Risk of motor vehicle collision with cannabis and alcohol use among patients presenting for emergency care

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ABSTRACT

Background: The objective of this study was to examine the relationship between cannabis and alcohol use and motor vehicle collision (MVC) risk among patients in the emergency department (ED).

Methods: This was a cross-sectional study of visits to EDs in Denver, CO, Portland, OR, and Sacramento, CA, by drivers who were involved in MVCs and presented with injuries (cases) and non-injured drivers (controls) who presented for medical care. We obtained blood samples and measured delta-9-THC and its metabolites. Alcohol levels were determined by breathalyzer or samples taken in the course of clinical care. Participants completed a research-assistant-administered interview consisting of questions about drug and alcohol use prior to their visit, context of use, and past-year drug and alcohol use. Multiple logistic regression was used to estimate the association between MVC, and cannabis/alcohol use adjusted for demographic characteristics. We then stratified participants based on levels of cannabis use and calculated the odds of MVC across these levels, first using self-report and then using blood levels for delta-9-THC in separate models. We conducted a case-crossover analysis, using 7-day look-back data to allow each participant to serve as their own control. Sensitivity analyses examined the influence of usual use patterns and driving in a closed (car, truck, van) versus open (motorcycle, motorbike, all-terrain vehicle) vehicle.

Results: Cannabis alone was not associated with increased odds of MVC, while acute alcohol use alone, and combined use of alcohol and cannabis were both independently associated with increased odds of MVC. Stratifying by level of self-reported or measured cannabis use, higher levels were not associated with increased risk for MVC, with or without co-use of alcohol; in fact, high self-reported acute cannabis use was associated with *decreased* odds of MVC (odds ratio [OR] 0.18, 95% confidence interval [CI] 0.05–0.65). In the case-crossover analysis, alcohol use alone or in combination with cannabis was associated with increased odds of MVC, while cannabis use was again associated with decreased odds of MVC.

Conclusions: Alcohol use alone or in conjunction with cannabis was consistently associated with MVC risk. However, the relationship between measured levels of cannabis and MVC was not as clear. Emphasis on actual driving behaviors and clinical signs of intoxication to determine driving under the influence has the strongest rationale.

1. INTRODUCTION

Decades of research have established that alcohol increases the risk for motor vehicle collision (MVC) in a dose-dependent manner (Peck et al. 2008, Taylor and Rehm 2012, Voas et al. 2012). Similarly, characterizing the relationship between cannabis and driving risk has become steadily more imperative (Aydelotte et al. 2019). As of January 2023, 37 states and the District of Columbia (DC) have legalized cannabis for use within comprehensive medical programs, of which 21 states and DC have also legalized cannabis for recreational use (DISA Global Solutions 2022). Cannabis has been observed to affect driving behaviors (Busardò et al. 2017, McCartney et al. 2021, Simmons et al. 2022) and have an additive or more-than-additive effect on driving when combined with alcohol (Chihuri et al. 2017). States that have legalized cannabis have observed greater cannabis-related visits to the emergency department (ED) (Roberts 2019), hospitalizations, and injury (Delling et al. 2019).

Current laws around cannabis and driving are highly heterogeneous, ranging from laws that simply prohibit any drug or any impairing substance to zero tolerance laws for cannabis to *per se* limits of 2 ng/mL or 5 ng/mL, or different thresholds depending on the presence or absence of alcohol (Governors Highway Safety Association n.d.). This is in part because detailed inquiry on cannabis and MVC-related injury, either alone or in combination with alcohol, faces a number of challenges (Cherpitel et al. 2017, Romano et al. 2017, Johnson et al. 2021). Drug tests used in the context of clinical care after MVC and injury are often qualitative, some of which measure metabolites that may be elevated for a long period of time after use, while others measure only the parent drug and do not detect metabolites. Thus, establishing a relationship between drug levels and a specific recent event is challenging. Many of the published studies have been performed in either simulated or strictly controlled settings (Downey et al. 2013, Busardò et al. 2017, Aydelotte et al. 2019, DISA Global Solutions 2022) or, conversely, examined fatal crashes (Callaghan et al. 2013, Martin et al. 2017, Aydelotte et al. 2019) (in which drug use information can be extremely limited) (Berning and Smither 2014). Studies of nonfatal cannabis-involved crashes have yielded conflicting results. For example, a National Highway Traffic and Safety Administration

study of 3,000 crash-involved drivers and 6,000 control drivers found cannabis use was not associated with crash risk after controlling for alcohol, age, and gender (Lacey et al. 2016), while a meta-analysis of 26 studies estimated a 32% increase in the risk of crash involvement among drivers who used cannabis compared with those who did not (Rogeberg and Elvik 2016, Rogeberg et al. 2018, Johnson et al. 2021).

