



Published in final edited form as:

*Curr Opin Psychol.* 2021 April ; 38: 75–79. doi:10.1016/j.copsyc.2021.03.003.

## Cannabis and Driving Ability

Eric L. Sevigny<sup>a</sup>

<sup>a</sup>Department of Criminal Justice and Criminology, Andrew Young School of Policy Studies, Georgia State University, 55 Park Place NE, Suite 519, Atlanta, GA 30303, United States

### Abstract

The aim of this review is to discuss recent evidence on cannabis and driving ability. In particular, the review examines experimental research on the acute effects of tetrahydrocannabinol (THC) on driving-related neurobehavioral skills and driving performance based on simulator and road course studies. The evidence indicates that certain driving abilities are significantly, albeit modestly, impaired in individuals experiencing the acute effects of THC. Treatment effects are moderated by dose, delivery method, recency of use, and tolerance development, with inconclusive evidence concerning the moderating influence of cannabidiol (CBD). Emerging research priorities include linking neurobehavioral deficits to specific decrements in driving performance, estimating the real-world implications of experimentally derived impairment effects, understanding how tolerance differentially affects driving impairment in different subgroups, and developing more evidence on CBD's potential role in mitigating THC-induced impairment.

### 1.1 Introduction

Road traffic crashes (RTCs) are a major cause of death and injury worldwide, and the leading cause of death among children and young adults aged 5–29 [1]. Cannabis is one of the most prevalent psychoactive substances detected in RTC-involved drivers [2]. Several recent meta-analyses estimate that cannabis intoxication and recent use produces a low to moderate increased crash risk, with reported odds ratios (ORs) ranging from 1.28 – 2.49 [3–7]. As more US states and countries liberalize legal access to cannabis, attitudes and behaviors surrounding cannabis-involved driving and associated RTC risk factors are drawing increased scrutiny from researchers and policymakers [8–10]. Against this backdrop, this review examines recent experimental research on the acute effects of cannabis on driving-related neurobehavioral skills and driving performance. This review does not focus on chronic cannabis use, which has also been shown to impair driving ability [11–13].

---

esevigny@gsu.edu.

Conflict of interest statement

Nothing declared.

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

## 2.1 Cannabis use and driving skills

Driving is a complex task requiring coordinated cognitive, visual, and motor abilities to be performed safely. Cannabis-induced impairments in driving performance therefore present a major threat to roadway safety. This section summarizes recent experimental evidence and systematic reviews concerning the acute effects of cannabis on driving ability, assessed across a range of neurobehavioral tasks relevant to driving and simulated or on-road driving performance metrics.

### 2.1.1 Experimental neurobehavioral research

Recent systematic reviews of experimental studies examining the acute neurobehavioral effects of tetrahydrocannabinol (THC), the main psychoactive compound in cannabis, consistently document significant impairments in memory, attention and concentration, psychomotor function, and executive functions such as problem-solving and impulse control [14–18]. The most recent and comprehensive of these reviews, McCartney et al.'s [15] meta-analysis of 80 primary studies, summarizes the experimental evidence across 11 cognitive performance domains, documenting a significant increase in peak-THC impairments of small to moderate size across nine functional areas (working memory, divided attention, sustained attention, information processing, tracking performance, fine motor coordination, reaction time, conflict control, and fluid intelligence). Conversely, the authors found no evidence that THC produces acute impairments in perception (sensory discrimination and time perception), but they cautioned against drawing a firm conclusion given the small number of included studies assessing perceptual impairments. Indeed, recent research by Ortiz-Peregrina and colleagues [19,20] that was not included in McCartney et al.'s [15] meta-analysis finds that THC produces significant deterioration in visual acuity, contrast sensitivity, depth perception, focusing ability, and straylight or glare response. More research is needed on the heterogeneous and potentially compounding neurobehavioral responses to THC, including the effects on visual disturbances under nighttime conditions when neurobehavioral demands are likely to be greater.

