*'s possible exacerbation effect.

Lacey *et al*. (2016) reported the absence of any effect of THC on the risk of crashing. Using information from their Appendix Q Table 7, a counts-based OR of 5.10 (3.4-7.7) can be calculated for BAC-only vs. THC&AOD-free, for BACs greater than 0.05. Using further information from the same table, a counts-based OR of 4.75 (2.0-11.6) can be calculated for THC&BAC-only vs. THC&AOD-free, for BACs greater than 0.05. There is no evidence of an exacerbation effect here.

Summary of the evidence for an exacerbation effect

Table 7.5 shows the numbers of drivers involved in calculations of the strength of the exacerbation effect for most of the eleven studies, along with the threshold BACs used to indicate the presence of alcohol.

Table 7.5: Numbers of drivers involved in investigations of an exacerbation effect

Study	Case-Control or Responsibility	Cut-Off BAC	N Alcohol Only Case / Responsible	N Alcohol Only Control / Not Resp.	Alcohol Only Total	N Alcohol with TCH Case / Responsible	N Alcohol with THC Control / Not Resp.	Alcohol with THC Total
Terhune, 1982	R	0.01	52	22	74	10	12	22
Williams, 1985	R	Zero	120	10	130	84	4	88
Terhune, 1992	R	Zero	678	67	745	35	2	37
Longo, 2000	R	Zero	225	25	250	12	2	14
Mura, 2003	CC	0.05	55	16	71	30	7	37
Drummer, 2004	R	0.01	720	39	759	42	1	43
Laumon, 2005	R	-			-			-
Gjerde, 2013	CC	0.02	97	23	120	7	2	9
Hels, 2013	CC	0.01	345	557	902	-	-	-
Poulsen, 2014	R	0.005	129	3	132	130	6	136
Lacey, 2016	CC	0.05	81	33	124	16	7	23

All eleven studies provided ORs for the relationship between the recent use of alcohol alone, expressed as a dichotomous variable, and crashing. A comparison of the ORs for alcohol alone

from Table 7.6 and for cannabis from Table 5.1 shows that alcohol has a much stronger effect on crashing than cannabis, which may have no effect at all.

Evidence for an exacerbation effect from each of the eleven studies is now considered in relation to the information in Table 7.6.

Table 7.6: Summary of evidence that is relevant to the possibility that cannabis exacerbates the effect of alcohol on crashing

Study	OR for Alcohol Only (Step 1 OR)	OR for Alcohol and Cannabis (Step 2 OR)	Single-Step (Exacerbation) OR	Evidence of an Exacerbation Effect?	Is the High-BAC Artefact Addressed?
Terhune, 1982	4.50 (2.6-7.9)	1.59 (0.6-3.8)		No	n/a
Williams, 1985	5.02 (2.2-11.3)	8.78 (2.9-26.8)		No	n/a
Terhune, 1992	4.83 (3.6-6.5)	8.35 (2.0-35.0)		No	n/a
Longo, 2000	8.05 (5.3-12.3)	5.37 (1.2-24.0)		No	n/a
Mura, 2003	3.8 (2.1-6.8)	4.6 (2.0-10.7)		No	n/a
Drummer, 2004	6.0 (4.0-9.1)*	Not provided	2.9 (1.1-7.7)	Yes	Yes
Laumon, 2005	8.51 (7.2-10.1)	14.0 (8.0-24.7)		Marginal	Probably
Gjerde, 2013	125 (69-225)	Not provided	0.83 (0.2-4.3)	No	n/a
Hels, 2013	9.79 (8.2-11.7)	Not provided	-	-	-
Poulsen, 2014	13.69 (4.3-43.8)	6.90 (3.0-16.0)		No	n/a
Lacey, 2016	5.10 (3.4-7.7)	4.75 (2.0-11.6)		No	n/a

* Probably for All alcohol rather than Alcohol alone; and probably for a BAC cut-off of 0.01

Hels *et al*. (2013) did not investigate the possibility of an exacerbation effect. And, as indicated in Table 7.6, they did not provide the information from which an exacerbation OR could be calculated.

In four of the studies (Terhune, 1982; Longo *et al*., 2000; Poulsen, Moar and Pirie, 2014; Lacey *et al*., 2016), there was obviously no evidence for an exacerbation effect because the OR for the combined use of alcohol and cannabis was less than the OR for the use of alcohol alone.

Gjerde *et al*. (2013) did not investigate the possibility of an exacerbation effect for cannabis. However, they did they provide information from which a counts-based exacerbation OR could be calculated (see Table 7.6). The OR of 0.83 (0.2-4.3) is less than 1.00, and therefore incompatible with an exacerbation effect.

Each of the five remaining studies (Williams *et al*., 1985; Terhune *et al*., 1992; Mura *et al*., 2003; Drummer *et al*., 2004; Laumon *et al*., 2005) reported results whose *direction* was consistent with an exacerbation effect. The rough rule-of-thumb being used here for a single OR to be statistically significant is that its 95% confidence interval should not include the value 1.00. The rule for the difference between two OR values is that their 95% confidence intervals should not overlap.

In three of the remaining five studies (Williams *et al*., 1985; Terhune *et al*., 1992; Mura *et al*., 2003) the 95% confidence intervals for the comparison of the two OR values overlapped to such an extent that the findings were obviously not close to being statistically significant. (The findings for Mura *et al*. (2003) were for the subset of subjects aged 26 or less, as they did not provide detailed results for the full sample.) Neither Terhune *et al*. nor Mura *et al*. addressed the high-BAC artefact, so it is possible that their non-significant results were marginally affected by it. However, Williams *et al*., *were* concerned about the high-BAC artefact, and addressed it through sub-group analyses presented in their Table 7. An analysis of that data shows that there

was no tendency for THC to be associated with the higher BACs, so there was no possibility that the high-BAC artefact could play a role.

The two studies that remain to be summarized are Laumon *et al*. (2005) and Drummer *et al*. (2004).

Although Laumon *et al*'s (2005) evidence hinted at the possibility of an exacerbation effect, their research methodology was so seriously compromised by various selection biases that their weak evidence for an exacerbation effect was not credible.

Drummer *et al*. (2004) were the only research team that claimed to have found an exacerbation effect. That claim is of questionable merit because Drummer *et al*'s MLR-based finding could not be reproduced here using a counts-based analysis, nor could it be replicated by Poulsen, Moar and Pirie (2014). Furthermore, there was a serious error in Drummer *et al*'s research design, which involved different selection timeframes for the drivers with alcohol-alone and alcohol-with-THC. While the implications of that problem for the size of the exacerbation OR are unknown, the findings should be considered to be of questionable evidential value.

Two of the most rigorous epidemiological studies of the effects of cannabis on crashing were conducted by Poulsen *et al*. (2014) and Lacey *et al*. (2016). In those studies, the OR for the combined use of alcohol cannabis was less than the OR for the use of alcohol alone, which is obviously inconsistent with an exacerbation effect.

It is concluded that there is no compelling overall evidence from the eleven studies for the existence of an exacerbation effect.

Where does the belief in an exacerbation effect come from?

It is often claimed that driving with a combination of cannabis and alcohol is worse than driving with alcohol alone. Given that this study has found no convincing epidemiological evidence for an exacerbation effect, it would be interesting to identify the epidemiological evidence-base for the claim. Of the five systematic reviews that were used in Part 2 of this report to identify epidemiological studies for inclusion in this study (Asbridge, Hayden & Cartwright, 2012; Li *et al*., 2012; Elvik, 2013; Hartman & Huestis, 2013; Rogeberg & Elvik, 2016a), only three investigated the effects on crashing of the co-use of cannabis and alcohol: Asbridge, Hayden and Cartwright, 2012; Li *et al*., 2012; and Hartman and Huestis, 2013. Those reviews are discussed below.

Asbridge, Hayden and Cartwright (2012, p. 3) noted that "In all studies assessing cannabis use in conjunction with alcohol, the estimated odds ratio for cannabis and alcohol combined was higher than for cannabis use alone, suggesting the presence of a synergistic effect". The four cited studies were: Drummer, 1995a; Longo *et al*., 2000; Mura *et al*., 2003 and Laumon *et al*., 2005. However, Drummer (1995a) was erroneously cited instead of Drummer *et al*. (2004). (The earlier Drummer study had actually reported that the risk of crashing after the combined use of cannabis and alcohol was *lower* than the risk for alcohol alone.) The four cited studies were all investigated earlier in this Part of the report, where it was concluded that they failed to provide any convincing evidence of an exacerbation effect.

Li *et al*. (2012, p. 70) said that "One of the studies included in the meta-analysis evaluated the effect of marijuana in combination with alcohol on crash risk and found that the combination confers an exceptionally heightened risk to driving safety". The study referred to was the Quebec Drug Study (Brault *et al*., 2004), which was discussed earlier in this report in relation to Table 2.2, where it was noted that it comprised a responsibility study nested within a case-control study. It was also noted that the findings of the case-control study were vulnerable to serious selection biases, such that the findings of the responsibility study were more likely to paint an accurate picture of the effects of drugs on crashing. The questionable case-control study produced a non-significant exacerbation effect for BACs above the legal limit in the US (BAC = 0.08), while the more robust responsibility study produced an effect in the opposite direction - a non-significant ameliorating effect (see their Table 3). These findings obviously provide no

justification for Li *et al's* hyperbolic claim that "marijuana in combination with alcohol … confers an exceptionally heightened risk to driving safety".

Under the heading *Combined Alcohol and Cannabis Intake*, Hartman and Huestis (2013, pp. 487-488) referred to only one epidemiological study, Drummer *et al*. (2004), that is directly relevant to the possible existence of an exacerbation effect. They noted that Drummer *et al*. had found that "THC-positive drivers with BAC values greater than or equal to 0.05 had a culpability OR of 2.9 relative to those with a BAC of greater than or equal to 0.05 alone, implying that THC enhanced alcohol's impairing effects". That finding was discussed earlier in this part of the report, where it was considered to be of questionable validity. Furthermore, the findings were not able to be replicated by Poulsen, Moar and Pirie (2014).

It is clear that the three systematic reviews were unable to discover any convincing evidence of an exacerbation effect. Given that failure, it would be interesting to know why the existence of an exacerbation effect is so often taken for granted in pronouncements by road safety agencies. The part of that story that relates to the introduction of 'cocktail offences' in Victoria is considered in detail in the next section. However, it is also worth briefly considering how the strength of the evidence for an exacerbation effect has been evaluated in road safety authorities in a country other than Australia.

In the UK, the Department for Transport commissioned an Expert Panel on Drug Driving to provide advice as to how the drug-driving legislation might be improved. The Panel's report (Wolff *et al*., 2013) included a section (pp. 69-71) on *Cannabis and alcohol in relation to driving*, where arguments were provided for the existence of an exacerbation effect. Some of the arguments were based on the findings of laboratory studies, and are not covered here, beyond emphasising that such findings are of secondary relevance, and that they tend to be over-interpreted, as discussed in Part 9 of this report. The Panel's report summarised the epidemiological evidence in the following terms: "In all studies assessing cannabis use in conjunction with alcohol, the risk estimate as an odds ratio for cannabis and alcohol combined was higher than for cannabis use alone, suggesting the presence of a synergistic effect". The four cited studies were: Drummer, 1995a; Longo *et al*., 2000; Mura *et al*., 2003 and Laumon *et al*., 2005. This unattributed summary was clearly extracted directly from Asbridge *et al*. 2012 (see above), even to the extent of including the erroneous citation of Drummer (1995a). Based on their acceptance of an exacerbation effect, the Panel advised that there should be a lower *per se* THC limit for THC combined with alcohol than for THC alone. The concern here is not so much that some material was lazily plagiarised by the authors of the Panel report. It is rather that flawed research results can uncritically be incorporated into systematic reviews, the findings of which can in turn uncritically be incorporated into policy advice to government.

Claims by Australian authorities about the combined effects of cannabis and alcohol

It has been claimed by various Australian government agencies that cannabis exacerbates the deleterious effects of alcohol. For example, in a pamphlet on drugs and driving that is available on the South Australian Government's road safety website 'Towards Zero Together' it is claimed that "The use of cannabis and alcohol together severely impairs driving ability and the effects are considerably greater than the effects of either substance taken alone" (accessed in July 2016).

Until recently, similar advice was provided on the VicRoads road safety website: "When users combine cannabis with alcohol, the hazards of driving can be much more severe than with either drug alone. … A small dose of cannabis can make the effects of a low BAC much worse" (see Attachment D). However, when provided with a draft of this report, VicRoads responded by improving the wording to say that: "When drivers combine cannabis with alcohol, the risk of crashing can be more severe than with either drug alone".

Government agencies can be paternalistic in not bothering to refer to an evidence base in their provision of information to the public, so it is not clear why the 'exacerbation hypothesis' has gained so much traction in Australia with respect to cannabis. One possible source is the paper by Drummer *et al*. (2004) which reported that the combined effect of THC with alcohol was 2.9

times worse than the effect of alcohol alone. That result was barely significant at the p = 0.05 level, but Drummer *et al*. (p. 244) concluded that "These data strongly suggest that THC does enhance the impairment caused by alcohol". As noted above, Drummer *et al*'s finding was the exception to the rule, was based on a flawed analysis, and was unable to be replicated by Poulsen, Moar and Pirie (2014).

Four studies not considered here are discussed in Attachment E

A case-control study by Chihuri, Li and Chen (2017) and a responsibility study by Dubois *et al*. (2015) were excluded from close scrutiny earlier in this review because they did not use the presence of THC in a body fluid to identify the prior use of cannabis. They are the only two published epidemiological studies that have a clearly stated focus (as expressed in their titles) on the exacerbation effect, and are therefore difficult to ignore in this part of the review, especially as they will probably be widely cited. The two studies are discussed in Attachment E.

A responsibility study by Romano, Voas and Camp (2017) was also excluded from close scrutiny earlier in the review for the same reason. It is also discussed in Attachment E.

Cannabis is not the only drug that could potentially exacerbate the effects of alcohol. So, the question arises as to whether an exacerbation effect exists for all illegal drugs combined. That question, which has been answered in the affirmative by Li, Brady and Chen (2013), is also discussed here in Attachment E, in the context of the Victorian 'cocktail offence'.

Laboratory evidence for the effects of cannabis on driving-related skills

In this and previous parts of the report there has been no reference to any of the literature on laboratory, simulator or on-road studies of the effects of illegal drugs and alcohol on driving-related skills. A distinction needs to be drawn here between evidence that is directly versus indirectly relevant to the relationship between the recent use impairing substances and crashing. Only the epidemiological evidence provided to this point in the report is directly relevant. In Part 9 of this report it is argued that the evidence for the impairing effects of cannabis is far weaker than is commonly understood, and poses no challenge to the interpretation of the epidemiological evidence that the prior use of cannabis is of little or no relevance to road safety. In Part 10 it is argued that the evidence for the exacerbating effects of cannabis on alcohol's effects on driving-related skills is also far weaker than is commonly understood, and again poses no challenge to the interpretation of the epidemiological evidence that the prior use of cannabis does not exacerbate the effect of alcohol on the risk of crashing.

Part 8: Odds ratios for various crash causes

OR for a range of BACs

Table 8.1 gives MLR-based odds ratios for two studies that have been considered previously in this report. Drummer *et al*'s (2004) responsibility study involved 3,398 fatally injured drivers in Australia. Lacey et *al's* (2016) case-control study, conducted in the U.S., involved 3,095 crashed cases, most of whom were uninjured, and 6,190 matched control drivers. So, the studies involved different levels of crash severity. The studies also had very different levels of alcohol involvement: 32.8% of Drummer *et al*'s total sample had measurable amounts of alcohol (see Drummer *et al*., 2003, Table 1), compared with only 3.7% for Lacey *et al's* total sample of cases and controls (see their Table 19).

Table 8.1: ORs for BAC levels from Drummer et al. (2004) and Lacey et al. (2016)

BAC Level	Drummer OR	Lacey OR
≤ 0.05	1.2	1.2
0.50 – 0.10	1.7	3.9
0.10 – 0.15	3.4	9.1
0.15 – 0.20	9.1	18.2
≥ 0.20	24.1	23.3

The ORs for the BAC levels from Drummer *et al*. (2004) are estimated from their Figure 1 (as discussed here in Attachment C). The ORs for Lacey *et al*. (2016) are taken from their Table 27 (using mid-range values). It is clear from Table 8.1 that there is a non-linear dose-response relationship between BAC and OR for both studies, such that the highest BACs are associated with very large ORs. Although there is some divergence of OR values between the two studies for mid-range BACs, they agree remarkably well for the lowest BACs (OR = 1.2 for BACs ≤ 0.50) and for the highest BACs (OR ≅ 24 for BACs ≥ 0.20).

Given that a BAC of 0.05 is the legal limit for most drivers in Australia and some other countries, it seems relevant to try to identify the corresponding alcohol-crash OR as accurately as possible. Only seven studies have been identified where a defendable estimate of the OR corresponding to a BAC of 0.05 can be obtained. Results in Table 8.2 are from three responsibility studies (R), and four case-control studies (C) all of which involved the strict matching of controls to cases.

Table 8.2: ORs corresponding to BAC = 0.05 from six studies

Study	Type	OR for BAC = 0.05
Borkenstein *et al*. (1964)	C	1.40
McLean, Holubowycz & Sandow (1980 , Table 3.4)	C	1.83
Perneger & Smith (1991, Table 3)	R	3.75
Preusser (2002, Table 2)	R	1.90
Drummer *et al*. (2004)	R	1.45
Blomberg *et al*. (2009)	C	1.38
Lacey *et al*. (2016, Table 27)	C	2.05

The results for Borkenstein *et al*'s (1964) 'Grand Rapids' study are as re-analysed by Hurst, Harte and Frith (1994, Figure 3). The result for Perneger and Smith (1991) represents the mid-point between their two lowest BAC categories, as given in their Table 3. The result for Preusser (2002) involves interpolating between the values given in their Table 2. The result for Drummer *et al*. (2004) represents the mid-point between the two lowest BAC categories, as given in Table 8.1 (above). Averaging across the seven studies gives an OR of 1.97 for a BAC of 0.05.

The cannabis-crash ORs from Table 5.4 for the eleven studies that are the focus of this report are compared with alcohol-crash ORs from the same eleven studies in Table 8.3. Where possible, ORs are provided for both a lower-range and a higher-range BAC.

Table 8.3: Comparison of ORs for cannabis and alcohol

Study	Responsibility or Case-Control Study	Cannabis-crash OR (95% CI)	Lower BACs and corresponding ORs (95% CI)		Higher BACs and corresponding ORs (95% CI)	
Terhune, 1982	R	2.14 (0.8-5.7)	< 0.10	2.22 (0.7-6.80)	≥ 0.10	5.36 (2.9-10.0)
Williams, 1985	R	0.46 (0.2-1.3)	< 0.10	2.30 (0.7-7.4)	≥ 0.10	6.83 (2.6-17.8)
Terhune, 1992	R	0.66 (0.3-1.6)	< 0.10	1.20 (n/a)	≥ 0.10	6.50 (n/a)
Longo, 2000	R	0.82 (0.5-1.5)	<0.08	2.87 (1.6-5.3)	≥ 0.08	14.64 (7.9-27.1)
Mura, 2003	C	1.88 (1.3-2.7)	All positive BACs: 4.64 (2.8-7.6)			
Drummer, 2004	R	2.70 (1.0-7.0)	All BACs ≥ 0.01: 6.00 (4.0-9.1)			
Laumon, 2005	R	1.78 (1.4-2.3)	<0.05	2.70 (2.1-3.5)	0.12-0.20	13.2 (9.1-19.1)
Gjerde, 2013	C	1.90 (0.8-4.6)	All BACs ≥ 0.02: 124.6 (69.1-224.9)			
Hels, 2013	C	1.91 (1.2-3.2)	<0.05	1.30 (0.9-1.9)	0.08-0.12	16.5 (9.6-28.2)
Poulsen, 2014	R	1.29 (0.7-2.3)	0.03-0.08	4.66 (0.6-35.6)	0.08-0.20	10.25 (2.5-42.5)
Lacey, 2016	C	1.00 (0.8-1.2)	= 0.05	2.03 (n/a)	= 0.15	13.55 (n/a)

In seven of the eight studies for which lower-range BAC results are available, the cannabis-crash OR is smaller than the low-range alcohol-crash OR. In the eighth study (Hels *et al*., 2013), the cannabis-crash OR is greater than the low-range alcohol-crash OR, but not significantly so. Given that most alcohol-affected crashes occur at higher BACs, it can be seen that the use of alcohol is associated with much higher crash risks than is the use of cannabis (which may have no effect at all on the risk of crashing). The unrealistically high alcohol-crash OR from Gjerde *et al's* (2013) study was discussed in Part 4 of this report.

ORs for the use of a mobile phone

Redelmeier and Tibshirani (1997) found that the risk of a crash when using a mobile phone was about four times higher than when the phone was not being used (OR = 4.3; 3.0-6.5). They reported a similar risk for hand-held and hands-free devices. McEvoy *et al*. (2005) also found that a driver's use of a mobile phone was associated with a four-fold increased likelihood of crashing (OR = 4.1; 2.2-7.7). Again, the risk was much the same for hand-held and hands-free devices. In their 2015 *Global Status Report on Road Safety*, the World Health Organisation concluded that there was a "four-fold increase in crash risk when talking on a mobile phone while driving" (p. 43). It therefore seems likely that the OR for crashing while using a mobile phone is about 4.0.

ORs for a range of vehicle speeds

From in-depth on-site crash investigations in metropolitan Adelaide, South Australia, Kloeden, McLean and Glonek (2002) estimated pre-crash speeds for 151 case vehicles involved in casualty crashes in 60 km/h speed zones. They obtained free speeds for 604 control vehicles that were matched with the case vehicles with respect to the crash location and time of day. The data were analyzed to produce ORs for levels of case-vehicle speeds in excess of mean site speeds (their Table 2.3). Their results are given here in Table 8.4.

The results for speeding in excess of mean site speeds are similar in some ways to the results for BAC levels. There is a non-linear dose-response relationship, such that the highest levels of speeding are associated with very high ORs.

Table 8.4: ORs for speed levels from Kloeden, McLean & Glonek (2002)

Case vehicle speed in excess of mean site speed	OR
+ 5 km/h	1.89
+ 10 km/h	4.12
+ 15 km/h	10.3
+ 20km/h	29.8

A result that is now well established, but which seemed surprising when it was first reported, is that driving at only 5 km/h above the mean site speed in a 60 km/h zone approximately doubles the odds of being involved in a casualty crash. By comparison with the findings in Table 8.2, it can be seen that driving at 5 km/h over the mean site speed is roughly equivalent to driving with a BAC of 0.05.

ORs for unprotected modes of transport

Table 8.5 provides some ORs from a selection of large-scale studies of the risks involved in cycling and motorcycling. The information on cyclists is from the U.K. Department for Transport (2014, Table RAS53001, p. 242). The information on motorcyclists is from Johnston, Brooks and Savage (2008). The values in Table 8.5 are Relative Risks (RRs) rather than ORs. The distinction is not important in this context, especially given that when RRs and ORs are calculated from the same set of data, the ORs will be greater than the RRs.

It can be seen that the casualty and fatality risks associated with the use of 'unprotected' modes of transport (i.e., bicycles and motorcycles) are very high. By comparison with the findings in Table 8.1, it can be seen that the risk of riding a bicycle is roughly equivalent to the risk of driving a car with a BAC in excess of 0.15, and that the risk of riding a motorcycle is roughly equivalent to the risk of driving a car with a BAC in excess of 0.20.

Table 8.5: Crash-risk RRs for some modes of transport, and ORs for road-user behaviors

Road User Group	Comparison Group	Rate	Region & Timeframe	RR
Cyclist fatalities	Car occupant fatalities **	Per cyclist / car occupant kilometer	UK 2003-2012	13
Cyclist casualties *	Car occupant casualties	Per cyclist / car occupant kilometer	UK 2003-2012	29
Motorcycle rider fatalities	Car driver fatalities	Per vehicle kilometer	Australia 2007	30
Motorcyclist serious injuries	Car occupant serious injuries	Per vehicle kilometer	Australia 2003-04	41

* 'Casualty' is killed or seriously injured. ** 'Car occupant' is a driver or passenger.

Contextualizing the OR for cannabis

It was concluded earlier in this report that there is no good evidence that the true value for the OR for cannabis and crashing is greater than 1.00. It was further concluded that, if the value were greater than 1.00, then it would be unlikely to be higher than 1.30.

Comparing an OR of 1.30 for cannabis with the ORs in Tables 8.1 to 8.5 shows that driving after the use of cannabis does not increases the risk of crashing as much as driving with a BAC of 0.05, or driving at 5 km/h above the mean site speed in a built-up area. Driving after the use of cannabis is also considerably safer than using a mobile phone while driving. And driving after the use of cannabis is far safer than riding a bicycle or motorcycle.

Tolerable risks

Despite frequent comments by politicians and others to the effect that a proposed countermeasure should be implemented "if it prevents a single injury", the reality is that crash risks are tolerated to different extents depending on the perceived benefits of the *status quo* and the pressures exerted by lobby groups. For example, despite the extraordinarily high risks of motorcycling (RR = about 30, see Table 8.5), there is rarely any serious attempt by Australian road safety authorities to reduce motorcycling exposure through advertising campaigns or other means, presumably because of the fear of offending the motorcycling fraternity.

The Australian Transport Council (ATC) was the body that brought together the Commonwealth, State, Territory and New Zealand Ministers who were responsible for road safety amongst other matters. The ATC has endorsed a commonly accepted rule-of-thumb in relation to crash risks:

> Speeds of just 5 km/h above average in urban areas, and 10 km/h above average in rural areas, are sufficient to double the risk of a casualty crash. This is roughly equivalent to the increase in risk associated with a BAC of 0.05 (ATC, 2008, p. 30).