The objective of the current study was to examine the risk of MVC attributable to cannabis alone and in combination with alcohol, using direct measurements of cannabis and alcohol in drivers presenting to emergency care. This method allowed us to obtain contemporaneous quantitative measurements from a clinically relevant patient population and examine risk at several threshold levels of cannabis. While the literature is mixed, based on the literature on cannabis's impact on driving skills and what we felt was the preponderance of research linking cannabis and driving injury, our hypotheses were that the overall risk of an MVC would be greater with cannabis use prior to driving compared with no cannabis use, greater with combined use of cannabis and alcohol compared with cannabis use alone, and greater with higher levels of cannabis.

2. MATERIALS AND METHODS

2.1 Study design

We conducted a cross-sectional study of emergency department (ED) visits by drivers who were involved in MVCs and presented with injuries (cases) and driving individuals who presented for a medical (noninjury) reason (controls). Research assistants (RAs) screened patients for eligibility, obtained informed consent from participants, and administered a detailed questionnaire approximately 30 minutes in length. Answers were entered directly into a REDCap form. RAs obtained blood and breathalyzer samples from study participants and reviewed the electronic health record (EHR) for each participant for additional visit-related data.

2.2 Study population

RAs recruited participants from the EDs of the study sites in Denver, Colorado, Portland, Oregon, and Sacramento, California. Eligible cases were adult (ages 18 years and older), English-speaking patients who presented to the ED within 8 hours of being in an MVC in which they were the driver. For each case, we screened consecutive patients arriving from the time of the MVC patient's presentation until we found an eligible control to participate in the study. To be eligible for the study, control patients needed to have been admitted to the ED for a noninjury problem and to have driven within the 8 hours prior to arrival in the ED to ensure that they were at risk for getting into an MVC, i.e., similar to cases except for the negative outcome of their driving.

At the Portland site, RAs recruited 24 hours a day, 7 days a week, from April 2017 to November 2019. At the two other sites, recruitment occurred between 7:00 a.m. and 12:00 a.m. from October 2018 to October 2019 (Denver) and November 2018 to November 2019 (Sacramento).The three study sites are urban, academic, Level 1 trauma centers in states where cannabis is legal for recreational use (Oregon legalized in 2014, Colorado in 2012, and California in 2016) (IIHS-HLDI 2022). However, they represented a range of facility characteristics, in terms of annual patient volumes (approximately 40,000

visits per year at the Portland site, 125,000 per year at the Denver site, and 80,000 visits at the Sacramento site) and differences in physical space and patient flow through the department. For example, the Denver site has an urgent visit portion of the ED that sees lower acuity visits and was used to recruit patients in addition to the main ED.

Patients in the custody of law enforcement and those presenting for psychiatric care were excluded from the study. Patients who were unable to provide consent on arrival (for example, due to critical illness or intoxication with drugs or alcohol) were followed until (1) they became clinically sober or otherwise regained consciousness and regained capacity to consent for themselves (based on a mini-mental exam) or (2) a Legally Authorized Representative (LAR) provided consent for the patient. Patients for whom an LAR could not be located were followed for the duration of their stay in the hospital and periodically assessed for capacity to consent. Participants received a $30 gift card for participating in the study.

This study was approved by the Institutional Review Boards of the respective institutions. We obtained a Certificate of Confidentiality from the National Institutes of Health due to the nature of the topics under study, including illicit drug use and risks to participant confidentiality.

