APPENDIX A

**Translating research into policy: An example from New South Wales**

In 2015, the state of Victoria was the first Australian jurisdiction to introduce ‘cocktail offences’ for driving after the combined use of alcohol and an illegal drug (cannabis, methamphetamine or ecstasy). The VicRoads (n.d.) website provides advice on the dangers of driving after the combined use of cannabis and alcohol: “Research shows that you increase your risk of crashing if you drive soon after taking cannabis, and if you combine cannabis with alcohol, the risk of crashing is higher than with either drug alone”.

New South Wales (NSW) followed suit in 2021 by establishing cocktail offences for the combined use of alcohol with cannabis, methamphetamine, ecstasy or cocaine (NSW: Legislative Assembly, 10 Feb 2021; NSW: Legislative Council, 18 Feb 2021). The scientific evidence provided to the NSW members of parliament by the NSW Centre for Road Safety in support of the cocktail-offences Bill comprised only one ambiguously expressed claim, which was cited by most of the participants in the parliamentary debates relating to the Bill in the lower and upper houses. Two examples are provided:

In his second reading speech to the lower house (NSW: Legislative Assembly, 10 Feb 2021: 5333), the Minister for Transport and Roads said:

Research has shown – a statistic that completely and utterly blows my mind – that the combination of drugs and alcohol increases the risk of a fatal crash by 23 times.

The spokesperson for the Opposition in the upper house also supported the Bill, in these terms (NSW: Legislative Council, 18 Feb 2021: 5104):

The Opposition is satisfied that the Bill is tied to risk factors. One of the facts that the Minister put on the table in his second reading speech was that research has showed the effects of combining drugs and alcohol increases the risk on the road by 23 times. ... I thank the team from the NSW Centre for Road Safety, some of whom are in Parliament today, for their work in providing that evidentiary basis. ... That single fact, that a combination of alcohol and drug driving increases the probability of causing a problem by 23 times, is persuasive.

The low level of scientific literacy evidenced by these and related comments in relation to the ‘23-times claim’ is lamentable. First, the claim that the risk of crashing is increased by 23 times is meaningless without being told the nature of the baseline risk. The crash risk from the use of psychoactive drugs with alcohol is certainly *not* 23 times greater than the risk from the use of alcohol alone. Presumably, one is supposed to assume that the baseline comprises the risk for a driver who has not used either drugs or alcohol. But the question then naturally arises as to the relation between the risk for combined use versus the risk for alcohol alone. In other words, the question arises as to whether there has been an exacerbation effect.

Second, the statement does not specify which drug or drugs are being combined with alcohol. Does the precise number 23 apply to *every* psychoactive drug? Does it apply to medicinal drugs such as benzodiazepines? And, in particular, does it apply to cannabis?

Third, the source of the information is not provided. The number 23 is treated as though it were a universally accepted number, rather than a speculative estimate from a particular epidemiological study.

Fourth, the number 23 is obviously cherry-picked to serve the intended purpose. There is no indication of how this number relates to comparable findings from the relevant literature. The reference to single studies rather than to review papers can be a sign of indifference to the broad body of relevant evidence.

We mentioned in the Introduction that a 2013 paper by Li *et al*. would be discussed later; and this is the appropriate place, because Li *et al’s* paper is the source of the 23-times claim. As noted above, the study by Li *et al.* is not included in the current systematic review because the cases in their case-control study were extracted from the FARS database (as discussed in our Methods section). Nevertheless, the paper deserves some attention here because of the way it has been exploited to facilitate the introduction of cocktail offences in NSW.

Li *et al’s* (2013) first claim, which is strongly supported in other studies, is that the use of alcohol presents a far greater risk of crashing than the use of any other psychoactive substance. The second is that the increase in the risk of crashing from the use of marijuana (83%) is far less than for narcotics such as opioids (203%), for stimulants such as amphetamines (257%), and for depressants such as benzodiazepines (383%). There is no indication in the recorded parliamentary debates that the NSW Centre for Road Safety briefed any of the MPs on the inconvenient truth that many medical drugs (none of which are tested for in NSW’s roadside drug-testing (RDT) program) present a far greater risk of crashing than cannabis (which *is* tested for).