In the case of drink-driving, it is legal in Australia for most drivers to drive with a BAC of up to 0.05. The ATC (2011, p. 88) explicitly acknowledges the compromise involved in setting the limit, which "strikes the right balance between societal values and public safety in relation to alcohol use". Given the rule-of-thumb above, it is evident that the ATC was prepared to tolerate drink-driving at BACs where the risk of crashing was nearly doubled.

Although the police in Australia are reluctant to discuss speed enforcement tolerances, it is likely that they are generally set in line with UK policing practice, where speeding below 10% over the speed limit is unlikely to be enforced (Association of Chief Police Officers, 2013). If so, the police would be tolerating levels of speeding where crash risks are commonly understood to be doubled.

Societal attitudes to the medicinal and recreational use of cannabis are changing, such that it could now be argued that a 30% increase in the risk of crashing after the use of cannabis (which is probably an over-estimate) 'strikes the right balance', especially when taking into account the high costs of enforcing cannabis-driving, and the injustices involved for many of the apprehended cannabis drivers who are unaffected by the drug at the time of their apprehension (as discussed in Part 12 of this report). At a minimum, the current zero-tolerance policy should be abandoned (as also discussed in Part 12).

General and specific causation

It may be of peripheral interest to note that there is a questionable rule-of-thumb in forensic science that has been applied in the translation of epidemiological evidence about a causal effect ('general causation' - such as a drug-crash OR of 4.50 for drug X) into evidence about the likelihood of causality in a particular situation ('specific causation' – such as driver Y's use of drug X was the cause of cyclist Z's death). The rule is that epidemiological evidence of a more-than-doubled risk of causation is a sufficient test for specific causation (Haack, 2014, Chapter 11). Despite its dubious validity (e.g., Greenland, 1999), the rule has often been applied in the American judicial system. It seems clear from the information provided in this report that cannabis has an OR of considerably less than 2.00 in relation to its possible role in crash causation. It follows that the rule-of-thumb could not be used to establish that a driver's use of cannabis had played a causal role in a crash.

Part 9: The limited relevance of studies of driving-related skills

Effects of cannabis on driving-related skills: DRUID results

A large-scale program of research on *Driving under the Influence of Drugs, Alcohol and Medicines* (DRUID) was undertaken in the E.U. to "provide scientific support to E.U. road-safety policy makers by making scientific-based recommendations concerning combatting driving under the influence of psychoactive substances" (Schulze *et al*., 2012a, p.5).

The DRUID program produced about 50 'deliverables' (i.e., reports), one of which described the results of a large-scale meta-analysis of the effects of psychoactive drugs on driving-related skills (Berghaus *et al*., 2011; as summarized in Hargutt, Kruger and Knoche, 2011, pp. 49-58). With an emphasis on the possible impairing effects of *medicinal drugs*, the meta-analysis focused on depressants (excluding barbiturates), antidepressants and antipsychotics. The only illegal drugs covered were cocaine and amphetamine (both stimulants) and cannabis. The report is a massive document: 772 pages long with 160 pages of references. It covered the results of 605 published studies, from which 13,191 'effects' were extracted. The types of skilled performance being measured were: attention, encoding & decoding, reaction-time, psychomotor tasks, tracking, visual functions and 'driving behavior'.

As is evident from the figures above, a single published study could report many 'effects', where an 'effect' is defined as the result, for a group of subjects, of a particular drug, at a particular concentration, at a particular time after administration, on a test of skilled performance. In the DRUID meta-analysis, drug effects were able to be analyzed by the concentration of the drug and by time-after-administration, but they were not able to be analyzed by the type of performance being measured, as all types of performance were considered to be equivalent. An effect was described in terms of its outcome, which could be: a statistically significant *improvement* in performance; a statistically significant *impairment* of performance; or *no difference* in performance. It was anticipated that most drug effects would be impairments.

It is interesting to note how the results of the DRUID meta-analysis were reported. For any robust phenomenon, results would be reported in terms of the strength of the effect. In contrast, because many of the drug effects were weak or non-existent, the DRUID meta-analysis reported only on whether or not an effect could be *detected* at a statistically significant level. The measures of the impact of a drug on performance were therefore the percentages of its effects that were impairments, improvements or made no difference.

The parts of the DRUID meta-analysis that focused on the effects of cannabis on driving-related skills (Berghaus *et al*., 2011, pp. 168-176 & 391-394 & 406) were based on 99 studies with a total of 916 effects. As very few of the effects were improvements, they will be ignored in the interest of simplicity (which should not be a problem as the apparent improvements were probably false positives). Two types of cannabis administration were studied: oral ingestion and the smoking of marijuana. The majority of studies involved smoking. In the interest of simplicity, the studies involving oral ingestion will be ignored. Results were given for three concentrations of THC: low, medium and high. As results for the low and medium concentrations were very similar, they have been combined in Table 9.1.

The results in Table 9.1 are for 885 effects from 78 studies. Overall, 46.9% of the effects (415 out of 885) were impairments. Another way of viewing that finding is that 53.1% of the effects failed to provide any evidence of a deleterious influence of cannabis on performance. Even in the first two hours after smoking marijuana, only 51.0% of the tests detected any impairment.

High concentrations of THC are associated with only a slightly higher proportion of impairment than low/medium concentrations (49.5% vs. 46.2%). Considering the results for only the low/medium concentrations, it seems that the detrimental effects of smoking marijuana persist for up to about four hours. The duration of impairment is less clear when considering the results for the high concentrations, where some level of impairment may persist for many hours. Despite

that possibility, the DRUID researchers (Hargutt *et al*., 2011, p. 53) concluded that THC has an "impairment that lasts very shortly".

Table 9.1: Cannabis effects by THC concentration and hours after administration

	Hours after administration					Totals
	1-2	**3-4**	**5-6**	**6-12**	**>12**	
Low and Medium concentrations of THC						
N Impaired	311	8	3			**322**
N Total	613	37	47			**697**
Impaired %	50.7%	21.6%	6.4%			**46.2%**
High concentration of THC						
N Impaired	66	13	2	4	8	**93**
N Total	126	28	5	9	20	**188**
Impaired %	52.4%	46.4%	40.0%	44.4%	40%	**49.5%**
All concentrations of THC						
N Impaired	377	21	17			**415**
N Total	739	65	81			**885**
Impaired %	51.0%	32.3%	21.0%			**46.9%**

There is some evidence that the impairing effects of cannabis are less problematic than might be implied by the DRUID meta-analysis. Cannabis is more impairing for *simple*, highly automatic driving functions than for *complex* driving tasks that require conscious control (Sewell, Poling & Sofuoglu, 2009). That contrasts with the situation for alcohol and most other psychoactive drugs, where the impairment is most pronounced for the complex tasks. So, it is possible that the laboratory-measured impairment levels reported by Berghaus *et al*. (2011) for cannabis are over-estimations of the levels of real-world driving impairment.

DRUID comparison of the impairing effects of cannabis and medicinal drugs

The DRUID researchers designed a metric, the *Degree of Impairment*, which enabled them to compare the total impairing effects of many different medicinal and some recreational drugs (Berghaus *et al*., 2011, pp. 27-44; Hargutt, Kruger & Knoche, 2011, pp. 49-58). The metric was based on two main aspects of the drug's impairment profile: the level of maximum impairment, and the duration of measurable impairment. The level of maximum impairment is measured by the percentage of all effects that are impairments at the time that the drug is having its strongest influence (e.g., from Table 9.1, the value for THC is 51.0%, at 1-2 hours after administration).

Table 9.2, which is a version of Table 1 from the main summary of the results of the DRUID program by Schulze *et al*. (2012b), compares the Degree of Impairment for a number of depressants and anti-depressants with the Degree of Impairment for cannabis (smoked marijuana). It can be seen that the Degree of Impairment from smoking marijuana is less than for standard doses of many different medicinal drugs.

That fact the use of cannabis falls short of causing the level of impairment that is associated with some medicinal drugs raises the question of how road safety researchers and policy advisors view the threats to road safety that are presented by the legitimate use of those medicinal drugs.

In a 2003 report for the Australian Transport Council on the development of drug-driving legislation, Dr. Morris Odell, the Acting Head of Clinical Forensic Medical Services at the Victorian Institute of Forensic Medicine, provided the following advice (p. 2):

> Any approach to limit the use of a specific drug in driving must not have a greater impact than the condition for which the drug is being taken. For example, it would

be counterproductive to limit the use of anticonvulsants [some of which are benzodiazepines] or antipsychotics if the use of these drugs allows drivers to be treated for conditions that allow them to drive safely. … When drugs are licit, it is unusual for them to be implicated in crashes if they are being taken as prescribed.

Table 9.2: How the Degree of Impairment for cannabis compared with the Degree of Impairment for a number of Depressant (top of table) and Antidepressant (bottom of table) medicinal drugs

Drug Class	Substance (Dose)	Common Name	Increasing Degree of Impairment
Depressants (Benzodiazepines and Z-Drugs)	Clobazam (lower)	Frisium	0
	Clobazam (higher)	Frisium	0
	Temazepam (lower)	Normison	0
	Zolpidem (low)	Ambien	0
	Diazepam (low)	Valium	17
	Temazepam (higher)	Normison	40
	Diazepam (low)	Valium	57
	Lorazepam (lower)	Ativan	64
	Cannabis (lower THC level)	**Marijuana**	**66**
	Cannabis (higher THC level)	**Marijuana**	**70**
	Triazolam (lower)	Halcion	89
	Oxazepam (lower)	Serapax	104
	Diazepam (medium)	Valium	112
	Flunitrazepam (lower)	Rohypnol	115
	Zolpidem (medium)	Ambien	119
	Oxazepam (higher)	Serapax	170
	Diazepam (high)	Valium	171
	Zolpidem (high)	Ambien	214
	Zopiclone	Zimovane	240
	Triazolam (higher)	Halcion	247
	Alprazolam	Xanax	369
	Lorazepam (higher)	Ativan	418
	Flunitrazepam (higher)	Rohypnol	461
	Lorazepam (higher)	Ativan	571
Antidepressants	Fluoxetine	Prozac	0
	Paroxetine	Paxil	0
	Imipramine	Tofranil	32
	Cannabis (lower THC level)	**Marijuana**	**66**
	Cannabis (higher THC level)	**Marijuana**	**70**
	Trazodone	Desyrel	87
	Mianserin	Bolvidon	185
	Amitriptyline (lower)	Elavil	327
	Amitriptyline (higher)	Elavil	380

This advice is consistent with the opinion of Voas *et al*. (2013a, p. 218) that "drivers who use prescribed controlled substances only as directed by their physician … are not generally a risk to other road users". Similarly, Dr Alain Verstraete, a major contributor to the DRUID project, who was also the Scientific Advisor to the Belgian government on the development of their drug driving laws, has said that he is "not convinced that driving under the influence of medicinal drugs taken in normal, prescribed doses significantly increases accident risk" (Huestis *et al*., 2011, p. 808).

It would seem that the laboratory evidence on the level of impairment caused by the use of cannabis is consistent with cannabis being of little concern to some road safety authorities.

Post-DRUID reviews of the effects of cannabis on driving-related skills

Since the completion of the DRUID program, two reviews have been published on the effects of cannabis on driving-related skills. In 2014, Verstraete and Legrand updated an earlier summary of the overall findings of the DRUID program (Verstraete *et al*., 2011). The reviewers briefly (pp. 33-38) considered all of the relevant laboratory, simulator and on-road studies, and concluded "Cannabis *may* impair some of the cognitive and psychomotor skills required to drive" (p. 94).

The second review (Hartman & Huestis, 2013) was undertaken at the U.S. Government's National Institute on Drug Abuse (NIDA) under the direction of Dr Marilyn Huestis, who, until her recent rretirement, was the director of a research program focusing on the effects of marijuana on driving-related skills. The reviewers noted that "Past experimental studies were often inconclusive because outcome measures lacked sensitivity and had not been tailored to specific THC effects" (p. 486). They therefore selected for review recently published studies involving performance measures that were likely to be sensitive to the effects of cannabis. In their Table 4, they summarised the results of seven laboratory studies of the effects of cannabis on various psychomotor skills, such as reaction time, memory and divided attention. They reported that, of the 28 test results, 16 (57%) showed some impairment, while 12 (43%) showed no effect. In their Table 5, they summarised the result of eleven simulator and on-road studies of the effects of cannabis on driving skills, such as headway maintenance, speed and weaving. They reported that, of the 40 test results, 24 (60%) showed some impairment, while 16 (40%) showed no effect. A reduction in speed, as recorded in four of the studies, was considered to be an 'impairment', despite the likely safety benefits. If speed reduction was re-classified as 'no effect', 20 (50%) of the 40 test results would be impairments, and 20 (50%) would be no effects.

As noted previously, about 50% of the earlier DRUID test results for the effects of cannabis on driving-related skills showed no effect. Despite their focus on the most sensitive measures of cannabis impairment, Hartman and Huestis (2013) reported similar results.

The NIDA researchers went on to undertake four large-scale studies of the effects of cannabis on driving-related skills, two of which were laboratory-based (Desrosiers *et al*., 2015; *Newmeyer et al*., 2017a), while the other two used a driving simulator (Hartman *et al*., 2015; Hartman *et al*., 2016). Those studies are discussed next.

Four NIDA studies of the effects of cannabis on driving-related skills

Desrosiers *et al*. (2015) published a paper on the 'psychomotor and neurocognitive' effects of smoking marijuana. Fourteen frequent and eleven occasional smokers were subjected to tests of three different types of skilled performance, 'critical tracking', divided attention and spatial working memory, as well as a test of risk-taking. The two groups of subjects (i.e., the frequent and occasional smokers) were tested repeatedly: there was a single pre-smoking test session at about 1.75 hours before smoking, and four post-smoking test sessions at about 1.5, 3.5, 5.5 and 22.5 hours after smoking. The exact testing times varied from task to task. The effects of smoking on task performance were measured in terms of the difference between the single pre-smoking (baseline) test score and the four post-smoking test scores.

The Critical Tracking Task (CTT) involves using a joystick to return a wandering target to the middle of its range. Desrosiers *et al*. (2015) found no effect of cannabis on CTT performance for either group at any time after smoking.

The Divided Attention Task (DAT) involves undertaking the CTT under distracting conditions. DAT performance was measured in five different ways: Control Losses, Tracking Errors, Hits (correct responses to the secondary, distracting task), False Alarms and Reaction Time. Desrosiers *et al*. (2015) found no effect of cannabis for three of the five DAT measures (Control Losses, Tracking Errors or False Alarms) for either group at any time after smoking. The researchers also found no effects of cannabis for the frequent smokers for the remaining two DAT measures (Hits and Reaction Time) at any time after smoking. However, they found small, but statistically significant, decrements in performance for the occasional smokers for the two

tasks at 3.5 hours after smoking. However, for those two measures, there were slight improvements for the frequent smokers during the same time, so it is likely that there would have been no overall change for the combined group.

Results for the DAT could have been analysed for the two groups separately or combined (as was done for the spatial working memory task – see below). Altogether, there was therefore the potential to find 60 statistically significant effects (for the 3 groupings of subjects x 5 DAT measures x 4 post-smoking test times). Of those 60, only 2 were reported as being statistically significant. Those two differences were not large, and could easily have been 'false positives'. The fact that there were 58 failures to demonstrate any impairing effect of cannabis on DAT performance is perhaps surprising, given that the CTT has been shown to be sensitive to impairments of attention (Petzoldt, Bellem & Krems, 2014).

In the N-Back Spatial Working Memory task, the subjects are asked to determine whether a given visual stimulus matches a stimulus that was presented either in the previous trial (1-back), or two trials previously (2-back), or three trials previously (3-back). The level of difficulty increases considerably from the 1-back version to the 3-back version. For each of the three versions, there were three measures of task performance: Accuracy, Reaction Time and False Alarms ('Errors of Commission').

Desrosiers *et al*. (2015, p. 256) acknowledged that they had found "minimal spatial working memory impairment following cannabis smoking". It would have been more accurate to say that no real evidence of *any* such impairment had been found. Of the 108 potentially significant effects (for the 3 groupings of subjects x 3 versions of the task x 3 levels of task difficulty x 4 post-smoking test times), only 3 were reported as being statistically significant, and one of those was an improvement! The fact that there were so many failures to demonstrate an impairing effect of cannabis on 'N-back' performance is perhaps surprising, given that the N-back test has been shown to be sensitive to some subtle changes that accompany the normal aging process (Wild-Wall, Falkenstein & Gajewski, 2011).

With respect to the test of risk taking and impulsivity (the Balloon Analog Risk Task – BART), Desrosiers *et al*. (2015, p. 258) acknowledged that they had found "no acute effect of cannabis smoking on risk-taking behaviour".

Only simple effects have been discussed here. There were, of course, hundreds of interaction effects that Desrosiers *et al*. (2015) could have investigated, and they reported on a few of them. It is difficult to make any sense of the few statistically significant, but weak, reported interaction effects.

It is clear that Desrosiers *et al*. (2015) have failed to provide any reasonable evidence for an effect of smoked cannabis on skilled performance or risk taking. However, that is not the impression that one would gain from reading their Conclusions (p. 259):

> We documented significant differences between occasional and frequent cannabis smokers in psychomotor … effects following cannabis smoking, with weaker effects in frequent smokers suggesting tolerance development. Impairment domains included those that play a key role in a driver's ability to accurately control a car or react to events on the road. These data help our understanding of cannabis' effects and will be valuable for interpretation of driving under the influence of cannabis and accident responsibility studies.

A more honest conclusion would have been to the effect that, despite the participants being involved in a battery of sensitive tests, no plausible evidence could be found of any detrimental effect of cannabis on skilled performance.

Newmeyer *et al*. (2017a) published a paper on the effects of smoked, vaporised and oral (in the form of a brownie) cannabis treatments, as well as placebo treatments, on three 'psychophysical tasks', taken from the Standardised Field Sobriety Test battery (SFST), which are routinely used by U.S. drug recognition experts (DREs). The first task was the 'Modified Romberg Balance' task

(MRB30), which involves the subjects standing still with their arms at their sides, heads tipped back and eyes closed, while estimating the passage of 30 seconds. The task is primarily evaluated in terms of the ability to estimate the elapsed time of 30 seconds. The second task was the 'One Leg Stand' (OLS), which involves the subjects raising one leg off the floor for 30 seconds with their arms at their sides while counting aloud in thousands. The task is evaluated in terms of various types of body instability. The third task was to 'Walk and Turn' (WAT), which is self-explanatory, except that the walking involves taking a specified number of heel-to-toe steps in both directions. The task is again evaluated in terms of various types of body instability, as well as the subjects' comprehension of and compliance with the detailed instructions on how to perform the task.

Eleven frequent and nine occasional marijuana smokers were subjected to all three psychophysical tasks. Each subject repeated the testing procedure four times, such that they were all tested for the effects of the four types of treatment (smoked, vaporised and oral cannabis and the placebo). After each treatment, the subjects underwent two rounds of testing: at about 1.5 and 3.5 hours post-treatment. There was no pre-treatment test session (so there were no baseline measures of performance). The effects of cannabis on task performance were measured in terms of the differences in performances under the placebo versus under each of the other three cannabis treatments.

A naive reader of the following words from Newmeyer *et al's* (2017a) Abstract could easily be convinced that the authors had found widespread deleterious effects of cannabis: "Oral cannabis administration impaired occasional cannabis users' performance on the OLS and WAT tasks compared to placebo, supporting other reports showing these tasks are sensitive to cannabis-related impairment. … These are important public health policy findings as consumption of edible cannabis products increases". The authors did, however, also note that "Significant effects following inhaled doses were not observed due to delayed tasks administration". However, a closer investigation of the full set of findings reveals that the vast majority of the findings were consistent with cannabis having no deleterious effects at all on any task performance. The experimental design offers a plethora of findings from which it is easy to cherry-pick a few to focus on. There are findings for: frequent and occasional smokers; smoked, vaporised and oral consumption of marijuana; the three main types of test outcome (as depicted in Newmeyer *et al's* Table 4 and Figure 2), and testing sessions at 1.5 and 3.5 hours post-dose. The combinations of those categories give 36 different findings. But many more potential findings can be created by combining the categories in different ways, such as by summing results over two of the three tasks, which the researchers have done. A more straightforward account of the full set of results might run as follows:

> There were two groups of subjects: frequent and occasional smokers of marijuana. It was expected that the use of cannabis would impair task performances for both groups. However no impairments were found, under any circumstances, for the frequent smokers. Marijuana was consumed in three different ways: smoked, vaporised and orally as cookies. As the effects of marijuana are mediated by THC in the blood, and as all three ways of consuming marijuana deliver much the same levels of THC to the blood, it was expected that similar impairments would result from all three ways of using marijuana. However, no impairments were found, under any circumstances, for smoking, which is the most prevalent way of using marijuana, or for using a vaporizer. The three SFST tasks selected for inclusion in the test battery (MRB30, OLS and WAT) were those used by DREs in their work, and should therefore be very sensitive to the impairing effects of cannabis. However no impairments were found, under any circumstances, for the MRB30. Furthermore, impairments were only found (under very specific circumstances) for the OLS and WAT when their results were combined. Testing sessions were held at 1.5 and 3.5 hours post-dose. Given that the effects of THC are known to be short-lived, it was expected that impairments would be much stronger at 1.5 hours post-dose. However, there were no differences in performance across the two session times. In summary, statistically significant impairments were found only for the occasional smokers of marijuana, and even then, they were found only for the consumption of marijuana in the form of a cookie, and even then, they were not found for the

MRB30, or for the other two SFST tests when considered separately. They were found only for the two SFST tests when combined. It is concluded that these three SFST tests, which are excellent at discriminating alcohol-affected (BAC ≥ 0.08) from sober (BAC < 0.08) drivers (Stuster, 2006) are, however, totally incapable of correctly identifying subjects who have recently used cannabis.

Hartman et al. (2015) recruited 18 occasional cannabis smokers into their experiment. On each of six days that were at least a week apart, each subject received one of six different combinations of cannabis and alcohol. The combinations comprised three levels of cannabis (placebo, lower and higher) along with two levels of alcohol (placebo and a moderate dose). The categories for the lower and higher THC concentrations were defined using a median split of blood THC concentrations. Testing was conducted in "the world's most sophisticated driving simulator" (p. 35). Although "hundreds of performance variables were monitored" (p. 26), Hartman *et al*'s paper focused on the results for four variables, all of which measured aspects of 'lane keeping' (which can otherwise be described as 'weaving'). The four lane-keeping measures were: standard deviation of lateral position (SDLP); standard deviation of steering angle; number of lane departures per minute; and maximum lateral acceleration.

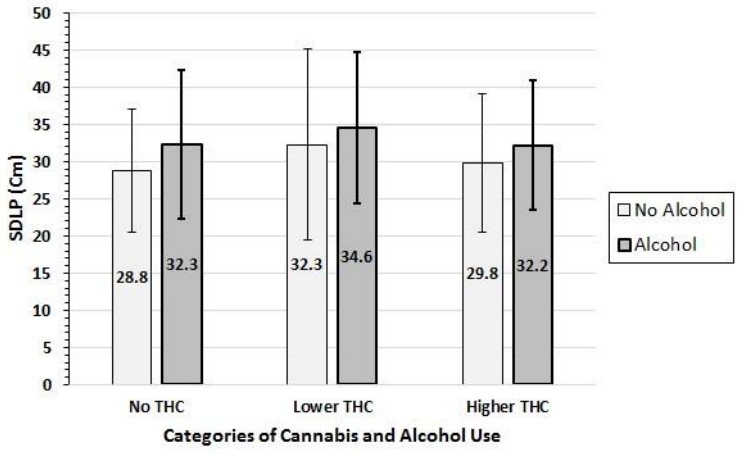
Hartman *et al*. (2015) found that three of the four lane-keeping measures were sensitive to the effects of alcohol, with the standard deviation of steering angle being the exception. In contrast, only SDLP was sensitive to the effects of THC. The results for alcohol will not be further considered. The negative results for THC in relation to three of the four lane-keeping measures will also not be further considered.

It is worth noting that SDLP is widely recognised as one of the most sensitive measures of the impairing effects of alcohol and drugs (Helland *et al*., 2016; Verster & Roth, 2014). SDLP is also sensitive to the level of driver distraction, and can therefore be employed to compare levels of intrusiveness of different distractors, such as the use of mobile phones (Ranney *et al*., 2013). Under simulated driving conditions, a typical SDLP is about 0.30 metres (30 centimetres).

According to a review of age-related performance decrements (Green *et al*., 2004), SDLP is affected by age, increasing by about 2 cm per decade from the age of 20 years. The existence of strong age effects was confirmed by Ranney *et al*. (2013, Figure 6) who found an increase in SDLP of about 2.5 cm per decade.

Figure 9.1 depicts the results for the effects of cannabis and alcohol on SDLP that were presented by Hartman *et al*. (2015) in their Table 5.