2.3 Measurements

Blood samples for tetrahydrocannabinol (THC) and its metabolites and breathalyzer readings for alcohol were collected after arrival to the ED and prior to consent, for timeliness, but were discarded if consent was not subsequently obtained. Plasma samples for cannabinoid testing were frozen at −80 °C and then thawed for analysis by High Performance Liquid Chromatography/Tandem Mass Spectrometry. RAs abstracted information from the EHR, including documented crash characteristics, disposition, and biosamples obtained for clinical use, including blood alcohol levels, into a standardized data form.

RAs administered a structured interview about the mechanism of the MVC or, for medical patients, the reasons for the visit to the ED, drug and alcohol use within 8 hours prior to the visit, context

of use, and past-year drug and alcohol use. An expanded instrument was used for cannabis to capture a wide variety of use beyond common forms (like joints) that are the focus of traditional instruments but may miss other products that have become readily available in states where cannabis is legal, such as edibles and hash concentrates. Participants were asked to estimate the amount of THC consumed in grams or milligrams, depending on what was appropriate for the type of cannabis product, and then normalized the measurements to grams. They were also asked to estimate the amount of alcohol consumed in ounces or milliliters. MVC participants were also asked about driving and drug and alcohol use during the same 8-hour period for each of the 7 days prior to the injury event. RAs were trained in nonjudgmental interviewing, including completing mock interviews observed by study investigators with feedback about verbal and nonverbal interactions.

Cannabis and alcohol use on the day of the ED visit was defined in two ways. As with previous studies (Asbridge et al. 2014), for the main analysis, an affirmative answer for cannabis use within 8 hours of the MVC or noninjury visit was considered as evidence of drug use contemporaneous with driving activity and an affirmative answer for alcohol use within 8 hours of the MVC or noninjury visit as evidence of alcohol use contemporaneous with driving. The self-report cannabis and alcohol use measures were cross-classified into four categories: cannabis use only, alcohol use only, both cannabis and alcohol, and use of neither. In addition to self-report acute use, we considered blood plasma THC levels > 0.5 ng/mL (the lowest detectable limit) and any detectable 11-OH-THC as evidence of likely acute use prior to driving (Asbridge et al. 2014). Similarly, any positive level on blood or breathalyzer testing was considered positive for alcohol.

2.4 Data analysis

Percentages were calculated to describe the study populations (cases and controls) in terms of demographics, visit characteristics, and drug use. Multiple logistic regression was used to estimate the association between MVC and cannabis/alcohol use adjusted for demographic factors, including gender, age, race and ethnicity, income, and disposition status.

We previously described the incomplete capture of recent drug use based on self-report or biosamples alone (Choo et al. 2022). For the current study, we created a combined variable, with recent drug or alcohol use defined as either self-report or a positive biosample. However, when examining the odds of MVC across levels of cannabis use, we used self-report and blood levels for delta-9-THC in separate models. A low to medium level of use for self-report data was defined as up to 1 g on the day of the MVC (corresponding to roughly three joints), with a high level defined as greater than 1 g. For biosamples, we defined a low level as ≤ 5 ng/mL and a high level as > 5 ng/mL (corresponding to the *per se* laws in some U.S. states that make it illegal to drive with this amount of THC in the body).

While sample size precluded stratifying by both cannabis and alcohol levels in detail, we examined the levels of alcohol use within cannabis groups, in case the level of alcohol was a confounder or modifier of the combined effect. Because the alcohol measurements were obtained at widely varying time periods, we normalized them by back-calculating blood alcohol concentration (BAC) to the first hour of presentation in the ED, using the equation (Gullberg 2007, Searle 2015):

$$\text{BAC (mg/dL)} = \text{BAC recorded} + ((100 \times \text{ethanol mass cleared per hour}) / (\text{Weight [in g]} \times \text{rho})) \times \text{[hours between } \textit{ED arrival} \text{ and sample]}$$

We used a standard ethanol clearance rate of 7.3g/h, Rho = 0.55 for women and 0.68 for men. If the measurement was obtained within 1 hour of ED arrival, we did not apply a conversion. If there was more than one measurement of alcohol level obtained, we used the one measured earliest after arrival in the ED.