In their Abstract, Li *et al*. (2013) also 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”. The baseline risk against which comparisons were made is the risk of fatal crash involvement for drivers who tested negative to both drugs and alcohol. The researchers found (see their Table 4) that the OR for the combined effect of all psychoactive drugs (medicinal and recreational) alone (i.e., without alcohol) was 2.2 (1.7-2.9), and for alcohol alone (i.e., without any other drug) was 13.6 (11.1-16.7). They also found that the OR for the effect of combining any drug with alcohol was 23.2 (17.8-30.3), which is greater than the sum of the component effects. They concluded that there was an interaction between drugs and alcohol whereby the combined effect is greater than the sum-of-the-part effects. So, while it is strictly correct to say, from their research, that “The combination of drugs and alcohol increases the risk of a fatal crash by 23 times”, it is far more relevant to say that “The combined use of drugs and alcohol increases the risk of fatal crash involvement by 1.7 times more than for alcohol alone” (where the ‘exacerbation OR’ of 1.7 for all drugs is obtained by dividing 23.2 by 13.6).

As the focus of our review is on cannabis, it should be noted that Li *et al.* (2013) found that cannabis alone had a much lower crash risk than the other categories of drug (many of which were medicinal). It should also be noted that Li *et al.* provided no evidence that cannabis *in particular* contributed to the alcohol-drug interaction effect. In fact, an almost identical study (Romano *et al.,* 2014), which was published a year after Li *et al’s* study, investigated the separate drug-alcohol interaction effects for cannabis alone and for all other drugs combined. They concluded: “The presence of drugs other than marijuana was found to be associated with an increase in fatal crash risk regardless of the driver’s BAC. The presence of marijuana, however, did not contribute to fatal crash risk” (p. 61).

In a follow-up study, Romano *et a*l. (2017) identified two major faults in Li *et al’s* (2013) research methodology. First, Li *et al*. had included information from states whose FARS coverage of drug data was exceptionally patchy and biased. Second, Li *et al.* failed to control for the effects of major confounders. We conclude that the study by Li *et al.*, which was widely cited in support of the introduction of cocktail offences in NSW, failed to provide *any* evidence in favour of such offences for the co-use of cannabis and alcohol.

*References for Appendix A*

Li G, Brady JE, and Chen Q (2013) Drug use and fatal motor vehicle crashes: A case-control study. *Accident Analysis and Prevention* 60: 205-210.

NSW: Legislative Assembly. (10 February, 2021) *Parliamentary debates (Hansard)*. <https://www.parliament.nsw.gov.au/hansard/Pages/home.aspx?s=1>

NSW: Legislative Council. (18 February, 2021) *Parliamentary debates (Hansard)*. <https://www.parliament.nsw.gov.au/hansard/Pages/home.aspx?s=1>

Romano E, Torres-Saavedra P, Voas RB, et al. (2014) Drugs and alcohol: Their relative crash risk. *Journal of Studies on Alcohol and Drugs* 75: 56-64.

Romano E, Torres-Saavedra P, Voas RB, et al. (2017) Marijuana and the risk of fatal car crashes: What can we learn from FARS and NRS data? *Journal of Primary Prevention* 38: 315-328.

VicRoads (n.d.) *Illicit drugs & road safety: How illicit drugs affect driving ability (Cannabis and driving)*. Retrieved November 5, 2022, from <https://www.vicroads.vic.gov.au/safety-and-road-rules/driver-safety/drugs-and-alcohol/illicit-drugs-and-road-safety>

**APPENDIX B**

**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 crash culpability. They are illustrated here with a worked example that uses the dummy data in Table B1. The interpretation of the groups in this table should be straightforward, with the possible exception of THC&AOD-free group, who are drivers with no cannabis, alcohol, or any other psychoactive drug in their system.

Table B1. Crash culpability and drug usage for a worked example

|  |  |  |  |
| --- | --- | --- | --- |
| **Group** | **Culpable** | **Not-Culpable** | **Total** |
| Cannabis: THC-only | 100 (r) | 100 (s) | 200 |
| Other drug (OD) combinations | 180 | 90 | 270 |
| Combined: THC&BAC-only | 120 (a) | 10 (b) | 130 |
| Alcohol: BAC-only | 800 (p) | 200 (q) | 1000 |
| Controls: THC&AOD-free | 900 (x) | 900 (y) | 1800 |
| **Total drivers** | **2100** | **1300** | **3400** |

In the calculations below, the values of the ORs are calculated directly from the information in Table B1, while the calculation of the values for the 95% CIs has required the use of statistical software.

At the outset, two features of the circumstances described by Table B1 should be explained. The first is that the data for cannabis-only in Table B1 is consistent with cannabis alone playing *no* direct causal role in crash culpability.

Cannabis-crash OR = (r/x)/ (s/y) = (100/900)/ (100/900) = 1.00 (0.7-1.3)

The second is that the data for alcohol-only in Table B1 is consistent with alcohol alone playing a strong direct role in crash culpability. The OR for BAC-only is:

Alcohol-crash OR = (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) with an OR for alcohol alone (as above). Finding a combined OR that was significantly greater than the OR for alcohol alone would be good *prima facie* evidence that cannabis had exacerbated the effect of alcohol.