Figure 9.1: Effects of cannabis and alcohol on SDLP from Hartman et al. (2015, Table 5)



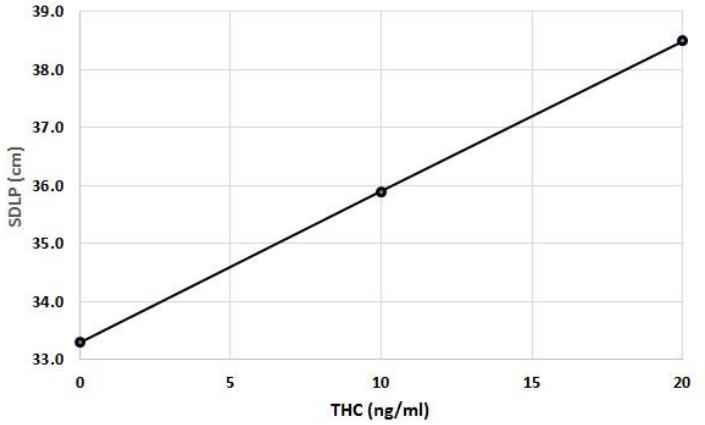
The 95% confidence intervals in Figure 9.1 were calculated from the standard deviations provided by Hartman *et al*. (2015). The experiment had a within-subject design (such that all

subjects were tested under all six conditions of cannabis and alcohol use), which makes it easier for relatively small drug and alcohol effects to achieve statistical significance. Nevertheless, it can be seen from Figure 9.1 that the effects of the cannabis and alcohol treatments are modest in comparison with the 95% confidence intervals. It is evident that there is no dose-response effect for THC, with or without alcohol, as the greatest increases in SDLP are associated with the lower levels of THC. At the lower levels of THC, the increases in SDLP above the 'No THC' treatment levels are 3.5 cm for THC alone, and 2.3 cm for THC in combination with alcohol. At the higher levels of THC, the increases in SDLP are 1.0 cm for THC alone, with no increase at all for THC in combination with alcohol.

Given that there was no dose-response effect of THC on SDLP, it is appropriate to estimate average values for the presence (versus absence) of THC. The overall effect of the presence of THC alone is an increase in SDLP of about 2.3 cm, and the comparable effect for THC in the presence of alcohol is 1.1 cm. When the effects of cannabis alone on SDLP are compared with the effects of normal aging (as reported above), it can be seen that the use of cannabis is equivalent to about a decade of aging. In the light of that comparison (given that no-one is suggesting that 40 year olds should be removed from the roads because of their age-related impairments), it would seem that the effects of cannabis on SDLP are trivially weak.

However, the effects of cannabis on SDLP were not reported as weak by Hartman *et al*. (2015), as indicated by their Figure 2, which is replicated here as Figure 9.2. This figure gives the impression that there is a strong linear dose-response relationship between the concentration of THC and SDLP. However, there was no such relationship in the raw results. The modelling procedure used by Hartman *et al*. has somehow conjured the linear relationship from incompatible raw data. The graph implies that an increase in SDLP of about 5 cm is found at the higher THC concentrations. That implication is also false. The graph has a strong visual impact that would have been considerably reduced if the origin had been at an SDLP of zero, rather than 33.0, and if the substantial error bars had not been omitted.

Figure 9.2: Effects of cannabis on SDLP from Hartman et al. (2015, Figure 2)



Assuming that the weak effects of THC on SDLP that were reported by Hartman *et al*. (2015) are real, there is a further matter to be considered: whether the size of the effect is influenced by factors that are unrelated to impairment. Hartman *et al*. stated that "We do not believe that conducting this study in a driving simulator, rather than on the road, represents a significant limitation" (p. 35). However, in a study that actually compared simulator with on-road SDLPs (Helland *et al*., 2013; 2016), it was found that, for some subjects, the SDLPs from the simulator were much larger than from the road, leading the researchers to conclude that the lack of perceived danger in the simulator sometimes causes reckless driving. It is therefore likely that the weak overall effects of THC on SDLP that were reported by Hartman *et al*. (2015) for simulated driving were larger than would have been obtained from an on-road driving test.

As noted above, the studies by Desrosiers *et al*. (2015), Newmeyer et al. (2017a) and Hartman *et al*. (2015) were all conducted at NIDA. All focused on a few islands of significant results in a sea on non-significance. All presented the few significant but weak results as though they were strong. NIDA's research programs have recently been criticised in the U.S. Congress for their biased attention to the harms of cannabis use (Committee on Oversight and Government Reform, 2014). One suspects that, at some point, the science stops and the proselytising starts for researchers who are directly funded by a government that has been strongly committed to the War on Drugs.

The DRUID meta-analysis (Berghaus *et al*., 2011) reported that cannabis caused roughly equal numbers of impairments and null effects. The reader of the DRUID review would naturally assume that the reported impairments were substantial. But if the impairments reported in the DRUID review are comparable with those reported by the NIDA researchers (using the most sensitive tests they could apply) they would be of little consequence for road safety.

Hartman *et al*. (2016) is the fourth NIDA-related study to be considered in this section. It explores the effects of cannabis on various aspects of speeding behavior. But before considering the results, some findings from the broader body of research on speeding will briefly be noted.

The first point to note is that speeding is now becoming recognized as the greatest contributor to fatalities on the roads (NTSB, 2017), especially given that a large proportion of alcohol-related fatalities are ultimately caused by speeding (NTSB, Figure 4). The second point, as previously noted in Part 8 of this report, is that the crash risks of travelling at only a few km/h above the mean speed for the location are considerable (Kloeden, McLean & Glonek, 2002), and far greater than many drivers realize (Mooren, Grzebieta & Job, 2013). The third point is that, despite an earlier view that driving slower than the mean travelling speed could increase the risk of crashing (e.g., Solomon, 1964), it is now recognized that driving slower than the mean does not increase the risk of crashing (Kloeden, McLean & Glonek).

Because Hartman *et al*. (2016) reported a sub-set of the findings of the study that was described above in Hartman *et al*. (2015), no further details of the experimental design will be mentioned here, except to note the additional performance measures that are reported in the 2016 paper. The researchers measured various aspects of speeding and speed-related behaviors, including: mean speed; the percent of driving time spent travelling 10% or more above the mean speed (% speed high); the percent of time travelling 10% or more below the mean speed (% speed low); and the mean following distance during headway maintenance. The results for cannabis alone are described here; the results for the effects of alcohol, with and without cannabis, are described in the next part of this report.

Hartman *et al*. (2106) found that the use of cannabis was associated with a decrease in mean speed, no change in % speed high, an increase in % speed low, and an increase in following distance. The researchers' modelling indicated that higher THC blood concentrations were associated with decreasing mean speeds and increasing headways. There are two different possible explanations for these results. The first is that the calming effect of cannabis directly affects travelling speeds and headways. The second, favored by Hartman *et al*., is that drivers choose to drive more cautiously as a means of compensating for the impairing effects of the use of cannabis.

To summarize the results of the four NIDA studies: The researchers have shown that most driving-related skills are not affected by the use of cannabis. The evidence that they present for the few instances of possible impairment is not convincing. On the other hand, when the focus is not on skills but on mood change, it seems clear that the calming effects of cannabis are manifested in slower travelling speeds and greater headways. Given the pervasive and deleterious effects of speeding on road safety, an overall conclusion that could easily be reached is that the use of cannabis is more likely to reduce than to increase the risk of crashing.

The paradoxical effects of illegal stimulants on driving-related skills

One major conclusion from the DRUID meta-analysis may seem counter-intuitive: it was that the illegal stimulant drugs cocaine and amphetamine (the latter being common in the E.U. but not in Australia), at recreational levels, are much more likely to *improve* than impair a range of driving-related skills (Berghaus *et al*., 2011 pp. 161-168). Although methamphetamine and ecstasy were not included in the meta-analysis, the researchers concluded from the available research that those stimulants, like amphetamine, would improve performance on driving-related tasks.

Perhaps those findings should not be surprising. Some stimulants are used at low levels by students as 'study aids' (Smith & Farah, 2011), and they are also prescribed to sufferers of attention-deficit hyperactivity disorder (ADHD) to improve their ability to concentrate (Swanson, Baler & Volkow, 2011). Stimulants are prohibited by the World Anti-Doping Agency (WADA) for use by athletes in-competition because of their performance-enhancing effects (Docherty, 2008); and they have been used by the armed forces for decades to improve the combat skills of military personnel, particularly when fatigued (e.g., Meadows, 2005). Given that stimulants have been known to improve performance in many fields for decades, it is not surprising that the findings in the field of road safety are consistent with previous research and practice.

As an aside, it should be noted that a critical review that was published soon after the completion of the DRUID program of research (Hart *et al*., 2012) confirmed the DRUID conclusion with respect to methamphetamine. The reviewers found that, when taken at typical recreational levels, methamphetamine improves performance on tasks such as reaction time, sustained attention, visuospatial perception, long-term memory and learning, for both infrequent and regular methamphetamine users. While some of the reviewed studies found no improvements on some tasks, there were no tasks for which performance was disrupted.

There is no doubt that the use of illegal stimulants is likely to improve driving-related skills. However, there is also no doubt that the use of illegal stimulants is a causal factor in road crashes. The lesson to be learned is that skilled performance may not be as relevant to road safety as many researchers and policy makers have supposed. Consistent with that fact is the fact that small decrements in skilled performance, as detected after the use of cannabis, are probably not relevant to road safety.

The effects of drugs on mood

The effect of drugs on driving-related skills is obviously not the only effect that is relevant to the risk of crashing. There is another factor that is often overlooked in the road safety literature: it is that drugs have effects on what can roughly be described as 'mood'.

Even for alcohol, the skill-reducing effects are probably of less consequence for road safety than the mood-altering effects (Curran *et al*., 2010). As expressed in a recent paper (Gonzalez-Iglesias, Gomez-Fraguela & Luengo, 2014, p. 22), "Contrary to popular belief, drinking is a road safety risk even at low alcohol levels; thus, 0.30–0.50 g/l suffices to impart omnipotent, false safety feelings, and to make drivers take increased risks and disregard precautions. This is especially so with accidents involving young drivers."

If this view were generally correct, it would be expected that alcohol-related crashes would be mediated more by risk-taking than by errors of skill. There is mounting evidence that that is so: speeding and the non-use of seatbelts are much more prevalent in alcohol-affected driver fatalities than in alcohol-free driver fatalities (Bogstrand *et al*., 2015; Phillips & Brewer, 2011; Romano & Voas, 2011; Stubig *et al*., 2012). Alcohol-motivated speeding is not an error of skill; it is a manifestation of bravado.

Beirness, Simpson and Williams (2006, pp. 12-13) support the view that the effects of drugs on skilled performance may not be as important as previously considered: "Laboratory findings are informative but limited as an indicator of actual on-road driving risks. … Laboratory tests can address the effects of drugs only on skills, not judgment, and the latter may be as important when

it comes to driving. Thus even if drugs are found to affect driving skills in laboratory tests, actual crash risk may or may not be affected." And in the words of a Research Note released by the NHTSA in relation to the on-road risks imposed by marijuana: "While useful in identifying how marijuana affects the performance of driving tasks, experimental and observational studies do not lend themselves to predicting real world crash risk" (Compton & Berning, 2015, p. 1).

It is clear from the evidence presented in this part of the report that laboratory studies are of limited relevance to the role of drugs in crash causation. The most trustworthy evidence must come from epidemiological research that *directly* investigates the effects of drugs on the risk of crashing, which is the approach adopted in this report.

A broader perspective on the relevance of skills to safety

If finely-honed driving-related psychomotor skills were relevant to road safety, it might be predicted that training in driving skills would be of some safety benefit, and that the causes of some crashes could be traced back to decrements in skilled performance. There is no evidence to support either of those predictions.

In a critical review of the literature on classroom and behind-the-wheel driver training programs, Peck (2011, p. 70) concluded that "One limitation with on-the-road training programs is that the primary focus is on skill; yet skill as measured by on-the-road tests has never been shown to be correlated with driver crash rates". In a similar vein, but with respect to post-licence driver training, Washington, Cole and Herbel (2011, p. 72) noted that "The consensus from the evaluation of countless advanced driver training programs is that these programs are a detriment to safety, especially for novice, young male drivers". And, in a rigorous case-control evaluation of 'Bike Ed', which is an Australian bicycle skills training program for school children, Carlin, Taylor and Nolan (1998, p. 22) concluded that "… this educational intervention does not reduce the risk of bicycle injury in children, and may possibly produce harmful effects in some children, perhaps due to inadvertent encouragement of risk taking, or of bicycling with inadequate supervision". It is clear from numerous reviews that training in driving-related skills is more likely to be detrimental than beneficial to road safety.

A number of researchers have attempted to classify the types of human failing that can play a causal role in crashing. For example Reason *et al*. (1990) concluded that there were four main types of driving 'error', as described in Table 9.3. They saw no need to include minor decrements in driving-related skills as one of their error categories.

Table 9.3: Examples of the four main types of aberrant behavior measured by the DBQ

Slips / lapses	Activate the turning indicator instead of the windscreen wipers
Mistakes	Underestimate the speed of an oncoming vehicle when overtaking
Unintended violations	Unknowingly, creep 5 km/h above the speed limit
Deliberate violations	Drive at 85 km/h in a 60 km/h zone

Other researchers have provided broad overviews of the types of inappropriate or inadequate driver behaviors that can cause crashes (e.g., Salmon *et al*., 2010; Wundersitz & Baldock, 2011). On reading these reviews, it is difficult to find any type of crash-producing human failing that could be described as a minor decrement in the performance of a basic driving-related skill.

It is concluded that modest decrements in the level of driving-related skills that are sometimes found in the laboratories that have studied the effects of cannabis on human performance are of little relevance to road safety.

Part 10: The exacerbation effect in relation to driving skills

Part 7 of this report examined the exacerbating effect of cannabis on the effects of alcohol in the context of epidemiological studies. In this part, the exacerbation effect will be examined, briefly and selectively, in the context of studies of driving-related skills. It should be remembered that the term 'exacerbation', as used in this report, refers to an interaction that can be sub-multiplicative, and even sub-additive. All that is required is that the impairing effect of cannabis and alcohol combined is significantly greater than the effect of alcohol alone.

Table 10.1 notes the conclusions reached in six post-2012 review articles about the exacerbating effect of the recent use of cannabis on impairments that are caused by the recent use of alcohol. Table 10.2 lists the original research studies (but not other reviews) that are cited in the six reviews as providing evidence for those conclusions.

Table 10.1: Conclusions reached in six recent reviews about the exacerbating effect of cannabis on impairments caused by alcohol

Review article	**Conclusion**
Beirness & Porath-Waller (2015)	Combining cannabis with even small amounts of alcohol greatly increased the negative effects on driving skills. (p. 3)
Bondallaz *et al*. (2016)	Several studies included laboratory and experimental results on alcohol and cannabis combination effects. Although some studies reported additive cannabis-alcohol impairments, others reported no interactions. Impairing effects of cannabis and alcohol interaction were also obvious in an on-road study. (p. 96)
Capler *et al*. (2017)	There is an additively impairing effect for cannabis and alcohol. Increased impairment, measured by the SDLP, when alcohol and cannabis are used concurrently has also been observed in driving simulator and on-road studies. (pp. 20-21)
Compton (2017)	Some studies have reported increased impairment on driving related skills when subjects are dosed on both alcohol and marijuana. In other cases, no increased impairment is found. The relative amount of both drugs ingested may help explain this confusing result. In some cases, the effects of alcohol may be so dominant that the additions of low doses of marijuana are not detectable. (p. 12)
Hartman & Huestis (2013)	Combining alcohol with THC exacerbated the observed effects, especially with respect to Reaction Time and SDLP. (p. 490)
Wong, Brady & Li (2014)	Various studies have demonstrated that the combined use of marijuana and alcohol is associated with significantly greater cognitive impairment than the use of one alone. (p. 3)

Table 10.2: The original research studies that are cited in the six recent reviews as providing evidence that cannabis exacerbates the impairments caused by alcohol

Review Article	**Cited Studies**
Beirness & Porath-Waller (2015)	Downey *et al*., 2013; Ramaekers, Robbe & O'Hanlon, 2000
Bondallaz *et al*. (2016)	Chait & Perry, 1994; Downey *et a*l., 2013; Hartman et al., 2015; Lenne *et al*., 2010; Liguori, Gatto & Jarrett, 2002; Ramaekers *et al*., 2011; Ramaekers, Robbe & O'Hanlon, 2000; Robbe, 1998; Ronen *et al*., 2010
Capler *et al*. (2017)	Downey *et al*., 2013; Ramaekers, Robbe & O'Hanlon, 2000
Compton (2017)	Robbe, 1998; Smiley, Noy & Tostowaryk, 1986
Hartman & Huestis (2013)	Chait & Perry, 1994; Lamers & Ramaekers, 2001; Lenne *et al*., 2010; Liguori, Gatto & Jarrett, 2002; Ramaekers, Robbe & O'Hanlon, 2000; Ramaekers *et al*., 2011; Robbe, 1998; Ronen *et al*., 2010
Wong, Brady & Li (2014)	Downey *et al*., 2013

Eleven different research studies are listed in Tables 10.1 and 10.2. The main findings of those studies are briefly summarised in Table 10.3.

Table 10.3: The main conclusions from the original research studies that are cited in the six reviews

Study	**Type of outcome measures**	**Is an exacerbation effect claimed?**	**Is the claim of an exacerbation effect substantiated?**
Smiley, Noy & Tostowaryk, 1986	On-road	Yes - additive	Possibly
Chait & Perry, 1994	Laboratory	No	
Robbe, 1998	On-road	Yes - additive	Yes
Ramaekers, Robbe & O'Hanlon, 2000	(Redundant)		
Lamers & Ramaekers, 2001	On-road	No	
Liguori, Gatto & Jarrett, 2002	Laboratory	No	
Lenne *et al*., 2010	Simulator	No	
Ronen *et al*., 2010	Simulator	Yes	Not strongly
Ramaekers *et al*., 2011	Laboratory	Yes - for one subtest	Generally not
Downey *et a*l., 2013	Simulator	Ambiguous	No
Hartman et al., 2015	Simulator	Yes	No

The main findings from each of the eleven studies with respect to the exacerbating effects of cannabis on the impairing effects of alcohol are briefly summarised below.

In a short conference paper, **Smiley, Noy and Tostowaryk (1986)** describe an on-road experiment using an instrumented car. They studied the effects of THC and low levels of alcohol, separately and combined, on various measures of driving performance. They concluded (p. 206) that "Results were in agreement with previous research in that both substances were associated with impairment, and that alcohol was associated with more risky behaviour and marijuana with more cautious behaviour". They noted that there was "no significant alcohol-marijuana interaction effect", but went on to conclude that "The lack of marijuana-alcohol interaction effects indicated that the drugs are essentially additive in their effects". Given that additive effects can qualify as exacerbation effects, it seems likely that they did find some exacerbation effects.

Chait and Perry (1994) used a battery of psychomotor and cognitive tasks in their attempt to demonstrate exacerbation effects. A number of alcohol effects were found, along with a few cannabis effects. However, no cannabis-alcohol exacerbation effects were found.

In his 'Study 4' **Robbe (1998)** investigated the effects of low and high doses of THC and a low dose of alcohol, separately and combined, on various measures of driving performance, using an instrumented car on highways in the Netherlands. He noted (p. S77) that "Standard deviation of lateral position (SDLP) in the road-tracking task was the most sensitive measure for revealing THC's adverse effects". He found significant main effects of alcohol alone and THC alone on SDLP "but no significant interaction" (p. S76). However, he did report an additive exacerbation effect for SDLP, as depicted in his Figure 4. He concluded (p. S77) that "The combination of THC with alcohol sufficient for attaining a BAC of about 0.04 has very severe effects on driving performance".

The paper by **Ramaekers, Robbe & O'Hanlon (2000)** provides a more complete description of the study described above by Robbe (1998). As it is redundant, it is not further considered here.

Lamers and Ramaekers (2001) investigated the effects of low doses of THC and alcohol, separately and combined, on various measures of driving performance, using an instrumented car on the streets of Maastricht. The subjects' visual search behaviour was recorded automatically, and their driving skills were scored on the Driving Proficiency Scale by a driving instructor who travelled with them in the car. There was no effect of the three treatments on driving performance as rated on the Driving Proficiency Scale. Although there was a 3% reduction in 'visual search frequency', the researchers concluded (p. 393) that "The effects of low doses of THC and alcohol on higher-level driving skills as measured in the present study are minimal".

Liguori, Gatto and Jarrett's (2002) study was designed to measure the separate and combined effects of marijuana and alcohol on (simulated) emergency braking (which could be a factor in

road crashes) and on body sway (as measured in field sobriety tests). *S*ubjects who regularly used both marijuana and alcohol took part in a laboratory experiment which involved investigating the effects of lower and higher levels of THC, and lower and higher levels of alcohol, both separately and combined. The lower doses of THC and alcohol were found to have no measurable effects. However, the higher dose of THC significantly increased body sway without affecting brake latency, while the higher dose of alcohol significantly increased brake latency without affecting body sway. There were no significant additive effects of THC and alcohol, when taken together in the higher doses, on either body sway or brake latency.

Lenne *et al*. (2010) used a driving simulator to study the effects of lower and higher doses of THC and lower and higher doses of alcohol, separately and combined, on many different measures of driving performance. They found some impairing effects of THC, but very few impairing effects of alcohol (possibly because even the higher dose of alcohol produced only low BACs). They apparently found no exacerbation effects, because they did not comment on any such effects, beyond noting in their Abstract that "Alcohol at the doses used had few effects, and did not produce synergistic effects when combined with cannabis".

In their Introduction, **Ronen *et al*. (2010**, p. 1856) observed that "The literature on the joint effects of THC and alcohol on driving is sparse and inconclusive". The researchers used a driving simulator to investigate the separate and combined effects of cannabis and alcohol on a wide variety of driving and non-driving tasks. Only the four driving tasks are considered here. The researchers did not pay much attention to the possible exacerbating effects of cannabis, although they did conclude in their Abstract that "Overall, the combination of alcohol and THC had the most intense effect after intake. This effect was reflected in performance impairments observed in the driving and non-driving tasks". However, their actual findings for the four driving tasks, as summarised in their Figure 3, were patchy. For example, while the use of alcohol caused an increase in mean speed, the addition of cannabis to the alcohol brought the mean speed back to baseline levels. It is difficult to see how that finding could be considered to be an intensification of an impairment. One of the other main outcome measures was the Root Mean Square (RMS) of steering wheel deviations, which is related to SDLP. There was no exacerbation effect for that measure, either. There was an apparent exacerbation effect for the other two driving measures: the RMS of lane position and the RMS of speed. As the RMS of lane position is a measure of SDLP, as is the RMS of steering wheel deviations, it is not clear why the two similar measures gave inconsistent results. And it is not obvious that the RMS of speed is really a measure of impairment. Overall, the evidence from Ronen *et al*. for exacerbating effects of cannabis in relation to driving performance is patchy and weak.

Ramaekers *et al*. (2011) investigated the effects of THC and alcohol, alone and in combination, on the cognitive performance of heavy cannabis users. A high dose of THC was administered along with lower and higher doses of alcohol. The drug and alcohol effects were evaluated against performance on four different cognitive tests, all of which were presumed to be relevant to the ability to drive safely. Alcohol alone significantly impaired performance on three of the tests, while THC alone did not significantly impair performance on any test. THC did not exacerbate the effects of alcohol on three of the four tests. The fourth test measured the subjects' ability to divide their attention between two tasks performed simultaneously. This Divided Attention Task (DAT) generated four measures of performance. THC did not exacerbate the effects of alcohol on three of the four sub-tests, but it did have an exacerbating effect on the fourth sub-test: 'Control Losses'. Overall, the evidence from Ramaekers *et al*. for exacerbating effects of cannabis in relation to cognitive performance is patchy and weak.

In their Introduction, **Downey *et al*. (2013**, p. 880) considered that "Previous research concerning the combined effects of alcohol and THC consumption is so far inconclusive". They used a driving simulator to detect many types of driving errors, which were then combined to produce two overall scores for 'driving impairment' and 'signalling adherence'. While there was some patchy evidence for exacerbation effects on some of the many individual measures, neither overall score was affected by alcohol alone, cannabis alone, or the combination of alcohol and cannabis. It is concluded here that Downey *et al*. have failed to produce any satisfactory evidence for a cannabis-alcohol exacerbation effect.

The study by **Hartman *et al*. (2015)** was discussed in some detail in the previous part of this report. Using a driving simulator they generated "hundreds of performance variables" (p. 26) from which they constructed four summary measures of 'lateral control', one of which was the Standard Deviation of Lateral Position (SDLP). In their Discussion, the researchers noted (p. 32) that "Past simulator studies were inconsistent regarding SDLP cannabis-alcohol interactions". No effects of cannabis alone or in combination with alcohol were found for three of the summary measures. In their Abstract, they claimed to have found an exacerbation effect, where "Cannabis-alcohol SDLP effects were additive rather than synergistic". The results used to support that claim are provided here in Figure 9.1. It can be seen that when the higher dose of THC is combined with alcohol, the SDLP is no greater than for alcohol alone. Their statistical modelling procedures somehow managed to conjure an exacerbation effect from the raw data. However, a straightforward interpretation of their results is that no such effect was found.

Overall, the evidence that cannabis exacerbates the impairing effects of alcohol is weak. The conclusions from the reviews in Table 10.1 are exaggerated. The only strong result was from the study by Robbe (1998) that used SDLP (weaving) as an outcome measure. Some further consideration of the relevance of that measure to road safety is called for.

There is widespread agreement that SDLP is the most sensitive available indicator of the impairing effects of drugs. For example, in their 2017 systematic review and meta-analysis of SDLP findings, Irwin *et al*. (p. 248) concluded that "SDLP appears to be a more sensitive indicator of driving impairment than other driving performance variables". And in another broad review of the use of performance tests to measure the effects of drugs on driving, Brookhuis (2014, p. 120) concluded "To date, SDLP has proved itself as the most valid and reliable indicator of performance deterioration".

However, it is not obvious that SDLP is of much relevance to road safety as a measure of the exacerbating effect of cannabis on the impairing effects of alcohol. It is widely acknowledged by researchers in the field that users of cannabis are generally aware of any possible drug-related impairments. Given the challenges to safe driving that are created by the use of alcohol, it is likely that cannabis users deploy their attention to the main safety-related driving tasks at the expense of keeping strictly in the centre of their lane.