Finally, we conducted a case-crossover analysis, using 7-day look-back data collected during the interview to allow each participant to serve as their own control. We examined driving days only and excluded those who reported a crash during the control period. Two models for this within-subject analysis were constructed: one, examining odds ratios (ORs) for alcohol, cannabis, and combined use; the second, adjusting further for any illicit drug use and day of the week. There was no adjustment for potential confounders, as participants were compared against themselves.

We repeated the analyses with further stratification by typical cannabis use patterns, in addition to stratifying by vehicle type for the case-crossover study. For typical past-year cannabis use, we categorized cannabis use into frequent (at least weekly) use or infrequent (less than weekly) use. For type of vehicle involved in MVC, we categorized vehicles into "open" vehicles, such as motorcycles or all-terrain vehicles (ATVs), or "closed" vehicles, such as cars, vans, or trucks.

3. RESULTS

Characteristics of MVC participants compared with medical participants are shown in **Table 1**. Of the 4,843 patients that were potentially eligible by EHR review, 4,625 were able to be approached to determine full eligibility, 2,877 were determined to be eligible, 1,398 provided consent and were enrolled into the study; one was missing MVC/medical classification and it could not be verified, so was excluded. MVC participants were more likely to be male and white, have private insurance, and have a higher monthly income compared with medical control patients. They were more likely to be admitted to the hospital during the visit, and more likely to have used alcohol prior to the visit than the medical controls. Medical controls, in contrast, were more likely to report past-year cannabis use.

Table 1: Characteristics of study participants, MVC and medical control groups

Characteristics	MVC (case) participants (N=817)	Medical (control) participants (N=580)	*p* value
Male gender (%)	61.0	42.1	**<0.001**
Age (mean, SD)	43.3 (18.0)	41.6 (14.7)	0.059
Race/ethnicity (%)			
White	66.8	61.5	**0.032**
Black	7.8	12.3	
Hispanic	19.9	21.7	
Others	5.5	4.6	
Education level (%)			
High school graduate or less	32.2	30.0	0.135
Some college	42.1	39.3	
College graduate or more	25.6	30.7	
Income — monthly after-tax (%)			
< $1500	25.3	32.8	**0.021**
$1,500–$3,999	44.4	40.8	
≥ $4,000	30.3	26.4	
Insurance			
Private	48.8	45.5	**0.040**
Medicare/Medicaid/Other	40.5	46.8	
None	10.7	7.7	
Trauma level (MVC)			
Full or 911 (%)	13.2	Not applicable	
Disposition			
Admitted (%)	51.7	27.0	**<0.001**
Injury severity (%)			
Admitted into trauma ICU (%)	22.4	Not applicable	
Motor vehicle type		Not applicable	
Car/truck/van	66.9		
Motorcycle/motor scooter	20.1		
Others (dirt bike, snowmobile)	13.0		
Reported past-year cannabis use (%)	43.7	50.3	**0.021**
Reported past-year alcohol use (%)	74.2	72.8	0.588
Reported acute cannabis use (%)	7.6	9.7	0.195
Positive cannabis biosamples (%)	19.9	19.3	0.798
Reported acute alcohol use (%)	13.9	3.2	**<0.001**
Positive alcohol biosamples (%)	13.9	2.8	**<0.001**

Note. Statistically significant differences are boldfaced.

SD = standard deviation.

3.1 Alcohol and cannabis use and risk of MVC

Table 2 shows the adjusted models for risk of MVC among all patients with alcohol use, cannabis use, and combined use of both cannabis and alcohol. Cannabis alone was not associated with increased odds of MVC, while acute alcohol use alone and combined use of alcohol and cannabis were both independently associated with increased odds of MVC. Of note, in the third model, only seven patients in the medical control group had combined use.

Table 2. Risk for MVC with alcohol, cannabis, and both (using either self-report or a positive biosample)

Models [1]	Medical (n)	MVC (n)	Adjusted OR [2]	95% CI	*p* value
Model 1: Any alcohol	26	132	3.81	(2.42, 6.01)	**<0.001**
Model 2: Any cannabis	108	162	1.11	(0.82, 1.50)	0.504
Model 3: Cannabis only	99	91	0.80	(0.57, 1.12)	0.190
Alcohol only	19	72	2.50	(1.45, 4.31)	**0.001**
Both cannabis and alcohol	7	59	6.91	(3.05, 15.66)	**<0.001**

Note. CI = confidence interval. OR = odds ratio. Statistically significant differences are boldfaced.