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

It can be seen that the OR of 12.00 (6.3-23.0) for the combined use of cannabis and alcohol (without any other drugs) is three times as great at the OR of 4.00 (3.3-4.8) for the use of alcohol alone. It can also be seen 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 as described above can be reduced to one. The single-step procedure involves the direct comparison of the odds for the culpable drivers of having THC&BAC-only vs. BAC-only (a/p) with comparable odds for the not-culpable drivers (b/q). If the single OR is significantly greater than 1.00, it might be concluded that cannabis has exacerbated the effect of alcohol on the risk of culpability. We describe the resulting OR as an ‘exacerbation OR’.

Exacerbation OR = (a/p)/ (b/q) = (120/800)/ (10/200) = 3.00 (1.6-5.8)

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 culpability are three times greater than the odds of alcohol alone being related to crash culpability. 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 there is a simple mathematical relationship between the exacerbation OR, the combined-crash OR and the alcohol-crash OR:

Exacerbation OR = Combined-crash OR / Alcohol-crash OR = 12.00/4.00 = 3.00 (QED)

It might be concluded that these analyses of the data in Table B1 have provided unequivocal evidence of an exacerbation effect. However, that conclusion could be premature, because the effects of possible confounders have not been taken into account. However, for most of the ORs reported in this review (including for the cannabis-crash ORs in Table 1), the possible distorting effect of confounders has been taken into account by embedding the simple calculations in complex multiple logistic regression (MLR) analyses where identified confounders are compensated for statistically.

**APPENDIX C**

**Table C1. Sources of the counts data included in Table 2**

|  |  |
| --- | --- |
| Terhune (1982) | Table 15, p. 87; unnumbered table p. 92 |
| Williams (1985) | Table 7, p. 23 |
| Terhune (1992) | Table 5.14, p. 68 |
| Longo (2000) | Table 1, p. 626 |
| Mura (2003) | Table 1, p. 81 (for total n < 27 years old); Table 2, p. 82 |
| Drummer (2004) | No alcohol or drugs: Table 2, p 243.  Alcohol only: Drummer *et al.* (2001), Table 1, p.4.  Alcohol and THC: Table 4, p. 244; and Drummer *et al.* (2001), Table 1, p.4. |
| Gadegbeku (2011) | Personal communication to MW from Bernard Laumon |
| Poulsen (2014) | Table 1, p. 122 |
| Lacey (2016) | Appendix Q, Table 7: THC results from oral fluid; BAC 0.05 and above vs zero; comparison of ‘Marijuana’ and ‘Negative’ |
| Martin (2017) | Table 6, p.11 (from %s of Responsible & Not-Responsible) |
| Brubacher (2019) | Table 2, p. 1621 |
| Drummer (2020) | Table 2, p.5 |

**APPENDIX D**

**Consideration of the evidence for exacerbation as provided in the twelve individual studies**

*Consideration of individual studies where the unadjusted exacerbation OR is 1.0 or less*

In five of the twelve included studies (Terhune, 1982; Longo *et al*., 2000; Poulsen *et al.*, 2014; Lacey *et al.,* 2016; Drummer *et al*., 2020), there was obviously no *prima facie* evidence for an exacerbation effect from the unadjusted analyses reported in Table 3, because the OR for the combined use of alcohol and cannabis was equal to or less than that for the use of alcohol alone, and the exacerbation OR was therefore equal to or less than 1.0. The reactions of the researchers to those null findings are now considered.

In relation to his analyses of his counts data as presented in our Table 2, **Terhune** (1982: 92) commented: “With such small numbers of cases the results must be considered inconclusive. Though they do *not* suggest a synergistic impairment effect when alcohol is combined with marijuana …, a more definite conclusion must await a larger study with necessary controls”.

In relation to their analyses of their counts data as presented in our Table 2, **Longo *et al.*** (2000) concluded:

There was no significant difference in culpability between the two groups: 90% of drivers who tested positive for only alcohol were culpable compared with 85.7% of drivers who tested positive for alcohol and THC (Chi-squared = 0.004, *p* > 0.05). This suggests that the effect of alcohol and THC was due mainly to the effect of alcohol. However, these results should be interpreted with caution as the number of drivers who tested positive for alcohol and THC was small.

In relation to their analyses, as reproduced in our Table 3, of their counts data, as provided in our Table 2, **Poulsen *et al*.** (2014: 127) concluded: “This study indicates a *lower* impact on crash risk when alcohol and cannabis use is combined, relative to alcohol by itself”. In other words, Poulsen *et al.* believe that their study indicates the possibility of an *ameliorating* effect of cannabis on risks from the use of alcohol, rather than an exacerbating effect.