Part 11: The evidence-base for the inclusion of cannabis in an RDT program

Summary of the evidence that cannabis is relatively benign in the context of road safety

It is evident from Parts 3, 4 and 5 of this report that the use of cannabis by drivers has not been shown to increase the risk of crash involvement. The evidence presented in Part 7 indicates that the use of cannabis by drivers does not exacerbate the effect of alcohol on the risk of crashing. Although cannabis has some deleterious effects on driving-related skills, as discussed in Part 9, the effects are "typically described by experts as 'modest' and are seldom long lasting" (Armentano, 2013a, p. 52). And, unlike subjects impaired by alcohol, drivers affected by cannabis are more aware of their impairment and often compensate effectively for it by driving cautiously (e. g., Robbe, 1995) or by refraining from driving (Armentano, 2013a, p. 53).

While the use of cannabis probably does not directly increase the risk of crashing, nor indirectly increase the risk by exacerbating the effects of alcohol, there is third way that cannabis could act to increase the risk of crash involvement. It is conceivable that, during a drinking session, a person who is also using cannabis might consume more alcohol than they otherwise would. This possibility was explored in an Australian study by McKetin *et al*. (2014) who identified "a strong association between stimulant intoxication and excessive alcohol consumption that was not observed for cannabis intoxication, suggesting that stimulant use is a complement to heavy drinking whereas cannabis use is not" (p. 444). In other words, when heavy users of cannabis chose to also drink alcohol, they do not drink any more than if they had chosen not to use cannabis. (While exonerating cannabis as a facilitator of heavy drinking, McKetin *et al*. have provided another good reason to continue to target stimulants in RDT operations.)

In 1994, Drummer concluded from some Australian responsibility analyses that "The absence of any positive effect of cannabis use on relative risk suggests that cannabis alone may not necessarily increase accident risk (and may even reduce it!)" (p. 46). In 1995, he again noted that "… cannabis tended to show a negative effect on relative risk when other drug groups showed an increase" (p. 429). He went on to speculate that "The most likely reason probably relates to the over-compensation of marijuana-using drivers on their driving skills. Over-compensation may be caused simply by slowing down and avoiding adverse driving situations. These observations do not seem to be related to whether Delta-9-THC or 11-carboxy-THC are measured …" (p. 429). The contention in this report is that Drummer's insights in the mid-1990s about the role of cannabis in crashing were correct. Since that time there has been much unbalanced reporting of the results of the epidemiological and laboratory evidence (as discussed in this report) and two unbalanced meta-analyses (as revealed by Rogeberg and Elvik in their 2016a review).

The 'Australian way': Harm minimization

Harm minimization is a policy framework that can be adopted by social and governmental agencies working in the areas of drug abuse. The framework focuses on reducing harmful drug use by interrupting the supply, reducing the demand and applying a range of strategies that reduce the possibility or extent of drug-related harm. Drug use is viewed as a health issue rather than a legal or criminal issue. The framework assumes that, because drug use will never be eradicated, the consequent harms should be understood and remedied where possible. It can be contrasted with a zero-tolerance approach which considers drug use to be a criminal and legal issue. The zero-tolerance framework assumes is that it is not the primary job of government to reduce harms, but rather to promote and enforce a policy of abstinence. The penalties for the use of illegal drugs can be severe.

With the futility of the US-led zero-tolerance War on Drugs becoming more evident, drug policies around the world are increasingly being developed within the harm-minimization framework (Douglas, Wodak & McDonald, 2012; Global Commission on Drug Policy, 2014; Hari, 2015; Sherman & Valenta, 2015). Cannabis is now understood to be at the low end of the harm scale (Lachenmeier & Rehm, 2015; Nutt, 2012; Nutt *et al*., 2007), and its beneficial effects are being

acknowledged worldwide, including in Australia, where a previous Prime Minister backed the legalization of medical marijuana (Dunlevy, 2014).

For the last thirty years, Australia's *National Drug Strategy* (Intergovernmental Committee on Drugs, 2015, p. 3) has had a "consistent and ongoing commitment to the harm minimisation approach". One of the defining features of that approach, which clearly distinguishes it from a zero-tolerance approach, is that it advocates a governmental response to an illegal drug that is proportionate to the harm done by the drug. A policy brief on *Drug use and road safety* that was published in 2016 by the World Health Organisation (WHO) advised that driving after using amphetamines (such as methamphetamine or 'ice') increased the risk of crashing by about 500%, while driving after the use of cannabis increased the risk by less than 30%. There is therefore a real sense in which, on those figures, the harms associated with amphetamine-driving are about fifteen times greater than the harms associated with cannabis-driving. To treat the two offences equally is like subjecting a drink-driver at a BAC of 0.20 to exactly the same penalties as a drink-driver at a BAC of 0.05. It would seem that Australia's "consistent and ongoing commitment to the harm minimisation approach" has failed to have much traction in the area of drug-driving road-safety policy and practice.

It is interesting to note that Professor Ross Homel, whose early work on deterrence theory (Homel, 1988) was instrumental in the introduction of Random Breath Testing (RBT) in Australia, considers that the inclusion of cannabis in Australia's RDT protocols is a disingenuous attempt to prosecute the War on Drugs under the guise of road safety (Hall & Homel, 2007). The findings of this review are consistent with that opinion.

An argument for removing cannabis from RDT programs: Product differentiation

The continued inclusion of cannabis in the RDT protocol could be counterproductive in two ways.

First, it could trivialize drug-driving road safety campaigns and government media releases. For example, when there is a news item such as "Drug-driving peril: Surge in positive detections among P-platers alarms authorities" (The Advertiser, 23 March, 2015), the reader will not know to what extent the 'peril' is due to methamphetamine and therefore of some real concern, or to cannabis and of much less concern. There is a danger of diluting the impact of drug-driving road-safety messages by including cannabis along with much more problematic drugs. This is particularly so in the current context of the previous Prime Minister's initiative to deal with the increasingly evident abuse of 'ice' (crystal methamphetamine) in Australia, through the establishment of a National Ice Taskforce to oversee a National Ice Action Strategy.

In 1987, South Australia became the first Australian state to decriminalize the personal use of cannabis. An argument for that initiative was that decriminalization would "send a clear message that cannabis is not regarded by the authorities in the same way as … drugs such as heroin and amphetamines" (Single, Christie & Ali, 1999, p. 3). It would now be appropriate for "the authorities" to send the same "clear message" in the context of drug-driving.

A second argument for removing cannabis from RDT programs: Human Rights

The second way that the continued inclusion of cannabis in the RDT protocol could be counterproductive was first raised by McDonald (2009). It is the possibility that a legal case could be made that RDT involves an abuse of human rights - especially where cannabis is the only drug involved in an RDT offence. However, human-rights protections are weak in Australia (Ricketts, 2004), and any such litigation would be more likely to be successful in Victoria or the ACT where human rights have some protection under state law. The ACT Human Rights Commissioner believes that significant human-rights issues exist in oral-fluid testing for illicit drugs where there is no reasonable suspicion that the driver is impaired by the drug (Watchirs, 2008). This matter is explored in some detail by Prichard *et al*. (2010) who explain that the RDT laws *prima facie* infringe three human rights: to liberty (by the driver being detained); to refuse self-incrimination (by the driver having to collaborate in his/her own prosecution); and to have

access to legal advice (which is not allowed before undergoing an RDT screening test). However, Pritchard *et al*. go on to explain that the infringement of those rights can be justified if doing so promotes the 'right to life' of other road users. So, there is a balance of human rights. The balance would favor current RDT legislation in relation to a drug such as methamphetamine where there is good evidence that it increases the risk of crashing, but should favor a potential litigant where there is evidence that use of the drug does not result in a meaningful increase in the risk of crashing, as is the case for cannabis.

There are precedents for cannabis being absent from a list of proscribed drugs: in the US states of Minnesota and Wisconsin, where there is a zero-tolerance approach to Driving Under the Influence of Drugs (DUID), cannabis has been exempted (Compton, Vegega & Smither, 2009, p. 13; Canadian Centre on Substance Abuse, 2014, p. 4).

It is concluded that there is no adequate justification for retaining cannabis as a proscribed drug in RDT protocols, and that to do so could decrease the credibility of RDT programs, and possibly trigger human rights controversies.

Inaccurate public information from VicRoads

On their road-safety Internet site, VicRoads had informed the public for many years that "Research shows that after recent use of THC the risk of being killed in a fatal crash is similar to a driver with a BAC of up to approximately 0.15" (see Attachment D). That claim was based on Drummer *et al*'s (2004) findings of a comparatively low OR of 3.7 (1.5-9.1) for BACs in the range 0.10–0.15, along with a very high OR of 6.6 (1.5-28.0) for 'the recent use of THC'. (To their credit, when provided with a draft of this report, VicRoads changed the wording to a more measured version: "Research shows that recent cannabis use increases your crash risk".)

Drummer *et al*'s (2004) findings were shown to be very questionable in Parts 3 and 5 of this report. VicRoads should have situated them in the broader research context, where it would have been evident that the findings were unrepresentative.

The exaggerated former claim by VicRoads can be contrasted with the balanced overview provided by Margaret Prendergast, General Manager, New South Wales Centre for Road Safety, when interviewed on 23 March 2015 by Tracy Bowden for the Australian Broadcasting Commission's 7.30 Report, where she said that "Road Safety authorities in every state are really worried about drug-driving. With cannabis you are about 1.3 times more likely to experience a crash. With amphetamines it's six times. With ecstasy it's about 1.6 times."

The inaccurate provision of public information by VicRoads on the risks of driving after the use of cannabis may have been motivated by the need to justify the Victorian Government's harsh drug-driving penalty structure in relation to the use of cannabis for 'Failing a roadside screening test', as provided in Table 11.1.

Table 11.1: The penalty structure in Victoria for 'Failing a roadside screening test'

Offence	**Penalties as at 16 August 2016**
First drug-driving offence – with an infringement notice	• Fine of $467 • Licence suspension: 3 months
First drug-driving offence – and you have to go to court	• Fine of up to $1,866 • Minimum licence cancellation: 3 months • The court may record a conviction
Second drug-driving offence	• Fine of up to $9,330 • Minimum licence cancellation: 6 months • The court may record a conviction
Third and subsequent drug-driving offences	• Fine of up to $18,660 • Minimum licence cancellation: 6 months • The court may record a conviction

The penalties in Table 11.1 cannot be justified from the road safety perspective in the case of cannabis.

Traffic police in Australia run parallel random and targeted enforcement campaigns. In the targeted campaigns, they have the capacity to give special attention to known drug-driving offenders. It is therefore likely that a known drug user would be caught for repeat offending, and subjected to the heaviest penalties in Table 11.1.

Inadequate public information from other Australian states

Victoria is not the only Australian state to have paid scant attention to the best evidence when providing public information on the risks of cannabis-driving. Table 11.2 presents some typical information on drug driving that is currently available on government road-safety websites across Australia.

Table 11.2: Some examples of public information on the risks of drug-driving

State	**Department**	**Information**	**Type of information**
NSW	Centre for Road Safety	Our research shows that the presence of illegal drugs is involved in the same number of fatal crashes as drink driving.	Prevalence
SA	Motor Accident Commission	Between 2010 and 2014, 21% of drivers/riders killed in road accidents had the presence of illegal street drugs in their system. In 2014, drugs overtook alcohol in the implication in fatalities.	Prevalence
SA	Department of Planning, Transport & Infrastructure	Laboratory testing, driving simulators and 'on road' testing has shown that these drugs can impair performance on driving-related tasks …. These types of drugs have been shown to have the potential to increase the risk of road crashes.	Psychology Epidemiology
WA	Mental Health Commission: *Drugs and Drinking Don't Mix*	Using cannabis affects a person's driving ability by: slowing the driver's reaction time, distorting the driver's perceptions and decreasing ability to coordinate appropriate reactions when driving. Driving while under the influence of cannabis is dangerous and greatly increases risk to the user and others on the road.	Psychology Epidemiology

In evaluating the relevance of such information it should be acknowledged that psychological evidence (such as, "Using cannabis affects a person's driving ability by slowing the driver's reaction time") and evidence about drug prevalences (such as, "the presence of illegal drugs is involved in the same number of fatal crashes as drink driving") are both less informative than epidemiological evidence (such as, "the recent use of cannabis increases the risk of crashing by 30%"). Even then, the quality of the published epidemiological studies is so variable that it is easy for a disingenuous government agency to cherry-pick a finding that is 'fit for purpose' (as discussed in the previous section). The best evidence does not come from individual studies, but from systematic reviews (which may include meta-analyses). But even then, the quality of the published reviews is variable, as discussed previously, with two of the most widely cited reviews (Asbridge, Hayden & Cartwright, 2012; and Li et al., 2013) failing to use ORs that have been adjusted for the effects of confounders. While it may not be easy for a government agency to identify and provide the best evidence available, it is clear from the information in Table 11.2, that very little attempt has been made to do so.

There are two further problems with the typical way that drug-driving information is provided by Australian government agencies. The first is that the messages are often about 'illegal drugs' rather than about a particular drug. From a road-safety perspective, the legal status of a drug is not particularly relevant. The focus on illegal drugs rather than individual drugs is indicative of motivation that springs from the War on Drugs rather than from a genuine interest in road

safety. The second problem is that purported facts are often provided without any attempt to indicate the source of the facts, leaving the inquisitive reader with no way of checking their veracity. It can be seen that Australians are not well served with respect to the provision of drug-driving information from government agencies.

Where to from here?

The aim of this part of the report has been to argue that cannabis should be removed as a proscribed drug from the Australian RDT protocols, because there has never been any satisfactory evidence that the use of cannabis increases the risk of crashing.

It is, however, acknowledged that this radical recommendation is unlikely to be implemented. Accepting that reality, the next part of the report considers the arguments for and against retaining the current zero-tolerance approach to the enforcement of the cannabis-driving offence.

Part 12: Arguments for and against zero tolerance

Duration of impairment for THC

In Part 9 of this report it was argued that the effects of cannabis on driving-related skills are too weak to be of any real relevance to road safety. Nevertheless, the effects are sometimes investigated within a sufficiently long timeframe to give some idea of the duration of any detectable impairments.

With respect to the results of the DRUID meta-analysis (Berghaus *et al*., 2011) that are summarized here in Table 9.1, the DRUID researchers (Hargutt *et al*., 2011, p. 53) concluded that THC has an "impairment that lasts very shortly". While the results in Table 9.1 are somewhat ambiguous, they could be interpreted as implying that the impairing effects of smoking cannabis last for up to four hours.

There are very few post-DRUID studies where the impairing effects of cannabis have been measured repeatedly after administration within a sufficiently long timeframe to give some idea of the duration of any impairment. One such study was reported by Ramaekers *et al*. (2009). The researchers repeatedly tested 12 occasional and 12 heavy cannabis users on a battery of driving-related performance tests over a period of 8 hours after smoking high-dose cannabis cigarettes. For the heavy users, there was no noticeable impairment on the main performance tests at any time after smoking, so there was no opportunity to measure the duration of impairment. Based on that finding, Ramaekers *et al*. (p. 274) concluded that the heavy users, possibly because of their development of tolerance to the effects of cannabis, would probably not be at an increased risk of crashing at any time after smoking. The researchers went on to conclude that most of the on-road exposure of THC-positive drivers would be from the heavy users. It follows that most of the THC-positive drivers on the road at any time would probably not be at an elevated risk of crashing. For the occasional users, there were some performance decrements that peaked during the first hour after smoking and then declined gradually. On three of the five main performance tasks, the impairments were no longer evident at 3 to 4 hours after smoking. On the remaining two tasks, the impairments were no longer evident at 5 to 6 hours after smoking.

As noted previously, Desrosiers *et al*. (2015) undertook a potentially relevant investigation, but failed to find any substantial impairing effects. If the data are interpreted as demonstrating any impairments, they would be present for only the first three hours after smoking (see their Figures 1 and 2).

It is concluded that the patchy evidence on the immediate, acute effects of cannabis on human performance indicates that any impairments are unlikely to last longer than about four hours.

Duration of the pleasurable effects of THC

A number of studies are in good agreement that the duration of the pleasurable psychological effects of smoking marijuana is three to four hours. Menkes *et al*. (1991) repeatedly measured the self-reported levels of 'subjective intoxication' of 13 cannabis smokers over a four-hour period after they had smoked a cannabis cigarette. They found that the effect peaked immediately after smoking, then fell steadily over the next two hours, before reaching a near-baseline level after three hours. Fabritius *et al*. (2013) repeatedly measured self-reported levels of 'intoxication' for 48 frequent or occasional cannabis smokers over a three-and-a-half-hour period after they had smoked a joint of pure cannabis. It was found that intoxication peaked immediately after smoking, then fell steadily over the next hour, before reaching a near-baseline level after about two-and-a-half hours.

A team of researchers affiliated with the U.S. National Institute of Drug Abuse (NIDA) have published a number of studies on the duration of various pleasurable psychological effects following the use of cannabis (Desrosiers *et al*., 2015; Hartman *et al*., 2016; Newmeyer *et al*., 2017b). Desrosiers *et al*. (2015) repeatedly measured self-reported levels of being 'high' for 25

frequent or occasional cannabis smokers over a six-hour period after they had smoked a cannabis cigarette. It was found that the high peaked immediately after smoking, then fell steadily over the next two hours, before reaching a near-baseline level after three or four hours. Hartman *et al*. (2016) repeatedly measured self-reported levels of being 'high', 'stoned', 'stimulated' and 'having a good drug effect' for 19 cannabis smokers over a nine-hour period after they had been administered a controlled dose of vaporized cannabis. Again, it was found that the pleasurable effects peaked immediately after smoking, then fell steadily over the next two hours, before reaching a near-baseline level after about three hours. In the study reported by Newmeyer *et al*. (2017b), twenty subjects were asked to rate the strength of the subjective cannabis 'high', and three other pleasurable feelings, immediately before using cannabis (to obtain baseline measures) and at 0.25, 0.50, 1.5, 2.5, 3.5 and 5.0 hours after. The strength of the pleasurable effects peaked at 0.25 and 0.50 hours after using cannabis, and fell steadily until reaching the baseline level at 2.5 to 3.5 hours after.

These results show that the pleasurable effects from using cannabis last for about three hours, and it seems likely that any impairing effects would have much the same duration.

The window of detection for THC in oral fluid

Australian RDT legislation makes it illegal to drive with any detectable level of THC in either oral fluid or blood. However, blood samples are only taken in relation to RDT operations if the driver is unable to provide a sufficient sample of oral fluid; so the focus in this section of the report is on oral fluid. Nevertheless, it should be noted that blood is the relevant body fluid in relation to the drug-testing of *crashed* drivers; and in South Australia, for example, more driver bloods than oral fluids are tested each year for the presence of drugs (Rositano *et al*., 2016, p. 128). No more will be said about the detection window for THC in blood except to note that Rositano *et al*. (p. 130) mention that the confirmatory cut-off for THC in the blood of South Australian road-crash victims is 2.0 nanograms of THC per milliliter of blood (2.0 ng/mL).

In the Australian RDT protocols, two or more drug-testing procedures for oral fluid are administered sequentially, with one or more screening tests preceding a confirmatory (evidentiary) laboratory analysis. It will normally be the sensitivity of the first screening test that is most relevant to the outcome for the driver, because no confirmatory testing will normally be conducted if the driver tests negative at the first stage. The sensitivity of both the screening and confirmatory tests are continually improving, so it is appropriate to first explore the *potential* window of detection for THC as limited only by the sensitivity of confirmatory testing, before considering the window of detection that actually pertains to the RDT enforcement regimes in Australia, where the potential sensitivity of the available screening and confirmatory tests may not be fully exploited.

The sensitivity of a confirmatory laboratory analysis can be described in terms of either a 'limit of detection' (LOD), which is the lowest concentration of the drug that can reliably be detected, or a higher 'limit of quantification' (LOQ), which is the lowest concentration of the drug that can accurately be quantified. In some of the literature, the lowest level used to confirm the presence of a drug is simply described as the 'cut-off', without clarifying whether it is an LOD or a LOQ. In this report, the term 'cut-off' will be used in relation to confirmatory testing without identifying the cut-off as an LOD or a LOQ. Confirmatory tests for THC typically have cut-offs in the vicinity of 0.5 ng/mL.

Niedbala *et al*. (2001), in their 'Study 1', repeatedly measured THC concentrations in the oral fluid samples of 10 cannabis smokers over a period of 72 hours after smoking "marijuana over a period of 20 to 30 minutes, according to their accustomed manner, with no external control over their smoking patterns" (p. 290). THC was reliably (i.e., consecutively) detectable in seven subjects up to the 16-hour mark and in two up the 24-hour mark, at levels above the 0.5 ng/mL cut-off. Beyond those times, there were some sporadic (i.e., non-consecutive) detections of THC all the way up to the 72-hour mark in four subjects. Unfortunately, the subjects were "under constant supervision" for only four hours, after which time "they were allowed to leave and

return at the designated collection times" (p. 290). Because of that flaw in the experimental design, the findings obtained beyond the four-hour mark are of questionable validity.

Toennes *et al*. (2010) repeatedly measured THC concentrations in the oral fluid samples of 24 cannabis smokers over a period of eight hours after smoking a single standard cannabis joint. THC was detectable in all samples at the eight-hour mark at levels that were well above the 0.5 ng/mL cut-off. Unfortunately, no samples of oral fluid were taken after eight hours, so the full duration of the detection window could not be determined. As the subjects were frequently tested on a set of psychomotor tasks during the eight-hour period, it can be assumed that they did not have the opportunity to smoke marijuana during that time.

A number of papers that deal with the longevity of THC in oral fluid over periods longer than eight hours have been published since 2010 by researchers affiliated with the U.S. National Institute of Drug Abuse (NIDA). Three NIDA studies that monitored subjects for 30 hours or more are discussed below. In the first two studies, the confirmatory laboratory analyses had a cut-off for THC of 0.5 ng/mL, but in the third study the cut-off was 0.2 ng/mL.

The results of the first NIDA study (Lee *et al*., 2011), which involved 28 'chronic' daily smokers of marijuana, and lasted, in the case of some subjects, for up to 33 days, will not be further considered here, as it was effectively replicated in the two subsequent NIDA studies. Another reason for overlooking this study is that, although the subjects resided in a "secure research unit", the researchers concluded (p. 1133) that the results had been contaminated by "new cannabis intake, although we do not know how this could have occurred".

The second NIDA study involved the detection of THC (above a 0.5 ng/mL cut-off) in the oral fluids of 14 frequent and 10 occasional users of cannabis over a period of 30 hours in a closed residential unit, after the subjects had each smoked a single standard cannabis cigarette. This study was reported on by both Anizan *et al.* (2013) and Newmeyer *et al*. (2014). For both the frequent and occasional smokers, THC was detectable in nearly all of them for up to 21 hours after smoking. For the frequent smokers, THC was detectable in the majority of them at the 30-hour time limit (and would have been detectable in some of them for longer). However, for the occasional smokers, THC was detectable in only one of them at the 30-hour limit.

The third NIDA study (Swortwood *et al.,* 2017a) involved the detection of THC, above a 0.2 ng/mL cut-off, in the oral fluids of 11 frequent and 9 occasional users of cannabis for periods of 72 hours in the case of the frequent smokers, and 54 hours in the case of the occasional smokers. The study was conducted in a closed residential unit. Each subject's THC concentration was measured regularly after smoking a single standard cannabis cigarette. (The experimental procedures were repeated for vaporized and oral cannabis administration, but only the results for the smoked cannabis administration are considered here.) From Swortwood *et al's* Figure 3, it can be seen that all of the frequent smokers tested positive for THC for the first 20 hours after smoking, most tested positive up to 40 hours, and about half of them were still testing positive at the 72-hour mark. The detection window was shorter for the occasional smokers. All tested positive for the first 10 hours after smoking, most tested positive up to 20 hours, and one continued to test positive up to 50 hours. However, none tested positive at the 54-hour mark.

An Australian-based study was published in 2015 by Odell *et al*., who are researchers affiliated with the Victorian Institute of Forensic Medicine (VIFM) in Melbourne. They investigated the kinetics in oral fluid (as well as in blood and urine) of THC concentrations in 21 high-dose cannabis users who volunteered to abstain from smoking while they resided in secure detoxification centres in Melbourne for seven days. The confirmatory drug-testing procedures for oral fluids had a cut-off of 1.0 ng/mL (which is double the cut-off level for most of the other studies discussed here). On admission, the subjects were asked when they had last smoked cannabis. With one possible exception of 'clandestine use', they did not smoke at all while they were in the secure accommodation. They were tested only once each day over the seven days. The results are difficult to summarize precisely, because the drug testing was conducted only once a day, and the first test was conducted at different time-delays after the last cigarette was smoked. Nevertheless, it can be concluded that THC was able to be detected in the oral fluid of one of the 21 subjects for up to 78 hours after the last use of cannabis. The detection windows for

the other subjects were shorter: three had windows of 50 or more hours, three had windows of 30 to 50 hours, four had windows of 20 to 30 hours, and the remaining ten had windows of less than 20 hours.

After smoking a cannabis cigarette, the concentration of THC in the oral fluid peaks almost immediately at a very high level that can be well over 1000 ng/mL (e.g., Swortwood *et al*., 2017a, Table 2). The concentration then falls very rapidly over the next hour or so, and less rapidly over the next two or three hours to reach mean level of about 10 ng/mL (with considerable variation around that mean) (e.g., Lee *et al*., 2012, Figure 1). It is the shape of the decay curve beyond the four-hour mark that determines the duration of the detection window for THC by confirmatory testing. Another factor is, obviously, the cut-off level of the confirmatory test (e.g., Swortwood *et al*., 2017a, Figures 1 & 3). As the findings discussed above indicate, the decay curves can have very different shapes for different subjects; with THC levels tending to decay more slowly for more frequent users of cannabis (e.g., Swortwood *et al*., 2017a, Figure 3).