[1] Model 1=alcohol use, Model 2= cannabis use, Model 3= combined use of both cannabis and alcohol.

[2] Adjusted OR controlling for site, gender, age, race/ethnicity, education, and income.

We also examined the relative levels of drug and alcohol use for study participants overall, both MVC and controls (not shown in Tables). Those who had both cannabis and alcohol did not appear to drink more alcohol than those having alcohol only. Comparing these two groups, the proportion of those having used alcohol only reported levels of drinking 0.1 to 2.0 drinks, 2.1 to 6.0 drinks and more than 6.0 drinks were 30.5%, 40.2% and 29.3%, respectively. For those having both cannabis and alcohol, the proportions for these three levels of alcohol volume were 21.7%, 52.2% and 26.1% (chi-square test *p* value = 0.57). Looking at biosamples, the mean BAC for those who reported both alcohol and cannabis use was 0.133%, while the mean BAC for those who reported alcohol only was 0.149% ($p = 0.68$).

3.1.2 Secondary analysis

Stratifying by typical (past-year) cannabis use (**Appendix Table A1**), cannabis use alone was associated with MVC only among infrequent (less than weekly) cannabis users, but not for those reporting frequent (weekly) cannabis use.

3.2 Risk of MVC at varying cannabis use levels

We then examined the odds of MVC based on levels of self-reported or measured cannabis use (**Table 3**), among study participants for whom we had this information. In this analysis, high self-reported acute cannabis use was associated with *decreased* odds of MVC (odds ratio [OR] 0.18, 95% confidence interval [CI] 0.05–0.65) when excluding patients with acute alcohol. Otherwise, there were no significant differences in MVC odds at the different levels of cannabis use, with or without alcohol. Specifically, higher biosample levels did not appear to distinguish those at risk for MVC in this analysis.

Table 3. Risk for MVC at variable acute cannabis levels (self-reported and biosample) and with and without alcohol (positive alcohol defined as either self-report use during period of interest or a positive biosample in ER)

	Medical (n)	MVC (n)	Adjusted OR [1]	95% CI	*p* value	Adjusted OR if cannabis only [2]	95% CI	*p* value	Adjusted OR if alcohol positive [3]	95% CI	*p* value
Self-reported											
None	505	644	1			1					
> 0 but <= 1 g (low to med)	26	27	0.75	(0.42, 1.33)	0.322	0.53	(0.28, 1.00)	0.052	NA [4]		
> 1 g (high)	14	9	0.49	(0.20, 1.18)	0.111	0.18	(0.05, 0.65)	**0.009**	NA [4]		
Biosamples											
None detected	396	578	1								
> 0 and <= 5 ng/mL (low)	52	66	0.94	(0.62, 1.44)	0.791	0.68	(0.42, 1.10)	0.114	2.06	(0.48, 8.84)	0.333
> 5 ng/mL (high)	43	78	1.21	(0.78, 1.86)	0.390	0.86	(0.53, 1.39)	0.532	3.83	(0.77, 19.92)	0.100

Note. CI = confidence interval. NA = not applicable. OR = odds ratio. Statistically significant results are boldfaced.

[1] Adjusted OR controlling for site, gender, age, race/ethnicity, education, and income.

[2] Among patients without acute alcohol (self-report of not drinking before event and BAC negative). For self-report, this consists of 20 MVC patients (85% reporting low use) and 40 medical patients (65% reporting low use). For biosamples, this consists of 92 MVC patients (47% low positive) and 88 medical patients (55% low positive).

[3] Among patients with acute alcohol (self-report of drinking before event or BAC positive). Consists of 52 MVC patients (44% low positive) and 7 medical patients (57% low positive).

[4] Estimates cannot be derived, as all medical control patients with acute drinking reported no cannabis use.