**Lacey *et al*.** (2016) did not analyze their data in the way we did in our Table 3. Instead, they created a number of statistical models of the shape of the dose-response curve relating BAC to crash risk (Figure 7, p. 59). Two of their models were identical, except with respect to the fact that one included only the effect of alcohol, while the other also included the effects of all other drugs (including cannabis). In commenting on the similar shapes of the two modelled curves, Lacey *et al.* observed that “Drug presence did not have a large impact on the alcohol crash-risk relationship. That is, there was no significant alcohol-by-drug interaction, which indicates that the presence of a drug, in addition to alcohol, did not increase crash risk”. Compton and Berning (2015) published an NHTSA ‘Research Note’ to summarize the main findings of Lacey *et al’s* study, in which they commented: “There was no difference in crash risk for THC-positive drivers who were also positive for alcohol … beyond the risk attributable to alcohol” (p. 5).

**Drummer *et al.*** (2020) did not analyze their data in the way we did in our Table 3. However, as reproduced here in Table 4, in their Table 2 they reported an adjusted OR of 16 (9.4-26) for alcohol alone, which was marginally smaller than the adjusted OR of 14 (4.4-46) for the combined effect of alcohol and cannabis. They made no comment on their failure to replicate their earlier purported demonstration of an exacerbation effect (Drummer *et al*, 2004; see below).

*Consideration of individual studies where the results indicate the possibility of an exacerbation effect*

In seven of the twelve included studies (Williams *et al*., 1985; Terhune *et al*., 1992; Mura *et al*., 2003; Drummer *et al*., 2004; Gadegbeku *et al*., 2011: Martin *et al*., 2017; Brubacher *et al*., 2019) the *direction* of results was compatible with the possibility of an exacerbation effect. However, there were only three studies (Drummer *et al.,* 2004; Gadegbeku *et al*., 2011; and Martin *et al*., 2017) where the researchers claimed to have demonstrated a statistically-significant exacerbation or equivalent effect. The comments of the researchers on these findings are now considered.

In relation to their analyses of their counts data as presented in our Table 2, **Williams *et al*.** (1985: 24) made comments to the effect that any exacerbation effect would be difficult to demonstrate: “The marijuana analysis was constrained by small numbers, and by the fact that, in the population studied, crash responsibility rates related to alcohol alone were greater than 90%, so that adding marijuana could not increase these rates by much”.

In relation to their analyses of their counts data as presented in our Table 2, **Terhune *et al.*** (1992: 69) acknowledged that “The question of alcohol-drug additive or interactive (synergistic) effects is an important one”. They compared culpability rates for alcohol and cannabis combined with culpability rates for cannabis alone (Table 5.15, p. 70), and found that the differences were not statistically significant, either at low BACs (below BAC = 0.10) or at high BACs (above BAC = 0.10). They commented that “Among the low-BAC drivers, the elevated responsibility rates at least suggest the possibility of drug contributions” (p. 69). They also observed that any incremental exacerbating effect of cannabis at high BACs would be very difficult to demonstrate because of the already very high baseline culpability rate of alcohol on its own (94%).

**Mura *et al*. (2003)** were mostly interested in their younger subjects (< 27 years old). For that sub-sample, in their Table 2, they reported an unadjusted OR of 3.8 (2.1-6.8) for alcohol alone, and an unadjusted OR of 4.6 (2.0-10.7) for the combination of alcohol and cannabis without any other drugs. Although the combined effect of alcohol and cannabis is slightly greater than the individual effect of alcohol, the 95% CIs are mostly overlapping, so the difference between the ORs is not statistically significant, and Mura *et al*. have therefore failed to demonstrate an exacerbation effect. However, the researchers were apparently not interested in the possibility of an exacerbation effect, as they said nothing about it.

We extracted counts data from Mura *et al*., as provided in our Table 2. However, our estimates of the ORs for alcohol alone and for alcohol and cannabis combined, as presented in our in our Table 3, differ somewhat from the values reported by Mura *et al.* in their Table 2. Where they report values of 3.8 (2.1-6.8) and 4.6 (2.0-10.7), we find larger values of 4.8 (2.7-8.6) and 6.0 (2.6-13.9). The relativities stay the same. However, the reasons for the discrepancy are not known.

The only researchers who claim to have demonstrated a statistically significant exacerbation effect are **Drummer *et al*.** (2004). As recorded in our Table 4, they reported an adjusted exacerbation OR of 2.9 (1.1-7.7). They concluded that their statistically-significant exacerbation OR “strongly suggests that THC does enhance the impairment caused by alcohol” (p. 244).