From the studies summarized above, it is clear that almost all cannabis smokers would have detectable levels of THC in their oral fluid for up to 10 hours after smoking, most up to 20 hours, many up to 30 hours, and a few for much longer periods of up to a few days, especially if they are heavy users.

By comparing the detection window for confirmatory analyses of THC in oral fluid with the duration of any impairing effects of cannabis (possibly up to four hours), it is evident that the duration of any impairment is likely to be much shorter than a typical driver's detection window, and vastly shorter for many drivers.

The THC cut-off for oral fluid in Australian RDT programs

As discussed above, currently available **confirmatory** tests for THC typically have very low detection thresholds (cut-offs), in the vicinity of 0.5 ng/mL, which enable the detection of THC in the oral fluid of cannabis users for many hours or days after using it. However, it is possible that Australian state forensic laboratories use higher (more conservative) cut-offs when reporting the presence of cannabis in the context of drug-driving enforcement, which would mean that THC in the oral fluid of cannabis users who are caught in RDT operations might be detected for only a few hours after using it. To come to an understanding of the likely detection window for THC that is relevant to Australian RDT operations, it is necessary to know the confirmatory cut-offs that are used.

The Australian Standard on *Procedures for specimen collection and the detection and quantification of drugs in oral fluid* (AS 4760-2006) was developed to provide guidance on the drug testing procedures that should be adhered to in workplaces and in medico-legal contexts. AS 4760 sets a 'target concentration' of 10 ng/mL to confirm the presence of THC. However, there is no requirement for government road-safety authorities to adopt the confirmatory cut-off that is recommended in the standard.

In a paper describing the first year of operation of RDT in Victoria (2004), Drummer *et al*. (2007, p. 105) reported (p. 105) that "Oral fluid on presumptive positive cases was sent to the laboratory for confirmation with a limit of quantification for THC of 2 ng/mL". Based on that statement, it seems reasonable to assume that the confirmatory THC cut-off was 2 ng/mL in 2004. That is a low level that would be consistent with an RDT detection window for THC of many hours or even days. However, if that were the case, the situation has improved since then. With respect to the operation of the Victorian RDT program from June 2009 to August 2010, Chu *et al*. (2012, Table 1) reported that the confirmatory test, in conformity with AS 4760, had a 'target concentration' of 10 ng/mL. Based on that statement, it seems reasonable to assume that the confirmatory THC cut-off was 10 ng/mL in 2010. When information was recently sought from the Victorian Government about the RDT screening and confirmatory cut-offs, the response was that the Government does not publish specific cut-off levels for its drug-testing regime, however they are prepared to advise that both the confirmatory and screening cut-offs are currently above the levels recommended in AS 4760 (10 ng/mL and 25 ng/mL respectively).

It is likely that the current cut-off level for laboratory confirmation of the presence of THC in the oral fluids of drivers in New South Wales (NSW) is particularly low, because there is reasonable evidence that drivers have been charged with cannabis-driving offences many days after their last use of cannabis (Police v. Carrall, 2016). The likelihood of a low confirmatory cut-off is supported by information provided in a 23 July 2015 letter from the Health Pathology agency in the NSW Government to Greens MP, David Shoebridge to the effect that "Minimum threshold amounts for saliva and blood drug testing are determined based on the capabilities of instrumentation and methodology". The NSW Police seem to agree with that approach. In their RDT Standard Operating Procedures (May, 2015) they note that "The program **DOES NOT** infer impaired driving or driving a motor vehicle under the influence of a drug. The program detects the **PRESENCE** of an illicit drug in a subject's oral fluid".

There is no publically-available information about the current THC cut-off levels for confirmatory RDT testing in any Australian jurisdiction. It is possible that the different jurisdictions have adopted different cut-offs for the purpose of reporting. It also seems likely that at least some of the jurisdictions conform to the 10 ng/mL cut-off as recommended in AS 4760.

Turning now to the sensitivity of the **screening** test: AS 4760 sets a 'target concentration' of 25 ng/mL to screen for the presence of THC. However, as noted above, there is no requirement for government road-safety authorities to use screening equipment with that cut-off.

Across Australia, RDT screening is conducted with a Securetec DrugWipe II Twin, which is distributed by Pathtech. The police in Australia, along with the Managing Director of Pathtech, are secretive about the DrugWipe II Twin's current nominal cut-off for THC. One fact that is known is that the Australian screening device is a member of a family of Securetec DrugWipe screening devices, whose sensitivities keep improving, and that the other members of the family currently have a nominal cut-off for THC of 5.0 ng/mL. However, according to the information recently provided by the Victorian Government, as noted above, the current cut off for the DrugWipe II Twin is above the AS 4760-recommended level of 25 ng/mL.

According to Beirness and Smith (2017, p. 57), the DrugWipe screening devices have been particularly unreliable in their ability to detect the presence or absence of cannabis, which has motivated the Australian police, in consultation with Securetec, to set a high cut-off level for the DrugWipe II Twin to minimize the number of embarrassing false positive results (whereby drug-free drivers are incorrectly classified as having used cannabis).

Drummer *et al*. (2007) evaluated the performance of the DrugWipe screening test that was used in the first year of the Victorian RDT program in 2004. At that time, its nominal cut-off for THC was 30 ng/mL (p. 106). Its performance with respect to false positives (where the screening test indicates that THC is present in oral fluid, but it is confirmed to be absent) was quite good (in accordance with the understanding of Beirness and Smith (2017), as noted above). Of the 13,176 roadside tests performed in 2004, there were only three instances of a false positive result for THC (Table 3). However, the DrugWipe's ability to detect the presence of THC in cannabis-positive drivers was abysmally poor. It correctly detected THC in only 15 of the 13,176 drivers tested (Table 3). Unfortunately, it was not possible for Drummer *et al*. to calculate an accurate false negative (miss) rate for the DrugWipe, because oral fluid was not routinely collected for confirmatory testing if the DrugWipe failed to detect the presence of proscribed drugs. However, oral fluid was collected for confirmatory testing if the DrugWipe screened positive for methamphetamine, and the analysis of those samples was revealing about the inability of the DrugWipe to detect THC. While, as expected, the DrugWipe failed to detect THC in 22 (96%) of the 23 drivers whose confirmed levels of THC were below the DrugWipe's nominal 30 ng/mL cut-off, it also failed to detect THC in 40 (89%) of the 45 drivers whose confirmed levels of THC were above the 30 ng/mL cut-off (p. 108). Many of the failed detections were for high levels of THC – up to 2,330 ng/mL (p. 108).

It is clear that the screening tests used in Victoria at the commencement of their RDT program in 2004 were incapable of detecting THC in most of the THC-positive drivers who were tested, including in many who had very high levels of THC. However, according to Drummer *et al*. (2007,

p. 109), that was not of particular concern to the Victorian road safety authorities because "It was thought that the devices had sufficient sensitivity to detect a number of drivers and hopefully provide a deterrence to the rest of the community". Perhaps that was correct. On the other hand, it is also possible that passing through an RDT station unscathed might have encouraged recent cannabis users to keep driving after using cannabis. It is assumed that the sensitivity of the DrugWipe screening device to THC has improved considerably since 2004.

A recent study by Swortwood *et al.* (2017) confirms that the notion of a strict cut-off value for a screening device is something of a fiction. These researchers investigated the sensitivities of two on-site oral fluid screening tests: the Drager DrugTest 5000 (DT5000) and the Alere DDS2. In their Discussion (p. 140), they observed that "Despite differences in screening cut-offs (5 vs 25 ng/mL of THC for DT5000 vs. DDS2), the two devices exhibited similar performance criteria. Additionally, no significant differences for [the duration of the THC detection window] were observed between the devices". It is obvious that the nominated cut-off values for screening devices are somewhat arbitrary, and that the DrugWipe II Twin could, at least sporadically, detect levels of THC that are well below its current nominal current cut-off (whatever that is).

Whatever the current cut-offs are for RDT confirmatory and screening tests in Australia, the RDT legislation simply refers to the 'detection' of illegal drugs, without specifying cut-off levels, which could potentially be very low, with correspondingly long detection windows. The paternalistic secrecy of the government authorities in regard to the cut-off levels is inappropriate in a society that seeks transparency about government operations, and especially about those operations that pertain to the possibility of committing an offence for which there can be severe consequences. Confusion about the confirmatory and screening cut-offs for THC in Australia, and also therefore about the duration of the THC detection window, is not much helped by advice provided by government agencies across Australia, as exemplified in Table 12.1. No relevant public information is provided by the road safety authorities in Western Australia or Tasmania.

Table 12.1: Public information from Australian State authorities on the RDT detection windows

State	Agency	Advice
NSW	Centre for Road Safety	Illegal drugs can be detected in your saliva by a Mobile Drug Test (MDT) for a significant time after drug use, even if you feel you are OK to drive. The length of time that illegal drugs can be detected by MDT depends on the amount taken, frequency of use of the drug, and other factors that vary between individuals. Cannabis can typically be detected in saliva by an MDT test stick for up to 12 hours after use.
VIC	Alcohol & Drug Foundation (referenced by the TAC)	Whether or not you have a positive test will depend on a number of factors: the size and potency of the dose, other drugs you may have used at the same time, and your body's metabolism. Cannabis: Random roadside drug testing can detect THC (the active ingredient in cannabis) for at least several hours after use. The test cannot generally detect use in previous days or weeks, although there have been reported cases of people testing positive to cannabis a few days after consuming.
QLD	Police	The saliva tests are designed to only react with the active ingredient of the relevant drug. The detection period for the active ingredient in the relevant drug varies depending on factors such as the quantity and quality of the drug that has been ingested, the frequency of use of the drug and the period of time since taking the drug. [No specific information is provided on the detection window for cannabis].
SA	Motor Accident Commission General Manager Road Safety	Michael Cornish said the new campaign tackles the issue of illegal drug use from the perspective of how long a user is likely to be impaired. "Our intention is to arm road users with the facts, and actively encourage them to wait until they are no longer affected before getting behind the wheel. The campaign sends a clear message that RDT can detect the impairing substance in marijuana for at least 5 hours, and maybe longer depending on the person."
SA	Dept. for Planning, Transport & Infrastructure	Brochure: The [DrugWipe Twin] devices used are able to detect THC (the active component in cannabis) for several hours after use. The exact time will vary depending on the amount and potency of the cannabis used and the individual metabolism. Inactive THC residue in the body of a driver from use in previous days or weeks will not be detected.

Variety of drug-driving enforcement regimes

Around the world, jurisdictions differ with respect to both the justification for apprehending a driver for a possible drug-driving offence, and the evidence required to establish that an offence has been committed. Table 12.2 attempts to depict the variety of possible enforcement regimes.

Table 12.2: The variety of enforcement regimes

		Evidence for an offence		
		Behavioral only	Behavioral & Toxicological	Toxicological only (*Per Se*)
Justification for apprehension	Behavioral (DUI)	Type 1	Type 2	Type 3
	None (RDT)	-	-	Type 4

The most common types of enforcement regime outside Australia (Types 1, 2 and 3) require a behavioral justification for apprehending a driver on suspicion of drug-driving. The observed behaviors may involve the mode of operation of the vehicle, such as weaving, or may be the result of the driver being required to undertake a field sobriety test at the roadside. The offences under such regimes are usually referred to as 'Driving under the influence' (DUI), 'Driving under the influence of a drug' (DUID) or 'Driving while impaired' (DWI). For convenience, these regimes will all be referred to as 'DUI'. A far less common type of enforcement regime, known as 'Roadside drug testing' (RDT), requires no justification for apprehending a driver for possibly engaging in drug-driving. Australia is the only country to have implemented large-scale RDT programs, which are conducted *randomly* (RRDT) in all Australian jurisdictions, and also in a way that *targets* likely drug-driving offenders (TRDT) in at least some of the jurisdictions.

The human rights elements in the U.S. legal system prohibit arbitrary detention, so there must always be a behavioral justification for apprehending a possible drug-driver. Consequently, all of the American states have DUI programs, and none has an RDT program. However, the DUI programs differ with respect to the evidence required to substantiate an offence. Because the states prosecutors have often found it tedious or impossible to prove that a driver was impaired under Type1 or Type 2 legislation, the U.S. government, with the support of many drug-driving experts, has strongly promoted the introduction of Type 3 *per se* drug-driving offences (DuPont *et al*., 2012: ONDCP, 2010; Reisfield *et al*., 2012; Voas *et al*., 2013a; Wong, Brady & Li, 2014). As of December 2014, twenty-one States have implemented *per se* DUI offences (GAO, 2015).

The situation in many developed countries is much the same as in the U.S. In 2015, the U.K. government enacted legislation to replace their Type 2 DUI offence with a Type 3 *per se* offence. The stated aim was to "reduce the wasted time, expense and effort involved for the Police, the Crown Prosecution Service and the Courts when prosecutions fail under the existing offence … of driving under the influence of drink or drugs (known as the 'impairment offence') due to the difficulty of proving impairment" (U.K. Department for Transport, 2013, pp. 4-5).

In 2011, nineteen of the twenty-eight E.U. countries had introduced Type 3 *per se* DUI offences, and three were in the process of doing so (Verstraete *et al*., 2011, Table 1).

Other countries are likely to travel down the same path. For example, Canada currently has a Type 2 DUI drug-driving enforcement regime, which is so tedious to manage that there are calls for it to be replaced by a Type 3 *per se* regime (Canadian Centre on Substance Abuse, 2014; Solomon & Chamberlain, 2014).

Although there is a growing consensus in favour of Type 3 *per se* offences, there are some dissenters who believe that impairment should always have to be proven through the direct observation of behavior (e.g., Armentano, 2013b).

Implementation of zero tolerance and impairment-based per se offences

A jurisdiction that has decided to establish *per se* drug-driving offences must make a further decision with respect to any proscribed illegal drug: whether to adopt a 'zero-tolerance' (ZT) approach, whereby it is an offence to have any detectable trace of the drug in a body fluid, or whether to define the offence in terms of one or more above-zero drug concentrations. Jurisdictions that choose the latter option generally do so in the belief that there is good evidence for a relationship between the drug's concentration and its degree of impairment, such that the cut-off concentrations can be described as 'impairment-based limits' (IBLs).

There are variants of the ZT and IBL approaches. For example, a ZT cut-off might actually be set slightly above zero to allow for any accidental passive intake of the drug. And for IBLs, there could be a single threshold cut-off level below which it is assumed that no impairment is likely, or there could be a number of cut-off levels that purportedly correspond to increasing degrees of impairment (as for drink-driving). And there can be hybrid regimes: jurisdictions that target medicinal drugs in their drug-driving programs may consider it appropriate to have an IBL approach for medicinal drugs along with a ZT approach for illegal drugs.

In contrast with the widespread approval for Type 3 *per se* drug-driving offences, there is little agreement as to the appropriateness of implementing a ZT or IBL *per se* regime with respect to illegal drugs. For example, in the U.S., of the fifteen states that had *per se* drug-driving offences in 2010, most (twelve) had ZT regimes (Lacey, Brainard & Snitow, 2010). By contrast, the view in most E.U. countries is that "… for population compliance, the cut-offs should be based on scientific risk analysis" (Verstraete *et al*., 2011, p.9), which means that the IBL *per se* approach is favored. However, because of the paucity of scientific evidence, E.U. jurisdictions that have adopted the IBL approach have had considerable difficulties in actually setting evidence-based cut-offs (Vindenes *et al*., 2012).

The history of the ZT vs. IBL debate in the U.K. reveals the motives behind the two approaches. The U.K. government commissioned Sir Peter North, a professor of law at Oxford University, to conduct a review of its drink- and drug-driving laws. In his report, North (2010) endorsed the 'fundamental principal' that "The law and penalties imposed should be focused on road safety (not on enforcement of wider law or policy on drugs and drink) and should reflect the degree of risk caused by impairment" (p. 5). He concluded that, when the evidence base was sufficient, the government should introduce "a new specific offence of driving with certain controlled drugs in the blood, at, or above, levels at which they are deemed to be impairing" (p. 12).

In 2012, the U.K. government appointed Kim Wolff, a Professor of Addiction Science at King's College, London, to chair an Expert Panel on Drug Driving, whose tasks included "To consider different sources of evidence to help establish the degree of risk associated with specific drugs in relation to road safety" (Wolff *et al*., 2013, p. 12). The Expert Panel recommended a THC threshold of 5 mg/mL in whole blood because "At this concentration, the risks for involvement in, responsibility for, or injury as a result of a traffic accident when driving under the influence of cannabis are significant compared to a driver who has not consumed cannabis" (p. 69).

Despite the strong recommendations of the government-appointed experts in favor of an IBL regime, the government introduced a ZT regime for reasons that are explained in a 2013 report by the U.K. Department for Transport:

> We believe that taking this tough approach to driving after taking these illegal drugs will serve as a strong deterrent to drug driving and will have benefits across Government and society as a whole. We consider that this approach will also have a greater potential to reduce the number of drug drivers and consequently will have the maximum impact in terms of improving road safety. It will bring about consistency in enforcement activities (in that it will be unlawful to drive with these drugs in the body at all in the same way that it is unlawful to possess or supply them at all), and it will help to ensure that members of the public will receive greater protection against the potential harm of these drugs and their misuse. … Setting higher limits would dilute the message to drug drivers, who would perceive

> such limits as meaning that it is "legal" to drive after taking certain amounts of illegal drugs. (pp. 5-6).

Clearly, while the U.K. Department for Transport is partly motivated by the need to improve road safety, it is also using road safety as a means of prosecuting the War on Drugs.

The position reached in the Part 11 of this report is that cannabis should be removed from the Australian RDT protocols. That might not happen. If so, the question arises as to whether the current ZT *per se* offence should be replaced by an IBL *per se* offence. There are two possible types of IBL offence structure that could be implemented: a single threshold-IBL, or a number of IBLs that purportedly correspond to different level of impairment (as, for example, in Norway: Vindenes *et al*., 2012). Only the single threshold-IBL is considered in this part of the report.

Setting a value for a threshold-IBL could, potentially, be justified in terms of epidemiological evidence or laboratory evidence or both. The credibility of those two types of evidence is considered in the next two sections.

Use of epidemiological evidence to set a threshold-IBL for THC

An interdisciplinary working group of international scientists convened in 2004 to identify an appropriate threshold IBL for THC in the blood, based on all of the available epidemiological and laboratory evidence (Grotenhermen *et al*., 2007). With respect to the epidemiological evidence, the group concluded (p. 1913):

> Overall, current epidemiological evidence on the effects of cannabis on accident risk is much less conclusive than for alcohol and must be considered insufficient for deriving a science-based legal limit for THC in blood.

Some years later, the DRUID researchers agreed with that opinion. They noted that most of the crash-related research involved only the *presence* of drugs and not their *concentrations*. It was because of the paucity of crash-based research that the directors of the DRUID program decided to use *laboratory* studies of impairment to establish appropriate IBLs for a variety of medicinal and illegal drugs (Houwing, Mathijssen & Brookhuis, 2012, p. 555; Schulze *et al*. 2012b, p. 5).

The same issue is explored in Part 6 of this report in relation to the risks associated with the use of cannabis, and the same conclusion is reached: epidemiological studies have failed to demonstrate any dose-response relationship between the concentration of THC in a body fluid and crash risk. So there is no satisfactory epidemiological evidence that could be used to set a threshold IBL for THC in any body fluid.

Use of laboratory evidence to set a threshold-IBL for THC

In a submission to the Australian Federal Parliamentary Inquiry into the Effects of Illicit Drugs on Families, the Victoria Police (2007) provided the following reasons for not incorporating IBLs in the Victorian RDT legislation (which set the framework for the rest of Australia):

> The physiological, pharmacological and toxicological aspects of drug use vary according to the circumstance; and the relationship between the level of drug present and the effect on driving cannot be established as easily as for alcohol. … Therefore a strong argument was made … to prohibit driving when an illicit drug such as methamphetamine, ecstasy or cannabis is present *at any level* in the body.

This justification by the Victoria Police for the introduction of ZT rather than IBL-based drug-driving offences has not been influential in the E.U. Under directions from the Council of Europe, the primary purpose of the DRUID research program was to review or conduct laboratory-based research that would identify concentrations of legal and illegal drugs that are equivalent to

particular BACs (such as 0.02, 0.05 and 0.08), so that drug-driving offences with above-zero IBLs might be established (Kruger *et al*., 2011, p. 5; Verstraete *et al*., 2011, p. 7).

Influenced by the findings from this type of research, some E.U. countries, including Germany, Finland and Norway, have introduced *per se* 'Driving Under the Influence of Drugs' (DUID) offences with non-zero IBLs, and penalties that reflect hypothetical levels of impairment. Norway treats illegal and legal drug use the same way, with the 'impairment limits' for each drug being determined by the drug's purported BAC-equivalent concentration (Vindenes *et al*., 2012). There are two impairment limits for each drug: the lower corresponding to a BAC of 0.05, and the higher to a BAC of 0.12.

The arguments in favour of IBL-based drug-driving offences that have been influential in the E.U. have not gained any traction in the U.S., where the National Highway Transport Safety Administration (NHTSA) agrees that drug-driving laws that specify impairment limits are not scientifically justifiable. In a 2009 Report to the US Congress, the NHTSA declared that "… specific drug concentration levels cannot be reliably equated with effects on driver performance", and that "Current knowledge about the effects of drugs other than alcohol is insufficient to allow the identification of dosage limits that are related to elevated crash risk" (Compton, Vegega & Smither, 2009, pp. 4 & 5).

The approach adopted by the NHTSA is supported in a paper by Reisfield *et al*. (2012) titled "The mirage of impairing drug-concentration thresholds". The authors agree that, for most drugs, there is no reliable relationship between the concentration of the drug and the level of impairment. They provide a further argument against attempting to establish IBLs: that the development of drug tolerances means that no plausible high-level IBL for the drug will be high enough to cause impairment in heavy users. Reisfield *et al*. are saying that BAC-equivalent drug concentrations are fictitious and that any drug-driving penalties based on them will be arbitrary.

Within the U.S. there is still general agreement among scientists that the implementation of IBL offences cannot be scientifically justified. From a large-scale study of over 5,000 drivers for whom the concentration of THC could be related to proficiency on various psychomotor tests, Logan, Kacinko and Beirness (2016, p. 3) concluded that "A quantitative threshold for *per se* laws for THC following cannabis use cannot be scientifically supported".

The views of Reisfield and the NHTSA have recently been endorsed by Hedlund (2017, p. 22) in his report to the U.S. Governors Highway Safety Association on *Drug Impaired Driving:*

> *Per se* laws with a limit greater than zero are modelled after alcohol *per se* laws, set at a BAC of 0.08 in the United States. They are apparently straightforward but conceal some thorny issues. The most fundamental is that setting a positive *per se* limit, such as 5 ng/mL for THC, implies that the limit is related to impairment and that all, or most, drivers have their abilities impaired at concentrations above the limit. The scientific evidence to establish such an impairment threshold for drugs simply does not exist, and may never exist.

In a second NHTSA report to Congress, on *Marijuana-impaired driving*, Compton (2017, pp. 11-12) observed that "These [laboratory and simulator] studies are conducted under carefully controlled conditions with precise measurements. Under these conditions even slight changes in performance are often statistically significant. Whether these often small changes in performance are practically significant (i.e., increase the risk of crash involvement) cannot be determined within this research framework". Compton's important distinction between *statistical* and *practical* significance is rarely taken as seriously as it should be by the researchers in the field. Compton (p. 27) also reaffirmed the longstanding NHTSA view that "The poor correlation of THC level in the blood or oral fluid with impairment precludes using THC blood or oral-fluid levels as an indicator of driver impairment". He went on to say (p. 28) that "A number of U.S. states have set a THC limit in their laws indicating that if a suspect's THC concentration is above [a specified] level (typically 5 ng/mL of blood), then the suspect is considered to be impaired. This *per se* limit appears to have been based on something other than scientific evidence".

It would seem that the adoption of *per se* IBLs, as recommended for the U.K. by Wolff and Johnston (2014) and by Wolff *et al.* (2013), and as implemented in a number of E.U. countries, is not based on scientific evidence.

The epidemiological and laboratory evidence used to justify the introduction of IBLs for THC is deficient. It might therefore be concluded, as has been done in Australia, that it is appropriate to have a ZT approach for illegal psychoactive drugs that are known to increase the risk of crashing. In doing so, it has to be acknowledged that ZT is a compromised response to a complex problem, and that not all the offenders who are penalized for a ZT offence will actually have an elevated crash risk at the time of the offence.

The injustice argument against a ZT approach for THC

In the first few sections of this part of the report, the duration of the detection window for THC in oral fluid was compared with the duration of any possible impairment following the use of cannabis, and it was concluded that the majority of drivers who were found in RDT operations to have used cannabis were not impaired by THC at the time. The Australian ZT approach is clearly targeting many cannabis users who present no increased threat to themselves or to other road users. The injustice involved is in stark contrast with the situation for alcohol. The extent of this problem has recently been recognized in New South Wales, where the excessive duration of the detection window for THC has been of concern to the Courts (e.g., Police v. Joseph Ross Carrall, 2016).

A paper that describes the injustice of Australia's ZT approach has recently been published by Quilter and McNamara (2017). They consider (p. 62) that "Drug driving laws should not be used as a *de facto* mechanism for punishing individuals who are suspected of having committed the crime of possession and/or self-administration of an illicit drug". They propose (p. 62) that the police in Australia "have been empowered to test for illicit possession/use in a way that would otherwise be regarded as inconsistent with Australian society's respect for civil liberties and the presumption of innocence".

Outside Australia, it is widely recognized (e.g., Grotenhermen *et al*., 2007; Wolff *et al*., 2013; Lee & Huestis, 2014; Wille *et al*., 2015) that the ZT approach is not an appropriate means of determining a cut-off value for THC in the context of road safety. Where the aim of the drug-testing regime is to identify drivers who might possibly be impaired by very recent drug use, the THC cut-off should be increased well above the ZT level (which might be an appropriate level in other legal contexts where it is necessary only to show that the person has previously used cannabis).