### 2.1.2 Experimental driving simulator and on-road research

Although neurobehavioral impairments can be indicative of poor driving skills, experimental simulator and road course studies provide more direct evidence of the acute effects of cannabis on driving performance. McCartney et al. [15] also meta-analyzed this body of research, synthesizing evidence across seven driving performance domains. Their analysis documents a significant increase in peak-THC impairments of small to moderate size for 'standard deviation of lane position' (SDLP; considered the gold standard outcome in driving safety research), other measures of lane weave, and reaction time. No significant effects were observed for either differences or variances in speed and car-following headway. These summary findings are generally consistent with two other recent reviews by Alvarez et al. [21], who narratively summarized 13 studies investigating cannabis impairment in young drivers, and Simmons (SM Simmons, PhD thesis, University of Calgary, 2020), who performed a meta-analysis of 81 studies investigating the effects of cannabis and alcohol on driving performance. A key divergence is that both Alvarez et al. [21] and Simmons conclude that drivers experiencing the acute effects of THC reduce

average driving speeds, likely as a compensatory response to perceived impairment, whereas McCartney et al. [15] was unable to draw this statistical inference despite an effect that trended in the same direction. In summary, drivers under the influence of THC weave more and are slower to react to stimuli (such as a roadside pedestrian). While it is also likely that drivers reduce their average speed to compensate for other performance deficiencies, additional confirmatory research is needed.

### 3.1 Moderators of acute THC effects on driving ability

Recent research indicates that certain neurobehavioral competencies and specific driving skills are significantly, albeit modestly, impaired in individuals experiencing the acute effects of THC. This section reviews recent research on key moderators of this association.

#### 3.1.1 Dose, delivery method, and recency of use

THC produces a dose-dependent effect on driving-related neurobehavioral outcomes [22]. More generally, McCartney et al.'s [15] meta-regression analysis demonstrates a significant dose-response association between THC and driving impairment across multiple performance domains. Consistent with research showing vaporization to be a highly efficient THC delivery method [23], McCartney et al. [15] also document a significantly greater effect of vaporized versus smoked cannabis on impairment. Although the bioavailability of THC varies by dose and route of administration [23], there appears to be little correlation between biological THC concentrations and impairment of neurobehavioral skills and driving performance indicators [24,25]. Indeed, detectable levels of THC in blood and oral fluid do not reliably discriminate recent cannabis use, especially among frequent users [26]. A key implication is that *per se* driving laws, which make it illegal to drive with THC blood concentrations above specified thresholds (e.g., 5 ng/mL), cannot accurately identify impaired drivers [24]. Perhaps the most reliable determinant of cannabis-induced impairment is time since exposure. The majority of THC's psychoactive effects occur within the first 2 hours of use, with any residual impairment subsiding during the subacute phase at 3–5 hours post-administration [10,23,27,28]. The actual cannabis impairment window will vary by factors such as the performance domain assessed, dose, route of administration, and individual characteristics. Meta-regression models reported by McCartney et al. [15], for instance, predict that meaningful impairment in SDLP among occasional users will last about 5 hours after smoking 10 mg THC but about 8 hours after vaporizing 20 mg THC. In light of such variability, new technologies and roadside protocols for detecting cannabis-impaired driving that do not rely on THC bioavailability markers offer promising avenues for future research [29–31].

#### 3.1.2 Tolerance development

Outside of treatment effects related to dose, mode, and timing, the development of cannabis tolerance can attenuate certain acute cognitive and driving performance deficits. Stronger evidence exists for the pharmacodynamic model of tolerance, in which acute effects are blunted by neuroadaptive responses to repeated cannabis exposure, than for the behavioral model, in which functional performance is maintained through volitional control and learned compensatory strategies [32,33]. In either case, tolerance development is more likely to

occur among high-dose cannabis users who partake daily at high frequency [33]. A recent driving simulator study of medically authorized daily cannabis users, for instance, showed a significant reduction in overall vehicle speed after subjects smoked a typical dose, but found no statistical differences in lateral control or braking latency [34]. As another example, Karoly et al. [30] found significant acute psychomotor impairments following use of high-potency cannabis among frequent users, although no significant differences were observed across other cognitive domains including attention and decision-making. Thus, tolerance development tends to be partial and manifest differently across performance domains, even among experienced users [32]. Developing coherent public policies on safe driving following cannabis use will need to address response heterogeneity as it relates to cannabis tolerance by accounting for the occasional recreational user as much as the medically authorized user who maintains a fixed dosing regimen [35,36].