3.2.1 Secondary analysis

Stratifying by typical cannabis use frequency (**Appendix Table A2)** demonstrated an association between lower measured blood delta-9-THC and MVC occurrence among infrequent cannabis users only. There was not sufficient data to complete the analysis of self-reported cannabis use among those with infrequent cannabis use, however. Again, small samples sizes limited our ability to identify associations between drug amounts and MVC risk.

3.3 Case-crossover analysis

In the case-crossover analysis (**Table 4**), alcohol use alone and combined use of alcohol and cannabis contributed to increased odds of MVC. Using cannabis was associated with decreased odds of MVC in both models. Adjusting further for any self-reported illicit drug use did not change these findings.

Table 4. Odds ratios (ORs) and 95% confidence intervals (CIs) from substance use using case-crossover analysis [1] (using self-report only)

Model 1	**OR**	**95% CI**	***p* value**
Acute alcohol/cannabis use			
Cannabis only	0.40	(0.21, 0.75)	**0.004**
Alcohol only	3.75	(2.43, 5.77)	**<0.001**
Both cannabis and alcohol	4.13	(1.82, 9.33)	**0.001**
Neither (ref)	1		
Model 2	**OR**	**95% CI**	***p* value**
Acute alcohol/cannabis use			
Cannabis only	0.36	(0.18, 0.70)	**0.003**
Alcohol only	3.89	(2.50, 6.04)	**<0.001**
Both cannabis and alcohol	3.06	(1.30, 7.22)	**0.010**
Neither (ref)	1		
Acute illicit drug use			
Yes	54.96	(16.69, 181.04)	**<0.001**
No (ref)	1		

Note. CI = confidence interval. OR = odds ratio. Statistically significant results are boldfaced.

[1] 1:7 matching, controls for day of week, excludes days in which participant reported not driving, and also excludes those who reported driving but had a crash during the control period; n = 602 for case periods, n = 2,836 for control periods.

3.3.1 Secondary analyses

When stratifying case-crossover analyses by vehicle type (closed vs. open, **Appendix Table A3**), the associations between use of cannabis alone and decreased odds of MVC were no longer present, and the associations between combined cannabis and alcohol use and increased odds of MVC were present for closed vehicles only. The associations between alcohol use alone and MVC remained for both closed and open vehicles. Stratifying by frequency of typical cannabis use (**Appendix Table A4**), use of cannabis alone was associated with decreased odds of MVC only among frequent cannabis users, while the association between combined cannabis and alcohol use and increased odds of MVC was present for infrequent cannabis users only.

4. DISCUSSION

Our study advances the understanding of substance use and driving safety in a number of ways. By using MVC-injured drivers and a control group of non-injured drivers, it offers real-world information that is more generalizable than observing driving behaviors in a simulated substance-use setting and more proximal than driving fatalities. A detailed look-back interview allows a complementary case-crossover analysis that provides another opportunity to examine the impact of cannabis use on MVC risk. With both interview and biosample information, it provides a more complete picture of cannabis use among patients in the ED.

Evidence of recent cannabis use was high among both case and control patients, which was not surprising in this study of EDs in states where cannabis was legal for recreational use. Our study supported an increased risk for MVC among those with acute alcohol and combined alcohol and cannabis use. Some of our findings suggested an absence of added risk (**Table 2**) or even reduced risk (**Tables 3, 4**) for MVC among those using cannabis alone prior to driving. This was somewhat unexpected, as high-risk driving behaviors have been described with cannabis use, legalization of cannabis has been associated with increased MVC-related healthcare visits (Lee et al. 2021), and literature reviews have

concluded that there is a low to moderate increased risk of MVC with cannabis use (Rogeberg and Elvik 2016, Cadieux and Leece 2017, Rogeberg et al. 2018).

On the other hand, our findings are similar to prior studies (Gmel et al. 2009) that show a decreased risk of injury with cannabis use, were not able to establish increased risk for MVC with cannabis alone (Cherpitel et al. 2021), or suggest that high estimates of increased risk with alcohol and drug combinations may be due to increased alcohol use when used with drugs (Cherpitel et al. 2013). There are physiologic explanations why motor skills involved in driving may not be significantly impaired among chronic users of cannabis (Karoly et al. 2022), and why testing levels may not accurately reflect pharmacodynamic effects (Spindle et al. 2021). Some studies have also suggested that cannabis users demonstrate greater awareness that they are impaired, may overestimate their impairment, and apply increased compensatory behaviors when driving, such as increasing the distance between themselves and other drivers (Sewell et al. 2009, Hartman et al. 2016). Such compensatory behaviors may not be present when combining alcohol and cannabis, consistent with our uniform finding (Tables 2, 4) of increased MVC risk with combined cannabis and alcohol use.