The stance of this report is that, if cannabis is to remain a proscribed drug under RDT legislation, the current ZT cut-off for THC is unjustifiable, and needs to be replaced by a threshold-IBL. Given that there is no adequate epidemiological or laboratory evidence that can be used to set a threshold-IBL for THC, a different approach is required. That approach is explored in the next section.

A pragmatic approach to setting an above-zero cut-off for THC

The pragmatic approach to setting a cut-off value for THC ignores the questionable epidemiological and laboratory evidence that has been used in some jurisdictions to set IBLs. Instead, it makes the plausible assumption that, if THC *did* produce any non-trivial impairments, it would most probably do so for much the same duration as its pleasurable psychological effects.

The pragmatic approach to setting a cut-off value for THC in oral fluid simply comprises identifying the concentration that is typically found at four hours after smoking cannabis. Given the large range of individual differences in THC concentrations at four hours post-use, the cut-off should probably be located near the median. While it is not necessary to identify and defend a particular value in this report, it does seem appropriate to provide a rough estimate. The time-

course of the elimination of THC from oral fluid has been investigated in many studies, and Table 12.3 provides some indicative findings from four of them (Fabritius *et al*., 2013; Lee *et al*., 2012; Menkes *et al*., 1991; Newmeyer *et al*., 2014). From these findings, a concentration of 10 ng/ml would seem to be a reasonable THC cut-off.

Table 12.3: THC concentrations in oral fluid at 3.5 to 6.0 hours after use

First author, Year, Source	N	Delay	THC concentration (ng/ml)
Fabritius 2013, Table 3	23	3.5 hrs	Median = 22; Range = 0 to 140
Lee 2012, p. 750	10	6.0 hrs	Mean = 9.4; Range = 2.1 to 44
Menkes 1991, Figure 1	7	4.0 hrs	Mean = 10; SE Mean = about 2
Newmeyer 2014, Figure 1	14	6.0 hrs	Median = 10

Given that the purpose of the task is now not to identify a potentially impairing level of THC in oral fluid, but rather to find a bio-marker of recent cannabis use, there is no longer any need for THC to be the target substance. What is required is to identify one or more substances, or relationships between substances, that demonstrate a reliable decay pattern following the use of cannabis. Some research teams are currently engaged in that enterprise (Fabritius *et al*., 2013; Lee *et al*., 2012; Lee *et al*., 2015; Moore *et al*., 2007; Newmeyer *et al*., 2014; Swortwood *et al*., 2017). One promising approach involves the analysis of exhaled breath (Coucke *et al*., 2016; Kintz *et al*., 2016).

If the 'recent-use' rationale were to be referenced by Australian road safety authorities in justifying the selected drug cut-off levels, they would be aligning themselves with the rationale adopted by Standards Australia in their *Procedures for specimen collection and the detection and quantification of drugs in oral fluid* (AS 4760-2006), which is that "An oral fluid specimen may be used to establish recent use at a workplace or at the roadside for drivers" (p. 10). In agreement with the stance adopted in this report, the standard goes on to emphasise that "It is not appropriate to relate the presence of drugs in oral fluid to impairment, but rather, to recent use".

Arguments for not providing drivers with information about drug cut-offs

In discussions with the author, some Australian road safety authorities have proffered two different arguments against providing drivers with information about the cut-off levels that are used in the screening and confirmatory tests for the three proscribed drugs. Only the cut-offs for THC are of interest in the context of this report.

The first argument relates to the fact that, unlike the graduated drink-driving laws, the drug-driving laws have zero tolerance for any detectable level of a proscribed drug. Consequently, the publication of thresholds is likely to encourage drug users to attempt to drive with drugs in their system, but remain 'under the limit' for detection. That is considered by the authorities to be unhelpful, because, for both alcohol and drugs, they are trying to motivate the community to "completely separate use from driving".

But that argument by the road safety authorities is misleading. In the case of drink-driving, the authorities are trying to "separate use from driving" only in the sense that they are trying to move towards a zero-BAC limit for driving. The authorities are not trying to prevent people from ever drinking alcohol. Nor is it their business to prevent people from ever using cannabis. So, the corresponding motivation in the case of cannabis-driving should be to prevent people from driving while they could possibly be affected by cannabis. That has nothing to do with zero tolerance. Given the exponential decay curve for THC (Compton, 2017, p. 5), the use of cannabis can, theoretically, be detected *forever* at vanishingly low levels. The zero-BAC equivalent for cannabis should be seen as the level reached at about four hours after using cannabis, by which time the acute effects of using cannabis have completely dissipated.

The second argument from the road safety authorities is that the publication of thresholds could be taken to imply that they are confident about dose-response relationships, where, in fact, the research does not allow for that confidence. The authorities argued that would be unwise provide informed drivers with any reason to consider them ignorant of the relevant research findings.

In responding to that argument, it can be agreed that the relevant research has failed to demonstrate any reliable dose-response relationships between the concentration of THC and either impairment or crash risk. But that potentially embarrassing fact can actually be ignored. As discussed above, a different rationale for setting a THC cut-off is readily available: it is to use a conservative (low) estimate of the THC concentration typically found at about four hours after using cannabis. In overtly referring to that rationale for the cut-off, in jurisdictions where there is a reasonable above-zero cut-off, the authorities do not have to pretend that there is an established dose-response relationship between the concentration of THC and impairment or crash risk. They simply have to acknowledge that, *if* there is any risk pertaining to the use of cannabis, then the risk will only last for up to four hours.

Nobody likes to be treated paternalistically. It seems unlikely that any driver could be harmed by the availability of road-safety-related information. Where that information is relevant to what constitutes a criminal activity, withholding the information from the public could be seen as an affront to natural justice.

Those who proffer paternalistic arguments in support of withholding road-safety information that is relevant to mature decision-making about when it is safe to drive should consider the possibility that their secrecy could be counter-productive. Rogeberg (2017) has presented the following example of how things could go wrong. Because cannabis users are more aware of their possible impairment than alcohol users, they are inclined to refrain from driving immediately after using the drug. But if they have been 'sold' the zero-tolerance message, and believe that they could be punished for drug-driving for up to a day or more after using cannabis, they might weigh up the pros and cons of driving immediately after using cannabis and decide to drive anyway, on the grounds that they might as well be hung for a sheep as for a lamb. In other words, it is plausible, in a jurisdiction with an appropriate above-zero confirmatory THC cut-off (and perhaps that is the situation in most Australian jurisdictions), that the lack of public information about the cut-off could, paradoxically, *increase* the amount of drug-driving at high concentrations of THC.

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Attachment A: ORs for a responsibility analysis vs. a case-control analysis

Consider a worked example of a responsibility analysis using the data in Table A.1. The study involves 1000 crashed drivers from two-vehicle crashes, 600 of whom are responsible for their crashes, while 400 are not-responsible. It is assumed that all drivers were tested for the presence of alcohol, which is the only drug involved. It is assumed that alcohol is detected in 30% of the responsible drivers, but in only 5% of the not-responsible drivers (consistent with alcohol playing a strong causal role in crashing). This data gives an alcohol-crash OR of 8.14 (5.0-13.2).

Table A.1: Numbers of drivers testing positive for alcohol in a responsibility study.

	Crashed Drivers N = 1000		
	Responsible	**Not Resp.**	**Total**
Alcohol +ve	180 (30%)	20 (5%)	200 (20%)
Alcohol -ve	420 (70%)	380 (95%)	800 (80%)
Total	600 (100%)	400 (100%)	1000 (100%)

Calculating the alcohol-crash OR from the responsibility study:

OR = [(Alc+ve Responsible) / (Alc-ve Responsible)] / [(Alc+ve Not-Resp) / (Alc-ve Not-Resp)]
= [180 / 420] / [20 / 380]
= **8.14**

It is now assumed that the responsibility study was embedded in a case-control study (see Table A.2), where the 1000 cases comprise the crashed drivers from Table A.1. However, their status as responsible or not-responsible for the crashes is now not relevant. Alcohol was therefore detected in 20% of the cases. It is assumed that the 1000 control drivers were randomly stopped at the roadside in such a way as to provide 1:1 matching with the case drivers. As for the cases, it is assumed that the 1000 controls were tested for alcohol, which was the only drug involved. Given that the control drivers, like the non-responsible case drivers, are representative of the population of drivers on the roads under the circumstances of the crashes, alcohol will be found in 5% of the controls. The prevalences of alcohol in the cases and controls are consistent with alcohol playing a causal role in crashing. This data gives an alcohol-crash OR of 4.75 (3.4-6.6).

Table A.2: Numbers of drivers testing positive for alcohol in a case-control study

	Cases (Crashed Drivers) N = 1000			**Controls**
	Responsible	**Not Resp.**	**Total**	**N = 1000**
Alcohol +ve	n/a	n/a	200 (20%)	50 (5%)
Alcohol -ve	n/a	n/a	800 (80%)	950 (95%)
Total	n/a	n/a	1000 (100%)	1000 (100%)

Calculating the alcohol-crash OR from the case-control study:

OR = [(Alcohol+ve Cases) / (Alcohol-ve Cases)] / [(Alcohol+ve Controls) / (Alcohol-ve Controls)]
= [200 / 800] / [50 / 950]
= **4.75**

It can be concluded that, when the subjects for responsibility and case-control analyses are drawn from the same overall study, the drug-crash ORs from the responsibility analysis will be larger than from the case-control analysis.

Attachment B: The mismatch problem

The discussion of the mismatch problem is probably best illustrated with a worked example that involves a responsibility study nested within a case-control study. There are 1000 crashed case drivers, 500 of whom were involved in single-vehicle and 500 in multi-vehicle crashes. There are 1000 control drivers who were randomly stopped on the roadside in such a way as to provide 1:1 matching with the case drivers. There are therefore 500 'single-vehicle' and 500 'multi-vehicle controls'. It is assumed that cannabis is twice as prevalent under the circumstances of the single-vehicle crashes. The results have been devised to be consistent with cannabis playing no causal role in crashing (such that the 'true' cannabis-crash OR is 1.00).

Case-control analysis

It is assumed that THC was found in the oral fluid of 20% of the single-vehicle cases and controls, but in only 10% of the multi-vehicle cases and controls. That is a plausible situation given that single-vehicle crashes are more frequent under the circumstances (such as time of day) where cannabis is more likely to be used. These percentages are consistent with cannabis not playing a causal role in crashing. The example is kept simple by not considering the involvement of alcohol or other drugs. This information is provided in Table B.1.

In calculating the case-control OR for THC, the distinction between single-vehicle and multi-vehicle crashes is not relevant because of the 1:1 matching between cases and controls.

Table B.1: Results for the case-control study where cannabis is more prevalent under the circumstances of single-vehicle (SV) than multi-vehicle (MV) crashes

	Cases N = 1000			**Controls N = 1000**		
Crash Type	**SV**	**MV**	**Total**	**SV**	**MV**	**Total**
THC-Positive	100	50	150	100	50	150
THC-Negative	400	450	850	400	450	850
Total	500	500	1000	500	500	1000

<u>THC-crash OR for the case-control analysis:</u>

OR = [(THC+ve Cases) / (THC-ve Cases)] / [(THC+ve Controls) / (THC-ve Controls)]
= [150 / 850] / [150 / 850]
= 1.00

The OR for THC for the case-control analysis is 1.00 (0.8-1.3), which is consistent with THC not increasing the risk of crashing. The ORs for single-vehicle and multi-vehicle crashes considered separately are much the same as for the combined analysis: for the single-vehicle sub-sample, the OR is 1.00 (0.7-1.4), and for the multi-vehicle sub-sample, the OR is 1.00 (0.7-1.5).

Responsibility analysis

If the 1000 cases in the case-control study are assessed for responsibility, the information about the cases can be subjected to a conventional responsibility analysis. Information about the 1000 controls is not relevant to the responsibility analysis. For the purpose of this example, it is assumed that all of the drivers involved in single-vehicle crashes are responsible for their crashes (which is the assumption in some published responsibility studies), and that 50% of the drivers involved in multi-vehicle crashes are responsible (a plausible assumption). It is further assumed that there is no relationship between the presence of THC and responsibility for the multi-vehicle crashes. This information is provided in Table B.2.

In calculating the cannabis-crash OR for a conventional responsibility study, the distinction between single- and multi-vehicle crashes is typically not considered to be relevant.

Table B.2: Results for the responsibility study where cannabis is more prevalent under the circumstances of single-vehicle than multi-vehicle crashes

	Cases N = 1000					
Crash Type	**Single-Vehicle**		**Multi-Vehicle**		**Total**	
Responsibility	**Resp**	**Not-Resp**	**Resp**	**Not-Resp**	**Resp**	**Not-Resp**
THC-Positive	100	0	25	25	125	25
THC-Negative	400	0	225	225	625	225
Total	500	0	250	250	750	250

THC-crash OR for the responsibility analysis:

OR = [(THC+ve Resp) / (THC-ve Resp)] / [(THC+ve Not-resp) / (THC-ve Not-resp)]
= [125 / 625] / [25 / 225]
= 1.80

This example demonstrates that, where cannabis plays no role in crash causation, but where it is also assumed to be more prevalent under the environmental and personal circumstances that pertain to single-vehicle than to multi-vehicle crashes, an exaggerated OR for THC will be obtained from a conventional responsibility analysis that incorporates both single- and multi-vehicle crashes. In this example, where the prevalence of cannabis under the circumstances of single-vehicle crashes has been set to be twice its prevalence under the circumstances of multi-vehicle crashes, the OR has increased by 80% from 1.00 (0.8 to 1.3) to 1.80 (1.1-2.8).

The mismatch problem can be eliminated by restricting the responsibility analysis to multi-vehicle crashes.

THC-crash OR for a responsibility analysis that is restricted to multi-vehicle crashes:

OR = [(THC+ve Resp) / (THC-ve Resp)] / [(THC+ve Not-resp) / (THC-ve Not-resp)]
= [25 / 225] / [25 / 225]
= 1.00

So, by eliminating single-vehicle crashes from the responsibility analysis, the OR for THC is reduced from 1.80 (1.1-2.8) to its true value of 1.00 (0.6-1.8).

Multiple logistic regression

The analyses to this point have been based on counts data. A second possible way of dealing with the mismatch problem in the responsibility analysis is to subject the full set of responsibility-analysis data (as provided in Table B.2) to an MLR analysis. When using only a cannabis-exposure variable to predict crash responsibility, the unadjusted MLR would give an OR of 1.80 (replicating the result above). However, when a covariate is included that codes for the distinction between single-vehicle and multi-vehicle crashes, the adjusted OR will reveal the uncontaminated effect of cannabis on crashing (no effect at all) with a THC-crash OR of 1.00.

For the data in Tables B.2, where 100% of the drivers involved in single-vehicle crashes are deemed to be responsible, a potential problem arises for the responsibility analyses that is known as 'quasi-complete separation' (QCS). For the purpose of this report it is assumed that QCS does not invalidate the results of the MLR. However, it is still advisable to conduct a separate MLR that is restricted to multi-vehicle crashes, for that is the only certain way of dealing with the mismatch problem.

Attachment C: BACs from Drummer *et al*. (2004)

Table C.1 provides estimates of the information that was provided only graphically by Drummer *et al*. (2004) in their Figure 1. The table shows that there are more fatally injured drivers for the highest BAC category (≥ 0.150) than for the lower BAC categories (< 0.150). Table C.1 also shows that alcohol-crash ORs increase steeply with increases in BAC.

Table C.1: Prevalences of All-alcohol drivers by BAC category, and MLR-based ORs from Drummer et al's (2004) responsibility study

BAC Group	Prevalence	OR
0.010 – 0.049	3.7%	1.2
0.050 – 0.099	3.4%	1.7
0.100 – 0.149	5.4%	3.4
0.150 – 0.199	8.3%	9.1
≥ 0.200	12.2%	24.1

The raw data that were analysed to provide the ORs in Table C.1 can be reconstructed, as below.

As a first step, frequencies (N) were obtained for each BAC group by multiplying their prevalences by the total number drivers in the responsibility analyses. That total, as given in Drummer *et al*'s (2004) Table 2, is 3,210. The additional information is provided in Table C.2.

Table C.2: Prevalences, Numbers and ORs for BAC-level groups

BAC Group	Prevalence	N	OR
0.010 – 0.049	3.7%	119	1.2
0.050 – 0.099	3.4%	109	1.7
0.100 – 0.149	5.4%	173	3.4
0.150 – 0.199	8.3%	266	9.1
≥ 0.200	12.2%	392	24.1
Totals	**33.0%**	**1,059**	

Drummer *et al*'s (2004) Table 2, gives the numbers of Responsible (1214) and Not-Responsible (376) drivers amongst the 1,590 drug and alcohol free (THC&AOD-free) 'control' drivers who were involved in the responsibility analyses. Table C.3 extends Table C.2 by including this information, in the bottom row.

Table C.3: The full set of data required to reproduce Drummer et al's (2004) Figure 1

BAC Group	Prevalence	N Resp	N Not-Resp	Total N	OR
0.010 – 0.049	3.7%	95	24	119	1.2
0.050 – 0.099	3.4%	92	17	109	1.7
0.100 – 0.149	5.4%	159	14	173	3.4
0.150 – 0.199	8.3%	257	9	266	9.1
≥ 0.200	12.2%	387	5	392	24.1
All-BAC Total	**33.0%**	**990**	**69**	**1,059**	**4.44**
THC&AOD-Free	**49.5%**	**1214**	**376**	**1,590**	**1.0**

For each BAC group, the numbers of Responsible and Not-Responsible drivers can now be calculated from the available information (the BAC group OR; the total number of drivers in the

BAC group; and the numbers of Responsible and Not-Responsible drivers in the THC&AOD-free control group). The calculated numbers are included in Table C.3. The total numbers of Responsible (990) and Not Responsible (69) alcohol-positive drivers are also included.

An OR can now be calculated for the whole group of the alcohol-positive drivers, as shown below:

<u>All-BAC (for BAC ≥ 0.05) vs. THC&AOD-Free</u>

OR = [(All-BAC Resp) / (THC&AOD-Free Resp)] / [(All-BAC NR) / (THC&AOD-Free NR)]
= [990 / 1214] / [69 / 376]
= 4.44 (3.4-5.8)

In their Table 3, Drummer *et al*. (2004) reported an OR for All-Alcohol of 6.0 (4.0-9.1). The reason that a lower value (4.44; 3.4-5.8) is found here is that Drummer *et al*'s calculations were for BACs extending down to only 0.05, while the value reported here is for BACs extending all the way down to 0.01.

Attachment D: Public Information from the VicRoads Road Safety Website
(Accessed 16 August 2016)

Cannabis & road safety

All forms of cannabis (marijuana) can contain different levels of mind-altering (psychoactive) drugs, the major substance being THC (delta-9-tetrahydrocannabinol), the main active chemical in cannabis. They also contain more than 400 other chemicals.

The THC in cannabis affects many skills required for safe driving:
- alertness
- the ability to concentrate
- coordination
- reaction time

These effects can last up to 24 hours after smoking cannabis. The THC in cannabis use can make it difficult to judge distances and react to signals and sounds on the road.

Research shows that after recent use of THC the risk of being killed in a fatal crash is similar to a driver with a BAC of up to approximately 0.15.

When users combine cannabis with alcohol, the hazards of driving can be much more severe than with either drug alone.

It is illegal to drive while affected by cannabis. There is no safe amount. For information on offences and penalties, see 'drug driving penalties' and 'combined drink and drug-driving penalties'.

Cannabis affects people in different ways

The effects of THC in cannabis depend on factors such as:
- how much is used
- the person's experience with the drug
- the person's physical and psychological state, which can be a complex mix of personal factors and environmental factors
- how long it has been since the person last used cannabis

Mixing drugs increases the danger

Using cannabis with other drugs, including alcohol, can markedly reduce your ability to drive safely. A small dose of cannabis can make the effects of a low BAC much worse. Some medicines, whether prescribed by a doctor or bought from a supermarket or pharmacy, can also increase the effects of cannabis.

Plan ahead

To reduce the risk of a serious accident, do not use cannabis or other drugs if you are going to drive. Make alternative arrangements, such as:
- designate a non-drinking and non-drug taking driver
- hire a taxi
- use public transport
- stay the night (make sure you are not still over the limit in the morning)
- arrange for someone to pick you up

Only accept a lift if you are certain the driver has not been drinking or using other drugs.

State Government of Victoria; Page updated 3 August 2015

Attachment E: Using FARS data to explore the effects of cannabis

The seven studies under consideration

The seven studies listed in Table 2.1 all drew their case drivers from the U.S. Fatality Analysis Reporting System (FARS; see below), in which the determination of the prior use of cannabis is through the toxicological identification of either THC or non-THC cannabinoids. Because these studies all relied on inadequate FARS toxicology, they were excluded from consideration in the main parts of this report. Some of the main features of the studies are listed in Table E.1.

Table E.1: The six studies under consideration in this Attachment

Authors	Year	Fatalities only (F) or Fatalities and Survivors (F&S)	Case-control (C) or Responsibility (R)	Reported a cannabis-crash OR?	Reported a cannabis-alcohol exacerbation effect?
Li, Brady & Chen	2013	F	C	Yes / Redundant	Yes / Redundant
Romano *et al*.	2014	F	C	Yes / Redundant	No
Dubois *et al*.	2015	F&S	R	Yes	Yes
Chihuri, Li & Chen	2017	F	C	Yes	Yes
Romano *et al*.	2017	F	C	Yes	No
Li, Chihuri & Brady	2017	F	R	Yes	Yes
Romano, Voas & Camp	2017	F	R	Yes	Yes

Two of the seven studies are redundant with respect to their cannabis-crash ORs. Li, Brady and Chen's (2013) study was expanded and refined by Chihuri, Li and Chen (2017). Romano *et al*'s (2014) study was refined by Romano *et al*. (2017). Both of the later studies provided re-worked estimates of the cannabis-crash ORs.

Cannabis-alcohol exacerbation effects, as explored in a number of these studies, are discussed towards the end of this attachment.

The studies by Li, Brady and Chen (2013) and Romano *et al*. (2014) were primarily focused on the question of whether *all* psychoactive drugs, considered together, might have an exacerbating influence on the effect of alcohol on crashing. None of the other studies investigated that possible relationship; they focussed on the effects of cannabis only.

Six of the seven studies are from only two research groups. The three that include Guohua Li as the corresponding author are from the Centre for Injury Epidemiology and Prevention (CIEP) at Columbia University. The three that have Eduardo Romano as the first author are from the Pacific Institute for Research and Evaluation (PIRE). The two groups have been involved in very similar research programs, from which they have reached some very different conclusions.

Four of the seven studies are case-control studies, and three are responsibility studies. The case-control studies all drew their control drivers from the 2007 U.S. National Roadside Survey (NRS; see below).

Six of the studies involved only fatally injured drivers. However, Dubois *et al*. (2005) also included drivers who survived their involvement in a fatal crash.

Before having a close look at some of findings, the limitations of the FARS database and NRS 2007 will be explored.

The FARS database in relation to cannabis-crash ORs

Overview of the FARS database

The National Highway Traffic Safety Administration (NHTSA) is an agency of the U.S. government. One of NHTSA's major activities is the maintenance of the Fatality Analysis Reporting System (FARS), which contains the data from a regular annual nationwide census of fatal crashes. To be included in FARS, a crash must involve a motor vehicle traveling on a road that is open to the public, and result in a death within 30 days. FARS has been operational since 1975 and has collected information on more than one million fatal crashes. It has information on over 100 variables that characterizes the crash, the vehicle, and the people involved. FARS data is used by the NHTSA to provide overall measures of highway safety, and to help identify possible crash countermeasures. It has also become a valuable resource for road-safety research in the U.S. and throughout the world.

A major limitation of the FARS database, from the perspective of the current study, is that the FARS variable that codes for the detection of cannabis fails to distinguish between THC and non-THC cannabinoids (Hartman & Huestis, 2014). It is for that reason that the six studies considered in this attachment were not considered in the main parts of this report.

In 2014, NHTSA released a Traffic Safety Facts Research Note titled *Understanding the limitations of drug test information, reporting and testing practices in fatal crashes* (Berning & Smither, 2014) which concluded that the FARS information on drugs is so patchy and inadequate that it cannot legitimately be used to "make inferences about impairment, crash causation, or comparisons with alcohol" (p. 3). And in a companion Research Note that was published the following year, Compton and Berning (2015, p. 1) observed that "Current limitations in the FARS dataset do not allow the calculation of unbiased, reliable and valid estimates of the risk of crash involvement that results from drug use".

The appropriate and inappropriate uses of the FARS database have been summarized by Romano *et al*. (2017), who conclude that:

- The FARS database should not be used to examine trends in drug use
- Neither should it be used to obtain precise estimates of a drug-crash OR
- However, "in some cases and under certain conditions, it could be used to assess the contribution of drugs to fatal crash risk *relative* to other sources of risk".

It would seem that FARS data cannot be used to obtain accurate *absolute* values for drug-crash ORs. However, it is possible that the data could nevertheless be used to obtain valid *relative* ORs for different types of drugs, and perhaps for drugs in relation to alcohol.

The views above, from official NHTSA publications, are supported by Logan *et al*. (2013) and Slater *et al*. (2016), who are particularly concerned by the incompleteness of the FARS information on alcohol and drugs. For example Slater *et al*. (pp. 122-123) commented that:

> Although the majority of FARS data are assumed to be relatively complete, certain variables, including alcohol and drug test results, are admittedly incomplete. In 2013, BAC results were known for 71% of drivers who were killed, and for only 28% of drivers who survived fatal crashes. … Drug test results were available for even fewer drivers: 57% for killed drivers, and 17% for surviving drivers.