### 3.1.3 Cannabinoid ratios and interactions

Most research on cannabis-impaired driving focuses on THC, but cannabis contains hundreds of other compounds that may affect driving ability. Recent impairment research has focused on the potential mitigating effects of cannabidiol (CBD), which is a major nonpsychoactive compound in cannabis. CBD, it is widely argued, attenuates certain adverse effects of THC, although the empirical evidence for this claim is decidedly mixed [37,38]. Recent cognitive and driving experiments examining the interactive effects of vaporized CBD and THC show that both THC-dominant and THC/CBD-equivalent cannabis impaired neurobehavioral and driving performance, whereas CBD-dominant and placebo cannabis did not [39–41]. Importantly, these findings may not extend to clinical populations, especially those who use pharmaceutical formulations of cannabis. A systematic review by Celius and Vila [42], for example, finds that Sativex, the THC/CBD-equivalent oromucosal spray, does not impair driving ability among multiple sclerosis (MS) patients, and may even improve performance due to enhanced cognition and reductions in spasticity. Thus, although CBD may moderate certain acute effects of THC such as anxiety [37,38], it does not appear to reliably protect against THC-induced driving impairments. Still, there is some evidence that CBD may reduce driving impairment in certain clinical populations, but more research is needed [15,42].

## 4.1 Emerging research priorities and challenges

This review elicits a number of research priorities and challenges. First, the neurobehavioral impairment research on THC is highly varied, and the systematic reviews summarizing this literature inconsistently categorize the primary study effects into different cognitive domains and subdomains [14–18]. Future review work in this area would therefore benefit from more consistent domain categorization of the neurobehavioral effects of THC [e.g., 43]. Moreover, road safety research would benefit from establishing clearer linkages between observed neurobehavioral deficits and functional decrements in driving performance [40], as some researchers are already doing [20].

Second, although cannabis significantly impairs driving ability, the magnitude of these impairments tends to be small. In McCartney et al.'s [15] meta-analysis, significant THC

impairments observed across 10 of 12 performance domains were considered small, with two effects reaching into the moderate range. There is some debate, then, about the extent to which these observed deficits meaningfully compromise roadway safety (MA White and NR Burns, unpublished). According to this critique, researchers need to more effectively grapple with the issue of “tolerable crash risks” for THC, similar to the limits currently in place for alcohol (e.g., BAC < 0.8). Given the incongruence between THC blood concentrations and measures of driving ability, valid approaches to determining cannabis-induced impairment for public health guidance and legal liability purposes are desperately needed. Research seeking to reliably and cost-effectively identify cannabis-impaired drivers should be prioritized [e.g., 29,30,31]. Because driving ability reaches across multiple performance domains, development of a summary ‘index of cannabis-impaired driving’ would also be a fruitful research endeavor.

Third, much of the experimental research on cannabis-related driving impairment excludes regular or daily cannabis users [e.g., 27,39]. Given tolerance development, selection effects associated with a primary focus on infrequent and occasional users are likely to be severe in much of the existing cannabis impairment research. More research is therefore needed that examines cannabis-related driving impairment in heterogeneous user populations, including clinical populations with daily regimented cannabis use [34]. Further, given that clinical populations may be more likely to use products with different THC:CBD formulations, more research is warranted on how different cannabinoid dose combinations affect driving performance.

## 5.1 Conclusions and policy implications

This review of the experimental literature on the acute effects of cannabis on driving ability confirms that THC significantly impairs certain neurobehavioral competencies and driving skills, although the impairments tend to be modest and reversible. These effects are also contingent upon treatment-related factors, including dose, route of administration, and recency of use. Tolerance development mitigates impairment of certain driving skills, but not consistently or equally across performance domains. CBD is a component of cannabis that may ameliorate specific negative effects of THC (e.g., anxiety), but it does not appear to fully moderate the performance deficits induced by THC, except possibly in certain clinical populations.

Several research priorities were noted for the field, including linking neurobehavioral deficits to specific decrements in driving performance, translating implications of experimental research findings on driving impairment to real-world conditions, understanding how THC tolerance affects impairment across different subgroups, and developing additional knowledge of CBD’s role in mitigating the acute impairing effects of THC on driving ability.