Our study suggests differences in risk depending on multiple factors, including drug tolerance (indicated by self-reported frequency of usual use), driving parameters, vehicle type (e.g., cars or trucks vs. motorcycles or ATVs, as we examined in this study), and use of cannabis alone or in combination with alcohol. Toxicologic or self-reported cannabis levels in our analyses did not appear to have a consistent relationship with MVC risk level (Table 3).

4.1 Limitations

Our study had a number of limitations. Risk estimates here may be affected by self-report. Controls may be more willing to report cannabis than cases, making the risk estimates biased in favor of a weaker relationship between cannabis use and MVC; in fact, we did observe a lower rate of self-reported use among MVC patients than among medical controls. However, we do not see this discrepancy for alcohol use, and combining the more objective biosample data into the outcome measure likely mitigated against this bias as well. Biosamples, too, provide only partial information, and information collected during the ER visit can only roughly estimate exact blood levels during actual driving. Drawing blood samples upon arrival, rather than waiting until after participants had been consented, provided delta-9-THC levels that were as contemporaneous with the prehospital driving event as possible. A study with a larger sample size would allow detailed quantification of cannabis and alcohol use, as well as other drug use, and sufficient power to compare risk at various levels of use. Our subanalyses by categories of vehicle type and baseline cannabis use also had small sample sizes, which may have obscured some associations between cannabis and alcohol use and MVC.

4.2 Conclusions

In this study, alcohol use was consistently associated with elevated MVC risk; however, the relationship between cannabis use alone at any level and MVC risk was less clear. The use of strict cut-offs of drug levels to gauge the influence of cannabis use on driving remains complex from a scientific and legal perspective, as the implication of measured levels are complicated by usual use, time and means of measurement, regular cannabis use patterns, and co-ingestion of alcohol. Our study reinforces that emphasis on actual driving behaviors and clinical signs of intoxication to determine driving under the influence has the strongest rationale, rather than specific drug-level thresholds (Wood and Dupont 2020).

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6. APPENDIX

Abbreviations

CI confidence interval
MVC motor vehicle collision
NA not applicable
OR odds ratio

Table A1. Risk for MVC with alcohol, cannabis, and both (using either self-report or a positive biosample) [1]

Models	Frequent cannabis users (>= weekly)			Infrequent cannabis users (< weekly)		
	Adjusted OR [2]	95% CI	*p value*	Adjusted OR [2]	95% CI	*p value*
Model 1: Any alcohol	6.74	(3.21, 14.12)	**<0.001**	3.18	(1.36, 7.46)	**0.008**
Model 2: Any cannabis	1.28	(0.80, 2.03)	0.302	2.81	(1.08, 7.29)	**0.033**
Model 3: Cannabis only	0.95	(0.57, 1.56)	0.826	1.90	(0.65, 5.53)	0.238
Alcohol only	3.42	(0.85, 13.84)	0.084	2.38	(0.96, 5.90)	0.060
Both cannabis and alcohol	7.93	(3.19, 19.69)	**<0.001**	NA [3]		

Note. Statistically significant results are boldfaced.

[1] Includes only patients reporting past-year cannabis use.

[2] Adjusted OR controlling for site, gender, age, race/ethnicity, education, and income.

[3] OR cannot be estimated for "both cannabis and alcohol" among infrequent cannabis users, as all those having "both cannabis and alcohol" were MVC-injured patients, while no medical patients had "both cannabis and alcohol."