The high level of missing information on the presence of drugs led both Logan *et al*. (2013) and Slater *et al*. (2016) to call for major improvements to the ways that drug information is obtained and incorporated into the FARS database.

In a recent personal communication, a senior U.S researcher who is very familiar with the strengths and weaknesses of the FARS database commented that "FARS is a sort of black box regarding drug information. Everything regarding drugs has to be said with extreme caution".

Selection for the likelihood of being affected by a drug

Whenever incomplete data are used in an epidemiological study, the possibility arises that selection biases are operating. As Slater *et al*. (2016, p. 123, paraphrased) observed in relation to some studies that used FARS drug data: "These studies can suffer from a selection bias when the risk factors of interest are associated not only with drugged driving but also with the chance of being selected for drug testing".

In a 2014 NHTSA Research Note, Berning and Smither (pp. 1-2) observed that "Lab tests are costly. A driver is more likely to be tested for drugs if there is information from the crash indicating that drugs may have been a factor". In other words, drivers are targeted for drug testing on the grounds that they are likely to have consumed drugs. The grounds would most obviously include having signs of drug impairment. However, there are many other plausible grounds for targeted testing, such as: being responsible for the crash; having a high BAC; having drug paraphernalia in the car; and being known to the police as a drug user. As described by Slater *et al*. (2016, p. 123): "Medical examiners/coroners and law-enforcement officials may be more likely to request drug testing for drivers who appear more impaired or have characteristics known to be associated with drug-driving (e.g., male, younger)".

That type of targeted selection, which is described here as 'selection for the likelihood of being affected by a drug' is directly relevant to the interpretation of results from case-control studies. Where there is targeted drug testing of case drivers, there will be an over-representation of drug users among the tested drivers (along with an under-representation among the untested drivers - who would normally be omitted from the drug-crash analyses), and a consequent exaggeration of drug-crash ORs.

The responsibility bias

One type of selection bias occurs when drivers are selected for drug testing on the grounds that they are likely to have been responsible for the crash they were involved in. That type of bias is particularly relevant to responsibility studies. Table E.2 provides information on the over-representation of responsible drivers in drug testing from FARS 2013 that is partly extracted from Slater *et al*. (2016, p. 123 & Appendix Table A.3) and partly calculated from the extracted information.

Table E.2: FARS 2013 drug-testing by crash responsibility and survival from Slater et al. (2016)

	Responsible		**Not Responsible**	
	Total N recorded in FARS	**% Drug-tested**	**Total N Recorded in FARS**	**% Drug-tested**
Fatality	6801	58.6%	4006	53.7%
Survivor	12618	23.3%	10871	10.3%
Overall	**19419**	**35.7%**	**14877**	**22.0%**

From Table E.2, it can be seen that substantially more responsible (35.7%) than non-responsible (22.0%) drivers are tested for drugs. In other words, in relative terms, responsible drivers are 38.4% more likely to be tested than non-responsible drivers. When broken down by fatalities vs. survivors, it can be seen that the discrepancy is greater for survivors. There is clearly a selection bias for drug testing in favour of responsible drivers in the FARS database, for both fatalities and survivors, for crashes that occurred in 2013, and presumably for every year that the FARS system has been in existence.

It may not be immediately obvious why the targeting of responsible drivers for drug-testing is likely to affect the size of a drug-crash OR. However, the link is fairly straightforward. Because the targeting is motivated by the need to discover why the responsible drivers caused their

crashes, it will introduce a selection bias for the presence of drugs in the responsible drivers. The over-representation of drugs in the responsible drivers will increase drug-crash ORs for both case-control studies (where the majority of drivers are responsible for their crashes) and responsibility studies (where the excessive presence of drugs in the responsible drivers will again increase drug-crash ORs).

The contaminating effects of the responsibility bias were recognized by Romano, Voas and Camp (2017), who noted that in their sample of 4294 drivers from two-car crashes who were selected from the FARS database for the years from 1993 to 2009, 64.7% were at fault for their crash (where, given the nature of the sampling, an unbiased selection of drivers would have resulted in 50% being responsible for their crash). From that fact, the researchers concluded that "The asymmetric distribution of drug test results between at-fault and not-at-fault drivers, may not be indicative of a drug contribution to the crash, but of officers' decisions to test for drugs only in the at-fault drivers" (p. 42). In other words, the researchers acknowledge that the statistically significant drug-crash ORs that they reported could be artefactual.

The low-testing-rate bias

Romano *et al*. (2014, p. 57) noted that in some U.S. states the toxicological testing of driver fatalities for the presence of drugs other than alcohol is conducted routinely, and at a high level, while in others the testing is done infrequently, and only if requested in relation to court or coronial proceedings. Consequently, two types of drug-testing regime can be distinguished: high rates of relatively untargeted testing; and low rates of relatively targeted testing. Given that targeted testing will produce higher drug prevalences, it follows that the States with lower testing rates should have artificially high drug prevalences, and correspondingly high drug-crash ORs. That type of selection bias will be referred to as the 'low-testing-rate bias'.

Romano *et al*. (2017, p. 322) examined the evidence for the low-testing-rate bias, and found that "The prevalence of drug- and marijuana-positive drivers in the FARS file was significantly higher in the states that routinely *do not* test for drugs (35.3% for any drug; 13.8% for marijuana-positive) than for those that test at least 80% of the drivers in the FARS file (19.9% and 9.3%, respectively)". The researchers concluded that: "in low-testing States, drug-based prevalences and risk estimates are biased upwards".

The applicability of the low-testing-rate bias is presumably not restricted to inter-state differences. The bias is presumably at work wherever there are relatively low testing rates, such as for the survivors of fatal crashes (in comparison with the fatalities). It would therefore be expected that drug prevalences and drug-crash ORs would be artificially increased for the survivors of fatal crashes.

A general principle involved here is that, wherever drug testing is optional (as distinct from routine or mandated), it will be targeted in such a way that drug prevalences and related drug-crash ORs are likely to be over-estimated.

The 2007 U.S. National Roadside Survey in relation to cannabis-crash ORs

Overview of NRS 2007

The four case-control studies listed in Table E.1 all drew their control drivers from the 2007 U.S. National Roadside Survey (NRS). According to Lacey *et al*. (2009a & 2011), the purpose of NRS 2007 was to estimate the prevalence of alcohol and drugs (over-the-counter, prescription, and illegal) in drivers on U.S. roadways. The survey involved randomly stopping drivers at 300 roadside locations across the U.S. Data were collected on weekends at night-time, and on Fridays during the daytime. The information was analysed to develop the first national prevalence estimates of alcohol- and drug-involved driving (Lacey *et al.*, 2009a, 2009b & 2009c).

Roadside data collection for NRS 2007 proceeded in a series of steps beginning with a police officer directing a random sample of drivers into an off-road survey site where an interviewer greeted them, informed them of the right to refuse participation, and obtained the necessary consents. The interviewer then asked some questions and conducted a breath test for alcohol. Participants were then offered $10 to provide an oral fluid sample for drug testing and answer some additional questions on drug use. There were some subsequent procedures that are not relevant in this context.

As indicated in Table E.3, 13,069 vehicles were selected by police officers to participate in the 2007 NRS. Of the selected vehicles, 1,949 (14.9%) ignored the police officer's signal to enter the survey site (having seen pre-signage that a "VOLUNTARY SURVEY" was being conducted). Of the 11,120 drivers who entered the survey site, 10,909 were determined to be eligible for survey participation (drivers were not eligible to participate, if, for example, they were under the age of 16 or could not communicate either in English or Spanish). Of the 10,909 drivers who were eligible to participate, 1,496 (13.8%) did not provide a valid breath sample for alcohol testing. And of the 9,413 drivers who provided a valid breath sample, 1,694 (18.0%) did not go on to provide a valid oral fluid sample for drug testing. Altogether, of the 13,069 drivers who were signalled to enter the survey site, 5,350 (40.9%) did not provide a valid oral fluid sample.

Table E.3: Sequence of events in the 2007 National Roadside Survey

Stages in the 2007 NRS	**N Drivers**
Signalled to enter the survey site	13,069
Stopped and entered the survey site	11,120
Eligible to be surveyed	10,909
Provided a valid breath sample for alcohol testing	9,413
Provided a valid oral fluid sample for drug testing	7,719

Non-response bias in NRS 2007

There would have been many reasons for driver to not proceed from one stage of the survey to the next. For example, the whole survey procedure required about 20 minutes, and many drivers would have had time constraints. Based on various types of evidence, Lacey *et al*. (2011, p. 344) stated that "the lack of time and 'survey saturation' were the most common reasons for refusal". They went on to conclude "that many of those who refused did so for reasons unrelated to substance use". However, that conclusion misses the point, which is whether or not many of those who had used 'substances' were among the 5,350 (from the potential pool of 13,069) who failed to provide an oral fluid sample.

Lacey *et al*. (2011, p. 348) were sufficiently satisfied with the rigour of NRS 2007 to say that "An important feature of this prevalence study is that it has laid the foundation for conducting a relative-risk case-control study for drugs other than alcohol". (The study prefigured here was published as Romano *et al*., 2014). In contrast, when reflecting on the lack of rigour of the roadside surveys that formed part of the multi-national E.U. DRUID case-control studies, Houwing *et al*. (2013, pp. 147 & 149) were less optimistic about the consequences of large non-response rates:

> A large share of non-response in a study increases the likelihood of a selection bias. This selection bias may lead to an underestimation of the share of illicit drug users, since drivers who were positive for illicit drugs can be assumed to be less likely to participate voluntarily because of the risk of being detected positive for drugs in the vicinity of the police who were present at the scene and took care of stopping the drivers. … The non-response rates in the roadside surveys showed … variations [between countries] with a range of between 0% and 52%. In Italy, non-response was non-existent since participation was mandatory. In Lithuania, Belgium and Finland the proportion of non-respondents at the roadside was very high at 25%,

> 48% and 52%, respectively. Based on this information, we assess that there was likely to be an overestimation of the odds ratios for illicit drugs in these three countries.

The NRS 2007 had an overall non-response rate for drugs of 40.9%, which would have been of considerable concern to Houwing *et al*. (2013). It is concluded that is implausible that NRS 2007 provided an accurate picture of the extent of drug-driving, especially with respect to the prevalence of *illegal* drugs.

Because of the 'non-response bias' in NRS 2007, there will be an under-representation of drug users among the tested drivers (along with an over-representation among the untested drivers), such that a case-control study which obtained its controls from NRS 2007 would be expected to over-estimate the value of any drug-crash OR.

Romano *et al*. (2017, p. 318) clearly recognized the nature of this problem:

> The main limitation of the 2007 NRS relates to the voluntary participation of the drivers. Although overall more than 70% of the drivers provided an oral sample, sampling bias in the NRS would exist if a greater proportion of drug-positive than drug-negative drivers were to decline participation in the survey. If the 2007 NRS underestimated the prevalence of drugs, then the crash risk estimates obtained by Li *et al*. (2013) and Romano et al. (2014) would have had an upward bias. Unfortunately, we were not able to examine this potential source of bias.

The likelihood that selection biases are introduced by drawing driver controls from NRS 2007 was also acknowledged by Li, Chihuri and Brady (2017, p. 343) who observed that "In case-control studies, high refusal rates for drug testing in controls recruited through roadside surveys may introduce severe bias to the estimated odds ratios".

Evidence that cannabis increases the risk of crashing

Cannabis-crash ORs from five non-redundant studies

The cannabis-crash ORs from the five non-redundant FARS-based studies are presented in Table E.4 (which re-presents some of the information that was provided in Table 2.2).

Table E.4: Main cannabis-crash findings for the four non-redundant FARS-based studies

Study	Responsibility (R) or Case-Control (C)	N Cannabis drivers contributing to the OR	Counts-based OR For Cannabis Only	MLR-based OR for Cannabis-Only
DuBois *et al*., 2015	R	3,387		1.2 (1.1-1.3)
Chihuri, Li & Chen, 2017	C	694		1.5 (1.2-2.0)
Romano *et al*, 2017	C	~382		1.3 (0.9-1.8)*
Li, Chihuri & Brady, 2017	R	2,409		1.5 (1.3-1.7)
Romano, Voas & Camp, 2017	R	101	1.3 (0.9-2.0)	

*The cannabis-positive variable includes drivers who are also positive to another drug

All five studies have cannabis-crash ORs that are greater than 1.0; and in three of the studies the difference is statistically significant (as defined by the value 1.0 being outside the 95% confidence interval). However, none of the ORs is as high as the widely accepted OR of 2.0 for driving with a BAC of 0.05.

A close look at the two case-control studies

Some of the main features of how the two research groups (Chihuri, Li & Chen, 2017 and Romano *et al*., 2017) selected their case drivers from the FARS database are described in Table E.5.

Chihuri, Li and Chen, (2017) reported a statistically significant cannabis-crash OR of 1.5 (1.2-12.0); while Romano *et al*. (2017) reported a non-significant OR of 1.3 (0.9-1.8).

Romano *et al*. (2017) conducted analyses showing that that the inclusion of the two states that did not test for cannabis (North Carolina and New Mexico) substantially reduced the cannabis-crash OR. It was therefore appropriate that both case-control studies excluded both states.

Table E.5: The coverage of FARS data for driver fatalities in the two case-control studies

Study	**Chihuri, Li & Chen (2017)**	**Romano *et al*. (2017)**
Years covered	2006, 2007, 2008	2006, 2007, 2008
Months covered	FARS months: 20 July – 1 December	All months of the year
U.S. states included	All continental states, but excluding two states that did not test for marijuana, and also excluding Maryland	Only the seven states that participated in NRS 2007, and had drug-testing for at least 80% of driver fatalities; but excluding two states that did not test for cannabis
2 states not testing for cannabis	Excluded	Excluded
Case-level data	Not used	Used
Total N FARS cases	1,944	~1,500 (Not provided)
Cannabis-crash OR	**1.54 (1.16-2.03)**	**1.27 (0.88-1.83)**
Exacerbation effect	Existence supported	Not investigated

Romano *et al*. (2017) also clearly demonstrated the contribution of the low-testing-rate bias by contrasting the cannabis-crash OR obtained when using FARS data from nine of the states with the highest drug-testing rates (over 80%) with the OR obtained when using data from all of the continental States. They found that the adjusted cannabis-crash OR was about 40% higher when using data from all of the continental states. Consequently, they did their best to eradicate the low-testing-rate bias from their own study by restricting the source of their FARS cases to seven of the continental states with the highest drug-testing rates (over 80%). In contrast, Chihuri, Li & Chen (2017) failed to restrict their analyses to the high-testing States. As a consequence, their cannabis-crash OR was inevitably overestimated.

Romano *et al*. (2017) availed themselves of individual-level data from both the FARS database and NRS 2007, such that their statistical adjustments for the confounding covariates could be done at the individual level. In contrast, Chihuri, Li & Chen (2017) used only grouped FARS and NRS 2007 data, such that their statistical adjustments could be done only at the group level, and were therefore less precise. However, it is not clear how the weaker design of Chihuri, Li & Chen's study affected their findings.

The ORs from the two case-control studies (Chihuri, Li & Chen, 2017; and Romano *et al*., 2017) do not provide any satisfactory evidence that the 'true' cannabis-crash OR is greater than 1.0, because the ORs are not large, and they would be expected to be afflicted by the all of the biases that pertain to the selection of FARS cases.

Additionally, the cannabis-crash ORs from the two studies would be expected to be exaggerated by the selection bias that most probably pertains to the selection of NRS 2007 controls. In that context, it is worth repeating Li, Chihuri and Brady's (2017, p.4) comment that "In case-control studies, high refusal rates for drug testing in controls recruited through roadside surveys may introduce severe bias to the estimated odds ratios".

A close look at the three responsibility studies

Dubois *et al*. (2015) reported a statistically significant cannabis-crash OR of 1.2 (1.1-1.3). Li, Chihuri and Brady (2017) also reported a significant OR of 1.5 (1.3-1.7). These ORs do not provide any satisfactory evidence that the 'true' cannabis-crash OR is greater than 1.0, because they are not large; and they are most probably artefactually increased by the bias that pertains to the over-selection of responsible drivers for drug testing, as described above.

The responsibility bias is expected to be particularly strong where low drug-testing rates are involved. Both studies included some low testing rates. Dubois *et al*. (2015) used FARS data for the years 1991 to 2008, while Li, Chihuri and Brady (2017) used data for the years 1993 to 2014. Drug-testing rates were low in the earlier years of those timeframes. Furthermore, as well as including fatally injured *drivers*, Dubois *et al*. (2015) included the drivers who *survived* their fatal crashes, for whom drug-testing rates are very low (see Table E.2).

The third of the three responsibility studies (Romano, Voas & Camp, 2017) deserves some special attention. The drivers, all from California, were selected from the FARS database in a way that should have improved the rigour of the study: Only two-car crashes were involved, and in each crash there was only one responsible and one not-responsible driver. However, there were numerous problems with this study. One was that the responsibility for each crash was assigned by the Californian Police, in such a way as to open the study to the bias arising from non-independent assessments (as discussed in Part 3 of this report). In the words of Romano, Voas and Camp (p. 42) "Limitations on the assignment of crash responsibility should not be ignored. Information on crash responsibility … comes from police reports. It is possible that errors or prejudice could have affected the accuracy of these reports. Issues such as whether the crash … involved alcohol have been shown to affect the officer's assignment of crash responsibility".

The study had a very high rate of exclusion of potential driver fatalities, because of the failure within the FARS system to routinely test for alcohol and drugs. Romano, Voas and Camp (2017, p. 40) noted that only 4,294 (37.9%) of the 11,328 otherwise-eligible drivers had a "known lab result". As noted previously, the inclusions were not random, but strongly favoured responsible drivers, introducing the likelihood of a strong 'responsibility bias' (as defined above).

Another major problem with Romano, Voas and Camp's (2017) study relates to the very unusual way that some of the results are reported. In their Abstract (p. 37) they conclude "We found evidence that, compared with drivers negative for alcohol and cannabis, the presence of cannabis elevates crash responsibility among drivers at zero BACs (OR = 1.89)." That conclusion (despite its awkward wording) seems straightforward: the cannabis-crash OR is 1.89 for the comparison of drivers with cannabis only and drivers who are drug-and-alcohol-free. But that interpretation is wrong. While the control group are drug-and-alcohol-free (as might be expected), 71 of the 172 drivers in the 'cannabis group' had also taken 'Other Drugs'. That is particularly problematic given that the unadjusted OR for Other Drugs (without cannabis or alcohol) is 2.11 (1.7-2.6), while the unadjusted OR for cannabis *alone* (as reported here in Table E4) is a non-significant 1.34 (0.9-2.0). Those unadjusted ORs were calculated from information provided by Romano, Voas and Camp in their Table 2. It is clear that the 'contamination' of the cannabis group of drivers with drivers who have also taken another drug has substantially increased the reported cannabis-crash OR from a value that would presumably be less than 1.34 (after adjustment for demographics), to the reported value of 1.89 (1.3-2.7) (which was adjusted for demographics, but not for the presence of 'other drugs').

Given that the non-significant, unadjusted cannabis-crash OR of 1.34 (0.9-2.0) has most probably been exaggerated by (1) not adjusting for demographic confounders, (2) the problem of non-

independent assessments, and (3) the responsibility bias, it is clear that Romano, Voas and Camp (2017) have failed to provide any evidence that the use of cannabis (alone) increases the likelihood of being responsible for a crash.

The FARS database in relation to exacerbation ORs

A number of biases have been identified above in relation to how FARS cases are selected for drug-testing. While those biases may all act to artefactually increase drug-crash ORs, they are not necessarily relevant to the ORs that represent the exacerbating effect of cannabis on the effect of alcohol on crashing.

High-BAC drivers provide a fertile ground for targeted drug testing

It is a well-established fact that the use of illegal drugs is more prevalent among drivers with higher BACs. For example, Lacey *et al*. (2009c, Table 39) reported that, among those drivers sampled at night-time in NRS 2007, the percentage of drivers testing positive for drugs (for all drugs, but with a large majority being illegal) increased with BAC, from 13.1% at zero BAC, to 23.9% at lower BACs (0.01 to 0.07), to 30.6% at higher BACs (0.08 and above). Further evidence of the strong relationship between illegal drug prevalence and BAC was presented in Part 7 of this report.

Given that the use of drugs is more prevalent among heavy drinkers, it follows that driver fatalities with high BACs should provide a fertile ground for targeted drug testing, especially for a jurisdiction that wanted to go beyond simply providing proof of impairment (for which the high BAC already comprises satisfactory evidence) to demonstrating the possible role of a psychoactive drug in the fatal crash.

The FARS database can be interrogated by anyone with internet access. Table E.6 gives the results of an investigation by the author of drug-testing rates among drivers with known alcohol-test results. The results are given for the three years from 2006 to 2008, and cover all hours of the day and all days of the week. The three selected years are the same as those used by Romano *et al*. (2014), Romano *et al*. (2017) and Chihuri, Li and Chen (2017). The results are broken down by zero, lower (0.07 and below) and higher (0.08 and above) BACs.

It can be seen from Table E.6 that, overall, only about 75% of the alcohol-tested drivers were also tested for drugs. Wherever there is incomplete coverage, it is reasonable to suspect that the excluded drivers are not randomly rejected, but that some systematic selection strategies are involved. Two acknowledged selection strategies are discussed below.

Table E.6: Cannabis results for fatally-injured drivers with known BACs from FARS 2006-2008

FARS 2006-2008	Known alcohol results	Drug-tested (with known results)			Tested positive for cannabis		
	N Alcohol -tested	N Drug-tested	As % of Column Total	As % of Row Total	N With cannabis	As % of Column Total	As % of Drug-tested Row Total
Zero BAC (0.00)	33121	25778	60.5%	77.8%	2249	45.7%	8.7%
BAC (0.01-0.07)	3328	2516	5.9%	75.6%	389	7.9%	15.5%
BAC (0.08-0.50)	20230	14336	33.6%	70.9%	2286	46.4%	15.9%
All BACs (0.00-0.50)	**56679**	**42630**	**100.0%**	**75.2%**	**4924**	**100.0%**	**11.6%**

The first strategy has already been discussed. It involves targeting drivers for whom there is some evidence of impairment. However, if the impairment-testing strategy were the only one involved, it would be expected that drug testing would be more prevalent among the (more impaired) high-BAC drivers, which is not the case. In fact, for the FARS population described in Table E.6, the high-BAC drivers are about 10% (relatively) less likely to be tested for drugs than zero-BAC drivers (70.9% vs. 77.8%).

That paradox can be explained in terms of a second selection strategy, which is discussed by Slater *et al*. (2016, p. 126) in the following passage:

> Drug testing rates were generally lower than alcohol testing rates. … This deserves some discussion, especially in light of recent statements acknowledging the widespread and counterproductive practice of omitting drug testing if a driver's BAC exceeds the legal limit (Berning & Smither, 2014; Logan *et al*., 2013). Because most state statutes do not distinguish between alcohol and drug impairment, and do not have greater penalties for alcohol-plus-drugs as opposed to alcohol alone, and because state criminal justice data systems do not distinguish between alcohol- and drug-related driving offences, there is little incentive to spend resources on drug testing when alcohol tests are positive. This issue applies primarily to surviving drivers who have the potential to face criminal charges for alcohol and/or drug-impaired driving based on these state statutes.

The second strategy is therefore to avoid testing drivers for the presence of drugs if they have already tested positive for illegal levels of alcohol (0.08 and above in the U.S.). That strategy can explain the paradoxically low level of testing of drivers with BACs of 0.08 and above (70.9%).

The two identified selection strategies (targeting alcohol-affected drivers who are likely to be drug-impaired, but overlooking higher-BAC drivers because further evidence of impairment would be redundant) may not immediately seem capable of providing an artefactual explanation for an exacerbation effect. But on further reflection, it can be seen that the two strategies should interact to create an exacerbation effect.

Given that there is sometimes no need to test high-BAC drivers for impairment (because they are already 'legally impaired'), the drug testing is likely to be motivated by curiosity about the role of drugs in the crash. The drug testing is therefore likely to be targeted to drivers who, for one reason or another, are considered likely to have taken drugs. For drivers with known alcohol and drug results, the targeted testing will result in a disproportionately high number of high-BAC drivers with positive drug tests. If those drivers were case drivers in a case-control study, the disproportionality would result in an artefactually increased exacerbation OR.

If the high-BAC drivers were targeted for drug-testing partly on the grounds that they were responsible for causing the fatal crash they were involved in, the more-targeted testing of the responsible drivers would lead to a disproportionate level of positive drug tests among the responsible drivers, and a consequent increase in exacerbation ORs for both responsibility studies and case-control studies (where the majority of drivers are usually responsible for their crashes).

The 2007 NRS in relation to exacerbation ORs in case-control studies

Non-response bias among alcohol-positive NRS 2007 control drivers

An artefactual explanation of an exacerbation effect that was derived from the conduct of NRS 2007 would need to be in terms of a selection bias among drink-drivers against the inclusion of those who had also used cannabis. One potential source of such a bias is immediately evident. The 'leakage' of NRS 2007 participants at various stages of the multi-stage survey is described in Table E.3. Of particular relevance here is the fact that, of the 9,413 drivers who provided a valid breath sample for alcohol testing, 1,694 (18.0%) did not provide a valid oral fluid sample for

drug testing. Given that many of the users of illegal drugs might prefer not to provide hard evidence of their drug-using habits or of their illegal drug-driving behaviours, it could reasonably be expected that there would be a disproportionate leakage of cannabis-positive drivers from the survey at that juncture (despite assurances of confidentiality). Such leakage would lead to an under-representation among drink-drivers of drivers testing positive for cannabis. As a consequence, an exacerbation OR from a case-control study would be artefactually increased.