Lastly, a number of policy implications can be derived from this review. First, because THC dose and recency of use are clearly associated with the level of impairment, policies that require clear labelling of cannabinoid content of regulated products, coupled with public service campaigns about minimum “wait” times after consuming cannabis, may assist

individuals with making responsible use decisions around driving [e.g., 44]. Current research also indicates that biological THC concentrations are not strongly correlated with impairment, so *per se* laws that criminalize driving above specific thresholds do not appear to be justified as stand-alone policy [24].

## Acknowledgements and funding

This research was supported in part by funding from the National Institute on Drug Abuse (NIH Award No.: R03DA046806).

## References and recommended reading

1. World Health Organization: Global status report on road safety 2018. Geneva: World Health Organization; 2018.
2. Christophersen AS, Mørland JG, Stewart K, Gjerde H: International trends in alcohol and drug use among motor vehicle drivers. In Alcohol, drugs, and impaired driving: Forensic science and law enforcement issues. Edited by Jones AW, Mørland JG, Liu RH: Taylor & Francis; 2020:510–561.
3. Els C, Jackson TD, Tsuyuki RT, Aidoo H, Wyatt G, Sowah D, Chao D, Hoffman H, Kunyk D, Milen M: Impact of cannabis use on road traffic collisions and safety at work: Systematic review and meta-analysis. *Can J Addict* 2019, 10:8–15. 10.1097/CXA.0000000000000046
4. Hostiuc S, Moldoveanu A, Negoii I, Drima E: The association of unfavorable traffic events and cannabis usage: A meta-analysis. *Front Pharmacol* 2018, 9. 10.3389/fphar.2018.00099
5. Rogeberg O: A meta-analysis of the crash risk of cannabis-positive drivers in culpability studies—avoiding interpretational bias. *Accid Anal Prev* 2019, 123:69–78. 10.1016/j.aap.2018.11.011 [PubMed: 30468948] \* This meta-analysis breaks new ground in developing novel synthesis methods for road safety researchers. The authors argue that traditional meta-analytic approaches to synthesizing culpability studies suffer from “interpretational bias” in which crash risks are overstated. Their proposed Bayesian statistical model adjusts for this bias so that culpability and total crash risk studies (e.g., case control) can be appropriately combined in a single meta-analysis. The paper applies the model to 13 published culpability studies.
6. Rogeberg O, Elvik R: The effects of cannabis intoxication on motor vehicle collision revisited and revised. *Addiction* 2016, 111:1348–1359. 10.1111/add.13347 [PubMed: 26878835]
7. Rogeberg O, Elvik R, White M: Correction to: ‘The effects of cannabis intoxication on motor vehicle collision revisited and revised’ (2016). *Addiction* 2018, 113:967–969. [PubMed: 29359364]
8. Hall W, Stjepanovi D, Caulkins J, Lynskey M, Leung J, Campbell G, Degenhardt L: Public health implications of legalising the production and sale of cannabis for medicinal and recreational use. *Lancet* 2019, 394:1580–1590. 10.1016/S0140-6736(19)31789-1 [PubMed: 31657733]
9. Lensch T, Sloan K, Ausmus J, Pearson JL, Clements-Nolle K, Goodman S, Hammond D: Cannabis use and driving under the influence: Behaviors and attitudes by state-level legal sale of recreational cannabis. *Prev Med* 2020:106320. 10.1016/j.ypmed.2020.106320
10. Ramaekers JG: Driving under the influence of cannabis: An increasing public health concern. *JAMA* 2018, 319:1433–1434. 10.1001/jama.2018.1334 [PubMed: 29582068]
11. Duperrouzel JC, Granja K, Pacheco-Colón I, Gonzalez R: Adverse effects of cannabis use on neurocognitive functioning: A systematic review of meta-analytic studies. *J Dual Diagn* 2020, 16:43–57. 10.1080/15504263.2019.1626030 [PubMed: 31232216]
12. Dahlgren MK, Sagar KA, Smith RT, Lambros AM, Kuppe MK, Gruber SA: Recreational cannabis use impairs driving performance in the absence of acute intoxication. *Drug Alcohol Depend* 2020, 208:107771. 10.1016/j.drugalcdep.2019.107771
13. Lovell ME, Akhurst J, Padgett C, Garry MI, Matthews A: Cognitive outcomes associated with long-term, regular, recreational cannabis use in adults: A meta-analysis. *Exp Clin Psychopharmacol* 2020, 28:471. [PubMed: 31670548]