Drummer *et al.* (2004) did not provide all the counts data from which an unadjusted estimate of the OR could be calculated. However, some missing information was given in an earlier conference paper (Drummer *et al*., 2001). That information is provided here in Table 2. An analysis of the data, as presented in our Table 3, gives a non-significant unadjusted exacerbation OR of 2.3 (0.3-17.0). So, the unadjusted OR as calculated by us is smaller than their adjusted OR - and non-significant. It would normally be expected that an adjusted OR would be smaller than the corresponding unadjusted OR, because the MLR re-allocates some of the drug-effect variance to the other covariates such as age and gender, but that is not the situation here. The reasons for this unexpected difference are unknown.

One concerning feature of Drummer *et al’s* (2004) study is that the statistical analyses underlying the calculation of the exacerbation OR (whether adjusted or unadjusted) were seriously flawed by having different sampling timeframes for the drivers with alcohol alone (10 years) and the those with both alcohol and THC (the last 2 to 5 years of the 10-year period - depending on the jurisdiction from which the data were provided). The implications of that defect for the size of the exacerbation OR are unclear.

Poulsen *et al.* (2014; as reviewed above) had intentionally designed their New Zealand study as a replication of Drummer *et al*’s (2004) Australian study. Using a considerably greater number of cannabis-and-alcohol-combined drivers than Drummer *et al*. (136 vs. 43), Poulsen *et al.* failed to replicate Drummer *et al*’s purported exacerbation effect. And, as also mentioned above, Drummer’s own research team (Drummer *et al.,* 2020) failed to replicate their earlier demonstration of an exacerbation effect when investigating hospitalized rather than fatally-injured drivers. In summary, we conclude that the evidence from Drummer *et al*. (2004) for an exacerbation effect is unconvincing.

Our Table 3 shows an unadjusted exacerbation OR of 2.1 (1.1-3.8) for the overall dataset analyzed by **Gadegbeku *et al.*** (2011), which implies a statistically-significant exacerbation effect where the odds of being culpable for the crash is doubled. The information in our Table 4 for Gadegbeku *et al.*was actually extracted from earlier analyses of the same overall dataset by Laumon *et al*. in 2005 (p. 3), who obtained an adjusted OR of 14.0 (8.0-27.4) for the combined use of alcohol and cannabis that was higher than the adjusted OR of 8.5 (7.2-10.1) for the use of alcohol alone. However, the fact that there is some overlap between the 95% CIs for the two ORs shows that the exacerbation effect did not achieve statistical significance. Nevertheless, the results are also compatible with a strong exacerbation effect. Overall, it is probably appropriate to describe the support by this study for an exacerbation effect as ‘marginally significant’. The researchers claimed to have demonstrated a multiplicative effect such that the drug-crash OR for joint use is the product of the separate drug-crash ORs for cannabis and alcohol. That claim is considered in our Discussion section.

The study by **Martin *et al*.** (2017) was conducted by the same French research team as was involved in the earlier study reported by Gadegbeku *et al.* (2011) and Laumon *et al.* (2005). As shown our Table 3, when we analyzed counts data from Martin *et al*., we failed to demonstrate an exacerbation effect - with a non-significant unadjusted exacerbation OR of 1.4 (0.5-3.7). Nevertheless, the researchers claimed to have demonstrated a multiplicative effect. That claim is also considered in our Discussion section.

**Brubacher *et al.*** (2019: 1621) say that “In the model that included a cannabis and alcohol interaction, the OR for BAC > 0% and THC ≥ 2 ng/ml was 1.62 (95% CI = 0.34– 15.7) times larger when both substances were detected compared to the individual effects of alcohol and cannabis alone, but this interaction was not statistically significant (P = 0.58)”. That information is provided here in Table 4. In email correspondence of 10 December 2022 with one of the authors (MW), Dr Brubacher explained that the OR was actually an adjusted exacerbation OR. So, it is not strictly an ‘interaction effect’ according to our terminology. Dr Brubacher also said that he would “caution about making too much of the effect as it was not statistically significant”.

**APPENDIX E**

**Evidence for exacerbation from experimental studies**

*A review by Simmons et al. (2022)*

We have not yet referred to any of the *experimental* literature on the impairing effects of cannabis in combination with alcohol on driving performance and driver behaviour. As for crash risks, we describe a joint deleterious effect that is greater than the deleterious effect of alcohol alone as an ‘exacerbation’ effect. Simmons *et al.* (2022) have recently published a systematic review with meta-analyses of the effects of alcohol and cannabis, alone and in combination, on driving performance and driver behaviour. We take their work as the starting point for much of our discussion in this appendix.