Evidence that cannabis exacerbates the effect of alcohol on the risk of crashing

Exacerbation effects from the four non-redundant studies

Chihuri, Li and Chen's (2017) case-control study is one of only two published epidemiological studies that has a clearly stated focus, as expressed in its title, on the 'exacerbation' effect (albeit without using that term): *Interaction of marijuana and alcohol on fatal motor vehicle crash risk: A case-control study.* The other is Dubois *et al*'s (2015) responsibility study, which is titled: *The combined effects of alcohol and cannabis on driving: Impact on crash risk.* Both studies reported statistically significant cannabis x alcohol interaction effects.

The two other FARS-based studies to have reported exacerbation effects are both responsibility studies: Li, Chihuri and Brady (2017) and Romano, Voas and Camp (2017).

None of the four studies provided 'exacerbation ORs' (as defined in Part 7 of this report) to quantify the interaction between cannabis and alcohol on the risk of crashing. Instead, they provided different types of evidence, as summarized in Table E.7. However, exacerbation ORs were able to be calculated for two of the studies (Chihuri, Li & Chen, 2017; and Li, Chihuri & Brady, 2017) from the counts data that was provided to the author by Guohua Li. And exacerbation ORs could also be calculated for Romano, Voas and Camp's (2017) study from the counts data that they provided in their Table 2.

Table E.7: Exacerbation effects from the four non-redundant studies

Study	**Wording used by the researchers to describe the evidence for an exacerbation effect**
Dubois et al. (2015)	"Drivers positive for both agents had greater odds of making an error than drivers positive for either alcohol or cannabis only" (p. 94)
Chihuri, Li & Chen (2017)	"A positive synergistic effect on fatal crash risk on the additive scale" (p. 1)
Li, Chihuri & Brady (2017)	"A positive interaction was present on the additive scale" (p. 9)
Romano, Voas & Camp (2017)	"Drivers with a BAC above zero but below 0.05 had a significantly higher culpability odds ratio than drug and alcohol negative drivers only when also positive for cannabis." (p. 41)

A close look at Dubois et al's (2015) responsibility study

In contrast with all of the other FARS-based studies, which involved only fatalities, Dubois *et al*'s (2015) responsibility study involved both fatalities and survivors.

Dubois *et al*. (2015) used FARS data for the years 1991 to 2008. Results provided in their Figure 1 indicate that drug-testing rates were very low in the earlier years of that period. And it is known that drug-testing rates among FARS *survivors* are particularly low. In fact, the overall attrition rate for the Dubois *et al*. study (considering both fatalities and survivors) was 79.2% (with 572,210 of the 722,220 potential subjects *not* being tested for both alcohol and drugs).

As noted previously, Slater *et al's* (2016) descriptive study of FARS data for the year 2013 found that responsible drivers were considerably more likely than non-responsible drivers to be tested

for drugs (see Table E.2). The difference in the timeframes of Slater *et al's* and Dubois *et al*'s (2015) studies is considered unlikely to be relevant to the fact that the rate of drug-testing for FARS drivers is generally higher for responsible than for non-responsible drivers. It follows that Dubois *et al*'s study would be expected to be affected by the 'responsibility bias', as described previously, especially given the high rate of driver attrition.

As reported here in Table 2.2, Dubois *et al*. (2015, p. 94) found a very small, but statistically significant, cannabis-crash OR of 1.16 (1.1-1.3) - which they inaccurately reported as being for 'THC alone' rather than for 'cannabis alone'.

Dubois *et al*. (2015) subjected their FARS data to complex statistical modelling procedures from which they found that cannabis exacerbates the effect alcohol in a way that is different at different BACs. For example, at a BAC of 0.05, the increase in the OR attributable to the co-use of cannabis was estimated to be 0.15, and at a BAC of 0.08 the increase was 0.11. These exacerbation effects are weak. A surprising implication of their statistical model was that, although cannabis has a weak exacerbating effect at lower BACs, it actually has a *protective* effect at moderate to high BACs! In that respect Dubois *et al*'s exacerbation finding is the opposite of that calculated here from Chihuri, Li and Chen's (2017) data, where an exacerbation effect was found to be present at only the *higher* BACs of 0.08 and above (see below).

Given that Dubois *et al*'s (2015) exacerbation effect is vanishingly weak, exists only at lower BACs, and can plausibly be explained by the 'responsibility bias', it is concluded that the researchers have not provided any convincing evidence that the prior use of cannabis exacerbates the effect of alcohol on the likelihood that drivers are responsible for the fatal crashes they are involved in.

A close look at Chihuri, Li and Chen's (2017) case-control study

The basic results from Chihuri, Li and Chen's (2017) case-control study are provided in Table E.8. The counts for cases and controls in the table were absent from their journal article, but were kindly provided by Guohua Li. The unadjusted ORs in the table were calculated from the counts. Some of the unadjusted ORs are not exactly equal to those reported by Chihuri, Li and Chen. The reason, as provided by Guohua Li in a personal communication, is that the research team made some minor miscalculations with respect to some of their unadjusted ORs (but not with respect to any of their adjusted ORs).

Chihuri, Li and Chen's (2017) FARS cases comprise drivers who were fatally injured across the U.S. in 2006, 2007 and 2008, with known BACs and known drug-test results. Their controls were drawn from NRS 2007. In Table E.8, case and control counts are broken down by three BAC groups (zero BAC, lower BACs and higher BACs) and by the presence/absence of cannabis.

Table E.8: Counts of fatally injured case drivers from the FARS database 2006-2008, and controls from the NRS 2007 roadside survey, broken down by BAC groups and the presence/absence of cannabis (from Chihuri, Li and Chen, 2017). Unadjusted ORs have been calculated.

Cannabis	Alcohol (BAC)	Cases	Controls	ORs
Negative	Zero	756	6724	Reference
Positive	Zero	65	395	1.46 (1.1-1.9)
Negative	0.01 to 0.07	125	408	2.72 (2.2-3.4)
Positive	0.01 to 0.07	15	50	2.67 (1.5-4.8)
Negative	0.08 and above	826	123	59.7 (48.7-73.2)
Positive	0.08 and above	157	12	116.4 (64.4-210.4)
	Total	**1944**	**7712**	
Negative	All positive BACs	951	531	15.9 (14.0-18.1)
Positive	All positive BACs	172	62	24.7 (18.3-33.3)

Chihuri, Li and Chen (2017) selected a relatively small number of cases (1,944) from the relevant FARS sub-population of fatally-injured drivers with known alcohol and drug results (42,630; see Table E.6). The reason for the restricted sample was to match their FARS cases with the controls from NRS 2007 with respect to sampling times. Consequently, their FARS case sample was restricted to those drivers who were killed in crashes on weekend nights or during the daytime on Fridays (at times when there is an increased prevalence of alcohol and drug use).

From Table E.8 it can be seen that Chihuri, Li and Chen's (2017) *unadjusted* OR for cannabis alone is 1.46 (1.1-1.9). Some comments were made on their *adjusted* OR for cannabis alone (1.5; 1.2-2.0) in Part 2 of this report.

The main focus of interest in the present context is whether cannabis exacerbates the effect of alcohol on the risk of crashing. Using the two-step procedure (as described in Part 7 of this report) it can be seen from the information in Table E.8 that the OR for the combined effect of cannabis and all non-zero levels of alcohol on the risk of crashing (24.7; 18.3-33.3) is greater than the OR for the effect of alcohol alone (15.9; 14.0-18.1). Given that the two 95% confidence intervals do not overlap, it can tentatively be concluded that an exacerbation effect has been demonstrated for all positive BACs.

Using the single-step procedure (as also described in Part 7) gives an exacerbation OR of 1.55 (1.1-2.1) for all positive BACs, as shown in Table E.9. Given that the 95% confidence interval does not include the value 1.00, it can again tentatively be concluded that an exacerbation effect has been demonstrated for all positive BACs.

Table E.9: Exacerbation ORs by BAC level for Chihuri, Li and Chen (2017)

Alcohol (BAC)	**Exacerbation OR**
Zero	1.46 (1.1-1.9)*
0.01 to 0.07	0.98 (0.5-1.8)
0.08 and above	1.95 (1.1-3.6)
All positive BACs	1.55 (1.1-2.1)

*Not usually described as an 'exacerbation OR'

From Table E.9, it can be seen that the exacerbation OR of 0.98 (0.5-1.8) that relates to lower-range BACs has a value less than 1.0, indicating that there is no exacerbation effect at those BACs. However, the exacerbation OR of 1.95 (1.1-3.6) that relates to higher-range BACs has a value greater than 1.0, with a 95% confidence interval that does not include the value 1.0, indicating that there is an exacerbation effect at those BACs. So, if there is a real exacerbation effect at work here, it is apparently operating only at the higher BACs of 0.08 and above.

Chihuri, Li and Chen (2017, pp. 3-4) reported finding a "significant interaction on the additive scale for the combined BAC levels, and for the separate BAC levels". They explained the nature of their interaction as being "a departure from additivity, i.e., whether the joint effects of alcohol and marijuana were in excess of the sum of their individual effects". Their finding of a supra-additive effect at low BACs was not replicated here using a different statistical approach. Their low-BAC supra-additive effect was quite weak, and they failed to provide a confidence interval for it; so it is not absolutely clear that they did find a real supra-additive effect at the low BACs. While their measure of cannabis-alcohol interaction is not exactly equivalent to an exacerbation effect as defined in Part 7 of this report, the difference should not be relevant to the findings reported here, because the evidential bar has been set low in this review through the way that the exacerbation effect is defined. In other words, where there is evidence of a 'positive synergistic effect on the additive scale', there should also be evidence of an exacerbation effect. It is unclear therefore why Chihuri, Li and Chen's apparent demonstration of a low-BAC supra-additive effect was not replicated here as a low-BAC exacerbation effect.

The finding of a real exacerbation effect at the higher BACs is still not proven, because the high-BAC artefact could be operating within that extensive range. It was noted in Part 7 of this report that strong evidence for an exacerbation effect could only be provided by a fine-grained analysis of the results by BAC levels. If, for example, exacerbation effects could be demonstrated for BAC ranges of 0.08 to 0.15, 0.16 to 0.25 and 0.26 and above, it might reasonably be concluded that real exacerbation effects had been discovered. Without such evidence, it remains possible that the high-BAC exacerbation effect obtained from Chihuri, Li and Chen's (2017) data is nothing more than the high-BAC artefact in disguise.

The statistically significant higher-BAC exacerbation OR of 1.95 (1.1-3.6) reflects a disproportionate (compared with the controls) number of fatally-injured case drivers from the FARS database for whom there is toxicological evidence of both high levels of alcohol and the presence of cannabis (16.0% vs. 8.9%; as given in Table E.9). One possible explanation for the over-abundance is that cannabis genuinely exacerbates the effect of alcohol on the risk of crashing (as assumed by Chihuri, Li & Chen, 2017). It is also possible that the overabundance is, at least to some extent, a result of the high-BAC artefact (as discussed above). However, there are two further plausible artefactual explanations for the overabundance. One relates to the selection of cases, and the other relates to the selection of controls. Both have been described above, and are therefore only briefly revisited below.

The artefactual explanation that relates to the selection of cases is based on the fact that high-BAC drivers provide a fertile ground for targeted drug testing. In that regard, it is interesting to note that a statistically significant exacerbation effect could be found only for higher-range BACs, which is consistent with the 'fertile-ground bias'.

The artefactual explanation that relates to the selection of controls is based on the fact that not all of the drivers who were tested for alcohol proceeded to be tested for drugs. If the attrition rate were higher for the cannabis-positive drivers at the higher BACs (consistent with the control-group prevalences in Table E.9) then the high-BAC exacerbation OR would be artefactually increased.

It is concluded that Chihuri, Li and Chen (2017) have not provided satisfactory evidence that the prior use of cannabis exacerbates the effect of alcohol on the risk of crashing. They have certainly not provided any evidence for such an effect at low BACs.

A close look at Li, Chihuri and Brady's (2017) responsibility study

The basic results from Li, Chihuri and Brady's (2017) responsibility study are provided in Table E.10. The counts for the responsible and not-responsible drivers in the table were absent from their journal article, but were kindly provided by Guohua Li. The counts are broken down by three BAC groups (zero BAC, lower BACs and higher BACs), and by the presence/absence of cannabis. The unadjusted ORs in the table were calculated from the counts.

Li, Chihuri and Brady's (2017) FARS drivers were killed during the 22 years from 1993 to 2014. They all had known BACs and known drug-test results. The responsible and not-responsible driver-pairs were all killed in two-vehicle crashes, where one of the drivers was clearly responsible for the crash and the other was an innocent victim. Those restrictive selection criteria resulted in a very high level of driver attrition. Of the 133,299 potentially relevant two-vehicle crashes, there were only 17,360 (13.0%) for which there were known drug-testing results for both drivers. With an 87.0% rate of attrition, it might be expected that there would be strong selection biases in operation. In some of the 17,360 two-vehicle crashes, both drivers were at least partly responsible. The analyses were therefore based on 14,742 crashes which involved one clearly responsible and one clearly not-responsible driver.

From Table E.10 it can be seen that Li, Chihuri and Brady's (2017) *unadjusted* OR for cannabis alone is 1.66 (1.5-1.8). Some comments were made on their *adjusted* OR for cannabis alone (1.5; 1.3-1.7) in Part 2 of this report.

Table E.10: Counts of fatally injured responsible and not-responsible drivers from Li, Chihuri and Brady (2017). Unadjusted ORs have been calculated.

Cannabis	Alcohol (BAC)	Resp	Not-Resp	OR
Negative	Zero	9,663	12,595	Reference
Positive	Zero	910	716	1.66 (1.5-1.8)
Negative	0.01 to 0.07	662	588	1.47 (1.3-1.6)
Positive	0.01 to 0.07	153	81	2.46 (1.9-3.2)
Negative	0.08 and above	2885	668	5.63 (5.2-6.1)
Positive	0.08 and above	464	82	7.38 (5.8-9.3)
	Total*	**14,737**	**14,730**	
Negative	All positive BACs	3,547	1,256	3.68 (3.4-3.9)
Positive	All positive BACs	617	163	4.93 (4.1-5.9)

*5 resp. and 12 not-resp. drivers had missing BACs, such that the totals do not sum to exactly 14,742

However, the main interest in the present context is whether cannabis exacerbates the effect of alcohol on the risk of crashing. Using the two-step procedure it can be seen from the information in Table E.10 that the OR for the combined effect of cannabis and all non-zero levels of alcohol on the risk of crashing (4.93; 4.1-5.9) is greater than the OR for the effect of alcohol alone (3.68; 3.4-3.9). Given that the two 95% confidence intervals do not overlap, it can tentatively be concluded that an exacerbation effect has been demonstrated for all non-zero levels of alcohol.

Using the single-step procedure gives an exacerbation OR (for Cannabis+Alcohol vs. Alcohol-only) of 1.34 (1.1-1.6) for all non-zero levels of alcohol, as shown in Table E.11. Given that the 95% confidence interval does not include the value 1.00, it can again tentatively be concluded that an exacerbation effect has been confirmed.

Table E.11: Exacerbation ORs by BAC level for data from Li, Chihuri and Brady (2017)

Alcohol (BAC)	Exacerbation OR
Zero	1.66 (1.5-1.8)*
0.01 to 0.07	1.68 (1.3-2.2)
0.08 and above	1.31 (1.0-1.7)
All non-zero BACs	1.34 (1.1-1.6)

*Not usually described as an 'exacerbation OR'

From Table E.11, it can be seen that the exacerbation OR of 1.68 (1.3-2.2) that relates to lower-range BACs has a value greater than 1.0, with a 95% confidence interval that does not include the value 1.0, indicating that there is an exacerbation effect at lower BACs. Similarly, the exacerbation OR of 1.31 (1.0-1.7) that relates to higher-range BACs has a value greater than 1.0, with a 95% confidence interval that has a lower bound of just over 1.0, indicating that there is marginal evidence for an exacerbation effect at higher BACs. These findings contrast with those from Chihuri, Li and Chen's (2017) case-control study, where there was no evidence for an exacerbation effect at the lower BACs.

Using their own particular approach to the demonstration of an interaction between cannabis and alcohol (as noted above), Li, Chihuri and Brady (2017, p. 345) reported that a "positive interaction was present on the additive scale". Their supra-additive interaction effect was shown to be statistically significant for all non-zero levels of alcohol considered together. However, they did not report separate significance tests for the lower (0.07 and below) or higher (0.08 and above) BACs.

The analyses undertaken as part of this review, and reported in Tables E.10 and E.11 did not take advantage of the pairwise nature of the dataset. However, Li, Chihuri and Brady (2017) did

employ a pairwise analysis, which would have increased their effect sizes and the statistical significance of their findings.

The statistically significant all-BACs exacerbation OR of 1.34 (1.1-1.6) reflects a disproportionately high number of fatally-injured responsible FARS drivers, compared with non-responsible FARS drivers, for whom there is toxicological evidence of the presence of both alcohol and cannabis (14.80% vs. 11.5%; as given in Table E.11). One plausible explanation for the modest over-abundance is that cannabis genuinely exacerbates the effect of alcohol on the risk of crashing (as assumed by Li, Chihuri & Brady, 2017).

However, the 'responsibility bias' (as discussed above) provides a further plausible explanation for the overabundance: If the FARS drivers were targeted for drug-testing partly on the grounds that they were responsible for causing the fatal crash they were involved in, the more-targeted testing of the responsible drivers would lead to a disproportionate level of positive drug tests among the responsible drivers, and a consequent increase in an exacerbation OR. . Given the massive attrition rate in Li, Chihuri and Brady's (2017) study, it would be expected that any such selection bias would be strongly expressed.

Given that the all-BACs exacerbation OR is not very large (1.34; 1.1-1.6), and that its presence can plausibly be explained by the 'responsibility bias', it is concluded that Li, Chihuri and Brady (2017) have not provided any convincing evidence that the prior use of cannabis exacerbates the effect of alcohol on the likelihood that drivers are responsible for the fatal crashes they are involved in.

A close look at Romano, Voas and Camp's (2017) responsibility study

The main results from Romano, Voas and Camp's (2017) responsibility study are provided in Table E.12. All of the fatally injured drivers had known BACs and drug results. The counts for responsible and not-responsible drivers, which are broken down by four BAC groups and by the presence/absence of cannabis, are taken directly from Romano, Voas and Camp's Table 2. The unadjusted ORs in Table E.12 were calculated directly from the counts.

Table E.12: Counts of fatally injured Responsible and Not-Responsible drivers from Romano, Voas and Camp, (2017). Unadjusted ORs have been calculated.

Cannabis	Alcohol (BAC)	Resp	Not-Resp	Total	ORs
Negative	zero	1398	1085	2483	Reference
Positive	zero	64	37	101	1.34 (0.9-2.0)
Negative	Below 0.05	76	70	146	0.84 (0.6-1.2)
Positive	Below 0.05	12	4	16	2.32 (0.7-7.2)
Negative	0.05 to below 0.08	47	24	71	1.52 (0.9-2.5)
Positive	0.05 to below 0.08	11	1	12	8.54 (1.1-66.2)
Negative	0.08 and above	517	99	616	4.05 (3.2-5.1)
Positive	0.08 and above	56	7	63	6.21 (2.8-13.7)
Negative	All positive BACs	640	193	833	2.57 (2.2-3.1)
Positive	All positive BACs	79	12	91	5.11 (2.8-9.4)

From Table E.12 it can be seen that Romano, Voas and Camp's (2017) unadjusted OR for cannabis is 1.34 (0.9-2.0). Some comments were made on that OR in Part 2 of this report.

However, the main focus of interest in the present context is whether cannabis exacerbates the effect of alcohol on the risk of crashing. Using the two-step procedure (as described in Part 7 of this report) it can be seen from the information in Table E.12 that, for each BAC category, there is a larger unadjusted OR for the combined effect of cannabis and alcohol than for alcohol alone. However, because of the small numbers involved, there is considerable overlap between the 95%

confidence intervals at all BAC levels, and it cannot be concluded that there is any convincing evidence for an exacerbation effect at any BAC level. When the results are combined for all positive BACs, the unadjusted OR for the combined effect of cannabis and alcohol on the risk of crashing (5.11; 2.8-9.4) is greater than the unadjusted OR for the effect of alcohol alone (2.57; 2.2-3.1). Because there is now very little overlap between the two 95% confidence intervals, it might be concluded that there is some borderline evidence for an exacerbation effect.

Applying the single-step exacerbation-OR calculations (as also described in Part 7) to the counts data provided in Table E.12 gives the unadjusted exacerbation ORs provided in Table E.13, for each BAC level separately, and for all positive BACs combined.

Table E.13: Unadjusted exacerbation ORs by BAC level for data from Romano, Voas and Camp, 2017

Alcohol (BAC)	Exacerbation OR
Zero	1.34 (0.9-2.0)*
Below 0.05	2.76 (0.9-9.0)
0.05 to below 0.08	5.62 (0.7-46.1)
0.08 and above	1.53 (0.7-3.5)
All positive BACs	1.99 (1.1-3.7)

*Not usually described as an 'exacerbation OR'

While none of the individual unadjusted exacerbation ORs for each of the three above-zero BAC levels in Table E.13 is statistically significant (as determined by a 95% confidence interval that does not include the value 1.0), the unadjusted exacerbation OR for all positive levels of alcohol combined is statistically significant (1.99; 1.1-3.7).

It can be seen that the highest (albeit not statistically significant) individual unadjusted exacerbation OR (5.62) occurred for the BAC range from 0.05 to below 0.08. Romano, Voas and Camp (2017, p. 41) reported roughly comparable findings from their MLR analysis:

> Among at-fault drivers, the prevalence of cannabis is higher at intermediate BACs [from below 0.05 to below 0.08] than at the extremes [zero, and 0.08 and above], albeit not statistically different. The elevated presence of cannabis among at-fault drivers at intermediate BACs also provides some support to the hypothesis that the use of cannabis contributes to crash responsibility in crashes in which the level of alcohol is under the legal threshold (BAC = 0.08).

However, given that Romano, Voas and Camp's (2017) bizarre definition of cannabis-positive drivers included many who tested positive for both cannabis and another drug (as discussed above), it is not possible to come to a clear interpretation of their results.

Given the borderline level of the evidence from Romano, Voas and Camp's (2017) study for a low-BAC exacerbation effect, and the many identified problems with their research design, it is concluded that their study does not provide credible evidence that the combined use of cannabis and alcohol exacerbates the risks associated with the use of alcohol.

The Victorian 'cocktail offence'

The Victorian Government has devised a special category of road safety offence for the combined use of any proscribed illegal drug and alcohol, which can be described as a 'cocktail offence'.

The findings of Li, Brady and Chen's (2013) FARS- and NRS 2007-based case-control study were cited by the responsible minister when announcing the establishment of the cocktail offences: "When drivers combine alcohol and illicit drugs they are on average *23 times more likely to be killed* in a crash compared with drivers who are drug and alcohol free" (Parliament of Victoria, 2014). That statement, of course, makes little sense on its own, as the OR of 23 could be due to

the alcohol alone. However, the implication of the statement is presumably that cannabis has been shown to exacerbate the effects of alcohol on the risk of crashing.

In their Abstract (p. 205), Li, Brady and Chen claimed that their results "indicate that drug use is associated with a significantly increased risk of fatal crash involvement, particularly when used in combination with alcohol". They found that the OR for the effect of all psychoactive drugs alone was 2.2 and for alcohol alone was 13.6. They then observed that the *OR of 23.2* for the effect of combining drugs with alcohol was greater than the sum of the component effects. So, they concluded that there was an interaction effect between drugs and alcohol whereby the combined effect was greater than the sum of the part-effects. The dangers of that logic have been discussed in this report in the context of the high-BAC artefact.

However, the reason for discussing the cocktail offence is not primarily to question the merits of introducing the offence (although there is some evidence, contrary to the findings of Li, Brady and Chen [2013], that psychoactive drugs in general do not exacerbate the effect of alcohol on the risk of crashing); rather, it is to question the merits of including *cannabis* as one of the drugs that can be involved in committing a cocktail offence. The evidence provided in Part 7 of this report and in this Attachment clearly indicates that cannabis has not been shown to exacerbate the effect of alcohol on the risk of crashing. It is concluded that there is no sound epidemiological evidence to support the inclusion of cannabis as a proscribed drug for the purpose of committing a cocktail offence, and that the Victorian legislation cannot be justified in that respect.

Some of the penalties relating to cocktail offences are severe, as shown in Table E.14. (Information on the requirement to have an alcohol ignition interlock fitted is not provided).

Table E.14: The penalty structure in Victoria for cocktail offences as at 16 August 2016

Offence	**Drink-driving *per se* penalties**	**Cocktail *per se* penalties**
First offence BAC 0.07 – 0.10	A fine (unspecified) Disqualification 6 months	A fine of up to $4,665 Disqualification 12 months min.
First offence BAC 0.15 or more	A fine (unspecified) Disqualification 15 months min. No vehicle impoundment	A fine of up to $4,665 Disqualification 21 months min. Possible vehicle impoundment 30 days
Second offence BAC 0.07 – 0.10	A fine (unspecified) Disqualification (unspecified) No vehicle impoundment	A fine of up to $13,995 Disqualification 24 months min. Possible vehicle impoundment 30 days
Second offence BAC 0.15 or more	A fine (unspecified) Disqualification 30 months min. No vehicle impoundment	A fine of up to $27,990 Disqualification 42 months min. Possible vehicle impoundment 30 days
Third offence BAC 0.07 – 0.10	A fine (unspecified) Disqualification (unspecified) No vehicle impoundment	A fine of up to $27,990 Disqualification 24 months min. Possible vehicle impoundment 30 days
Third offence BAC 0.15 or more	A fine (unspecified) Disqualification 30 months min. No vehicle impoundment	A fine of up to $41,985 Disqualification 42 months min. Possible vehicle impoundment 30 days