Table A2. Risk for MVC at variable cannabis levels (self-reported and biosample) (not further splitting by with and without alcohol given small sample size)

	Frequent cannabis users (>= weekly)			Infrequent cannabis users (< weekly)		
	Adjusted OR [1]	95% CI	*p value*	Adjusted OR [1]	95% CI	*p value*
Self-reported						
None	1			1		
> 0 but <= 1 g (low to med)	0.64	(0.33, 1.24)	0.184	NA [2]		
> 1 g (high)	0.47	(0.18, 1.18)	0.107	NA [2]		
Biosamples						
None detected	1					
> 0 and <= 5 ng/mL (low)	1.12	(0.62, 2.03)	0.709	3.81	(1.08, 13.47)	**0.038**
> 5 ng/mL (high)	1.58	(0.88, 2.83)	0.126	1.45	(0.20, 10.72)	0.718

Note. Statistically significant results are boldfaced.

[1] Adjusted OR controlling for site, gender, age, race/ethnicity, education, and income.

[2] OR cannot be estimated because of empty cells for medical patients.

Table A3. Odds ratios and 95% confidence intervals from substance use using case-crossover analysis by vehicle type (closed vs. open vehicle) [1]

	Predicting MVC from closed vehicle (car, truck, van)			Predicting MVC from open vehicle (motorcycle, all-terrain vehicle)		
Model 1	**OR**	**95% CI**	***p value***	**OR**	**95% CI**	***p value***
Acute alcohol/cannabis use						
Cannabis only	0.47	(0.21, 1.03)	0.060	0.89	(0.27, 2.90)	0.843
Alcohol only	4.57	(2.61, 8.02)	**<0.001**	3.06	(1.17, 8.04)	**0.023**
Both cannabis and alcohol	3.30	(1.23, 8.82)	**0.017**	4.94	(0.57, 43.22)	0.149
Neither (ref)	1			1		
Model	**OR**	**95% CI**	***p value***	**OR**	**95% CI**	***p value***
Acute alcohol/cannabis use						
Cannabis only	0.45	(0.20, 1.01)	**0.003**	0.81	(0.23, 2.79)	0.734
Alcohol only	5.15	(2.88, 9.21)	**<0.001**	3.07	(1.17, 8.07)	**0.023**
Both cannabis and alcohol	2.58	(0.91, 7.34)	**0.010**	4.27	(0.49, 36.78)	0.187
Neither (ref)	1			1		
Acute illicit drug use						
Yes	108.65	(14.55, 811.12)	**<0.001**	16.86	(1.81, 157.28)	**0.013**
No (ref)	1			1		

Note. Statistically significant results are boldfaced.

[1] 1:7 matching, controls for day of week, excludes those who didn't report driving during control period, and also excludes those who reported driving but had a crash during the control period.

Table A4. Odds ratios and 95% confidence intervals from substance use using case-crossover analysis by frequency of typical cannabis use [1]

	Frequent cannabis users (>= weekly)			Infrequent cannabis users (< weekly)		
Model 1	**OR**	**95% CI**	***p value***	**OR**	**95% CI**	***p value***
Acute alcohol/cannabis use						
Cannabis only	0.35	(0.22, 0.56)	**<0.001**	0.56	(0.14, 2.22)	0.406
Alcohol only	3.30	(1.74, 6.25)	**<0.001**	2.02	(1.03, 3.94)	**0.040**
Both cannabis and alcohol	1.14	(0.53, 2.44)	0.737	8.11	(1.64, 40.02)	**0.010**
Neither (ref)	1			1		
Model 2	**OR**	**95% CI**	***p value***	**OR**	**95% CI**	***p value***
Acute alcohol/cannabis use						
Cannabis only	0.36	(0.22, 0.57)	**<0.001**	0.48	(0.11, 2.13)	0.336
Alcohol only	3.10	(1.61, 5.97)	**0.001**	2.17	(1.07, 4.39)	**0.030**
Both cannabis and alcohol	0.90	(0.41, 1.96)	0.791	7.123	(1.33, 38.15)	**0.022**
Neither (ref)	1			1		
Acute illicit drug use						
Yes	8.16	(3.51, 18.98)	**<0.001**	25.14	(8.52, 74.19)	**<0.001**
No (ref)	1			1		

Note. Statistically significant results are boldfaced.

[1] 1:7 matching, controls for day of week, excludes those who didn't report driving during control period, and also excludes those who reported driving but had a crash during the control period.