Simmons *et al*. (2022: 2) included only those experimental studies that were conducted in driving simulators, on closed road courses or on public roads. They excluded experimental laboratory studies of psycho-motor skills, for much the same reasons as given by Owens and Ramaekers (2009: 52):

A wide range of experimental studies have assessed drug effects on laboratory test performance over the last three decades. Although various investigators have claimed that their task or task-battery taps driving-related skills, most studies show no proof for such a claim, or even a reasonable theoretical rationale. In general, investigators have employed a wide range of laboratory tests measuring aspects of perception, attention, motor control, cognitive function or central-nervous-system (CNS) arousal that are assumed to underlie safer driving. However, none of these tests has ever been shown to closely predict driving performance or traffic accidents.

Simmons *et al*. (2022) reported results for eight dependent variables, all of which were selected on the basis of Fuller’s (2005) theory of driver behaviour for [arguably] being directly relevant to road safety: crashes (simulated); hazard reaction time; lateral position variability (‘weaving’); time-out-of-lane (TOL); total number of lane excursions; speed; speed variability; and speed exceedances.

Simmons *et al.* (2022) reported that, for those outcomes where cannabis *alone* had an impairing effect, the strength of the effect was equivalent to that of alcohol at a BAC of about 0.05. However, they paid particular attention to the impairing effects of the *combined* use of alcohol and cannabis. As reported in their Table 3 and Supplemental Figures E51 to E74, they found no evidence of *exacerbation* for six of their eight measures. However, they did find some positive evidence in relation to both weaving and TOL. These two measures are related, because TOL is a consequence of excessive weaving (see Ramaekers *et al.,* 2000, Figure 3).

Four studies were included in the meta-analysis for weaving (Hartman *et al.*, 2015; Ramaekers *et al.*, 2000; Ronen *et al.*, 2010; Sexton *et al.*, 2002), but only one for TOL (Ramaekers *et al.*, 2000). The findings are summarized here in Table E1 (where RMSLP is an alternative measure of SDLP). It should be noted that the target BACs were quite low, in the vicinity of 0.05, for all four studies.

Table E1 shows that Hartman *et al.* (2015) found no evidence for an exacerbation effect. The table also indicates that there is no evidence for exacerbation from Sexton *et al’s* (2002) study. However, that evidence could perhaps have been described as ‘marginal’: although Sexton *et al.,* in their Table 22, describe their exacerbation effect as ‘non-significant’, Simmons *et al.* (2022, Figure E59) report that it is statistically significant under one of their three meta-analytic modelling assumptions. It can be seen from Table E1 that only two of the four studies on weaving (SDLP/RMSLP) report evidence of an exacerbation effect, such that the overall evidence for an exacerbation effect for lane control at low BACs is patchy.

**Table E1**. Exacerbation findings from Simmons *et al.* (2022) for lane control

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Study (First author, Date) | Measure | Study Type | Target BAC | Evidence for Exacerbation? |
| Hartman, 2015 | SDLP | Simulator | 0.065 | No |
| Ramaekers, 2000 | SDLP | On-road | 0.05 | Yes |
| Ronen, 2010 | RMSLP | Simulator | 0.05 | Yes |
| Sexton, 2002 | SDLP | Simulator | 0.05 | No |
| Ramaekers, 2000 | TOL | On-road | 0.05 | Yes |

Three factors should be taken into account when considering the relevance of the exacerbation of *weaving* (as evidenced in Table E1) to the exacerbation of *crash risk*: (1) exactly *what* is being measured by an increase in weaving at low BACs; (2) any ameliorating effects of the co-use of cannabis; and (3) the limited contribution of the co-use of cannabis to crash causation at high BACs. These factors are considered below.

*What is actually being measured by an increase in weaving at a low BAC?*

Ramaekers (2017) has argued that weaving (as measured by the standard deviation of lateral position – SDLP) is the ‘gold standard’ measure of driving impairment from the use of alcohol and other psycho-active drugs. He identifies 2.5cm. as the ‘clinically relevant’ mean increase in SDLP, because that is the increase typically found from alcohol at a BAC of 0.05. Simmons *et al.* (2022) concluded that the use of cannabis on its own had an impairing effect equivalent to that of alcohol at a BAC of about 0.05, such that cannabis on its own also increases mean SDLP by about 2.5 cm. Given the major role played by weaving in the identification of impairment from drug use, it is important to understand exactly *what* is signified by a modest increase in weaving, as found for low BACs or from the use of cannabis, so that the relevance of weaving to road safety can be assessed.

Verster and Roth (2011) provide an excellent description of how SDLP is measured, along with an overview how SDLP has been used to assess the effects of drugs on driving performance. Basically, SDLP is a measure of the width of the ‘weaving zone’ around a driver’s mean position in the lane. More precisely, SDLP is the standard deviation of a driver’s moment-to-moment lateral displacements from their mean position. Let us consider the situation for a typical car whose width is 1.90 m. (Holder, 2021) on a typical lane whose width is 3.50 m. (Fanning *et al*., 2016). Let us assume that the driver’s mean position corresponds to the middle of the lane. Under those circumstances, the mean distance between the side of the car and the edge of the lane (the ‘lateral zone’) is 0.85 m. (or, 85 cm.) As the car ‘weaves’ from side to side it encroaches into the lateral zones by an amount that is determined by the SDLP. Let us consider only the lateral zone on the shoulder side of the road. A distance of 20 cm. is a typical SDLP for an unimpaired driver (Verster and Roth, Figure 6). By the nature of a standard deviation, the driver will encroach into the lateral zone: by as far as 20 cm. (1 SD) for 68% of the time; as far as 40 cm. (2 SDs) for 95% of the time; and as far as 60 Cm. (3 SDs) for 99% of the time. The road shoulder at the edge of the 85 cm. lateral zone will not normally be reached. If we assume that the normal use of cannabis increases the SDLP by 2.5 cm., then the ‘cannabis-impaired’ SDLP will be 22.5 cm. Following the arithmetic steps above, the driver will still not encroach so far into the 85 cm. lateral zone as to reach the shoulder of the road (with 68% of the encroachments as far as 22.5 cm; 95% as far as 45.0 cm; and 99% as far as 67.5 cm).

It should be noted that the discussion below will relate only to *modest* increases in SDLP, in the vicinity of 2.5 cm., as caused by the use of alcohol at a BAC of 0.05, or by the recent use of cannabis. We propose that use of the term ‘impairment’ to describe such effects is arguably not justified. In contrast, the term is certainly justified to describe the effects on SDLP of alcohol at moderate or high BACs, or of some medicinal drugs. For example, Louwerens et al. (1987, Figure 1) reported an increase in SDLP of about 9.0 cm. for female participants at a BAC of 0.14; and Verster et al. (2002, Table 1) reported an increase of 9.4 cm. from the use of alprazolam (which is a benzodiazepine). Following the arithmetic steps above, the use of alprazolam would cause the driver to occasionally weave across the 85 cm. lateral zone and onto the shoulder (with 68% of the encroachments as far as 29.4 cm; 95% as far as 58.8 cm; and 99% as far as 88.2 cm). While such encroachments would not normally be dangerous, especially where there was a sealed shoulder, the corresponding encroachment on the other side of the car, on a two-lane road, could cause a collision.

So, what does a ‘clinically-relevant’ 2.5 cm. increase in weaving signify? In agreement with Ginsburg (2019: 611), we suggest that such an increase is not *intrinsically* dangerous. We acknowledge that our suggestion is controversial. For example, Simmons *et al.* (2022) assume that all eight of their driving-related outcomes, including lane control, are directly relevant to road safety. However, our stance is also supported by Salvucci and Beltowska (2008), who found increases of 3.0 to 4.0 cm. in mean SDLP (i.e., larger than the ‘clinically relevant’ increase of 2.5cm) in their simulator experiment on the impairing effect of a cognitive distractor (memory rehearsal). They commented that “Although the effects we have noted are statistically significant, they are fairly small in magnitude”, and went on to conclude that “In many situations, the small additional deviation resulting from memory rehearsal would likely not amount to any appreciable differences with respect to driver safety”.

So, what *does* a small increase in weaving signify? Within the Human Factors literature (e.g., Angell *et al*., 2006; Engstrom *et al*., 2017; Fuller, 2005; Salvucci and Beltowska, 2008) the level of weaving, as measured by SDLP, is interpreted as an indicator of the overall mental and physical workload involved in many driving situations. As a general rule, although there are some exceptions (see, e.g., Li *et al.,* 2018), as the workload increases, so does SDLP. That occurs because steering is a tracking task (McGehee *et al.,* 2004), and, as such, comprises a low-level, largely autonomous, component of the overall workload. So, when the workload is heavy, mental resources are diverted from lower-level driving tasks such as steering (as reflected in SDLP) to higher-level tasks such as paying attention to an approaching potential driving hazard.

The overall workload, as reflected in mean SDLP, can be increased by many driving circumstances, such as: the complexity of the road geometry (e.g., Rosey and Auberlet, 2012); the presence of roadside distractors such as billboards (Shaw *et al.*, 2019); and the driver’s involvement in a secondary task such as looking intently through the rear-view mirror (Wang *et al.,* 2019) or using a mobile phone for texting (e.g., Ortiz *et al.,* 2018). SDLP is also deleteriously affected by limits on workload capacity as imposed by old age (e.g., Ortiz-Peregrina *et al*., 2020), sleep loss (e.g., Mahajan and Velaga, 2022), the use of psychoactive medications (e.g., Jongen *et al*., 2018), or the use of alcohol (e.g., Helland *et al.,* 2016).

The reason for this digression into the functional anatomy of weaving is to question weaving’s status as an ‘impairment’, particularly at the relatively low levels of increased weaving caused by the use of cannabis. These modest increases in weaving should more correctly be thought of as an indication that mental resources are being redistributed from lower- to higher-level cognitive functions. That redistribution is not necessarily diagnostic of an increased risk of crashing. To the contrary, the redistribution serves the purpose of road safety by allocating safety-relevant mental resources to where they are most needed.

*Possible ameliorating effects of the co-use of cannabis*

Let us now consider what the studies summarized in Table E1 have to say about the effect of the co-use of cannabis on alcohol-induced speeding. Ramaekers *et al.* (2000) had nothing to say, because their subjects were not permitted to reduce speed, even if keen to do so. Hartman *et al.* also had nothing to say in their 2015 paper, because their speed-related results were reported in a separate paper in 2016. In that paper (Hartman *et al*., 2016: 1427), they noted “The only significant (THC x alcohol) interaction effect detected was for ‘percent speed high’ … This indicates possible mitigation of alcohol effects by THC on time spent above the speed limit”. They concluded (p. 1427): “While alcohol reduces accurate self-assessment of intoxication and increases risky driving behaviors, drivers under the influence of cannabis are more likely aware of potential impairment and decrease speed to compensate, allowing a greater time to react to changing circumstances”. Ronen *et al.* (2010: 1864) came to a similar conclusion: “As might be expected from their separate effects, under the combination of THC and alcohol speed was not significantly different than in the placebo sessions; probably because the two drugs counteracted each other”. And, in the words of Sexton *et al*. (2002: 25):

Results using the [UK] Transport Research Laboratory’s driving simulator confirm the results from previous studies. There was a reduction of average speed and an increase in minimum time headway on simulated motorway driving when participants had the active dose of cannabis, *regardless of the alcohol dose*. This strongly suggests that the participants as drivers are aware of their impairment, and attempt to compensate for their impairment by driving more cautiously.

The evidence from Simmons *et al’s* (2022) review for ameliorating effects of the co-use of cannabis on the proclivity of alcohol-affected drivers to speed is no more than suggestive. While the authors of the reviewed studies are inclined to support such an effect (as above), Simmons *et al.* were unable to find any statistically-significant supporting evidence from their meta-analyses. In relation to the *separate* effects of cannabis and alcohol, they concluded (p. 10): “With respect to speed, cannabis and alcohol had opposite effects. Cannabis led to decreases in speed, whereas alcohol led to increases in speed, with generally greater increases in speed at higher BAC levels”. However, with respect to the *combined* effects they concluded (p. 10): “The hypothesis that cannabis and alcohol counteract each other on speed is not substantiated here”. However, they feel the need to qualify that conclusion by observing that: “A lack of evidence for an effect is not evidence for a null effect”.

Given the prominent role of speeding in crash causation (e.g., Job and Brodie, 2022), and particularly in relation to alcohol-involved crashes (Bogstrand *et al*., 2015; Phillips *et al*., 2015), any ameliorating effect of the co-use of cannabis on the proclivity of alcohol-affected drivers to speed could reduce the risk of crashing for co-use to below that for alcohol alone. In other words, the beneficial effects of the co-use of cannabis on alcohol-related speeding could easily outweigh any possible deleterious effects of cannabis on the exacerbation of weaving.

*The limited contribution of the co-use of cannabis to impairment at high BACs*

It can be seen from Table E1 that the evidence for the exacerbation of weaving comes from two studies (Ramaekers *et al*., 2000; Ronen *et al*., 2010) with target BACs of about 0.05. The choice by the researchers to limit their exploration of exacerbation effects to low BACs is presumably deliberate. Although they do not discuss this matter, it seems likely that they understand that the incremental exacerbating effects of cannabis on weaving are unlikely to be discernible at high BACs where alcohol on its own has very strong impairing effects (Irwin *et al*., 2017).

*Overall conclusion from the experimental evidence*

A distinction needs to be drawn between evidence that is *directly* relevant to the exacerbating effect of cannabis on the risk of crashing versus evidence that is only *indirectly* relevant: only the *epidemiological* evidence, as summarized in the body of this review, is directly relevant. We consider that the findings of Simmons *et al*. (2022) in relation to the indirectly-relevant *experimental* evidence do not seriously challenge our conclusion from the epidemiological evidence that the co-use of cannabis is unlikely to exacerbate the effect of alcohol on the risk of crashing.

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