14. Broyd SJ, van Hell HH, Beale C, Yuecel M, Solowij N: Acute and chronic effects of cannabinoids on human cognition—a systematic review. *Biol Psychiatry* 2016, 79:557–567. 10.1016/j.biopsych.2015.12.002 [PubMed: 26858214]
15. McCartney D, Arkell TR, Irwin C, McGregor IS: Determining the magnitude and duration of acute  $\delta$ 9-tetrahydrocannabinol ( $\delta$ 9-THC)-induced driving and cognitive impairment: A systematic and meta-analytic review. *Neurosci Biobehav Rev In Press*. 10.1016/j.neubiorev.2021.01.003\*\* This recently published groundbreaking meta-analysis and meta-regression study comprehensively synthesizes the evidence on the effects of THC on cognitive skills and driving performance from the experimental research published from 2000–2020. The scope and quality of this first-of-its-kind is exemplary, and will stand as state-of-the-art for some time to come. Supplementary material includes a spreadsheet that allows input of dosing and time lapse parameters in order to estimate impairments effect sizes across different performance outcomes.
16. Oomen PP, van Hell HH, Bossong MG: The acute effects of cannabis on human executive function. *Behav Pharmacol* 2018, 29:605–616. 10.1097/FBP.0000000000000426 [PubMed: 30199388]
17. Prashad S, Filbey FM: Cognitive motor deficits in cannabis users. *Curr Opin Behav Sci* 2017, 13:1–7. 10.1016/j.cobeha.2016.07.001 [PubMed: 27482533]
18. Chow RM, Marascalchi B, Abrams WB, Peiris NA, Odonkor CA, Cohen SP: Driving under the influence of cannabis: A framework for future policy. *Anesth Analg* 2019, 128:1300–1308. 10.1213/ANE.0000000000003575 [PubMed: 31094805]
19. Ortiz-Peregrina S, Ortiz C, Casares-López M, Jiménez JR, Anera RG: Effects of cannabis on visual function and self-perceived visual quality. *Sci Rep* 2021, 11:1–11. 10.1038/s41598-021-81070-5 [PubMed: 33414495]
20. Ortiz-Peregrina S, Ortiz C, Castro-Torres JJ, Jiménez JR, Anera RG: Effects of smoking cannabis on visual function and driving performance. A driving-simulator based study. *Int J Environ Res Public Health* 2020, 17:9033. 10.3390/ijerph17239033\*\* This driving simulator study of visual function and driving performance provides recent evidence on a relatively understudied neurobehavioral domain. Significant impairments are observed in visual and driving performance. The authors also report correlations between visual and driving outcomes, indicating, for instance, that impaired stereoacuity is associated with greater lane weave.
21. Alvarez L, Colonna R, Kim S, Chen C, Chippure K, Grewal J, Kimm C, Randell T, Leung V: Young and under the influence: A systematic literature review of the impact of cannabis on the driving performance of youth. *Accid Anal Prev* 2021, 151:105961. 10.1016/j.aap.2020.105961
22. Boggs DL, Cortes-Briones JA, Surti T, Luddy C, Ranganathan M, Cahill JD, Sewell AR, D'Souza DC, Skosnik PD: The dose-dependent psychomotor effects of intravenous  $\delta$ 9-tetrahydrocannabinol ( $\delta$ 9-THC) in humans. *J Psychopharmacol* 2018, 32:1308–1318. 10.1177/0269881118799953 [PubMed: 30255720]
23. Spindle TR, Cone EJ, Schlienz NJ, Mitchell JM, Bigelow GE, Flegel R, Hayes E, Vandrey R: Acute pharmacokinetic profile of smoked and vaporized cannabis in human blood and oral fluid. *J Anal Toxicol* 2019, 43:233–258. 10.1093/jat/bky104 [PubMed: 30615181]
24. Arkell TR, Spindle TR, Kevin RC, Vandrey R, McGregor IS: The failings of per se limits to detect cannabis-induced driving impairment: Results from a simulated driving study. *Traffic Inj Prev* 2021:1–6. 10.1080/15389588.2020.1851685\*\* This simulated driving experiment examines the effect of cannabis with different ratios of THC:CBD on driving performance. A key finding of the study is that THC blood concentrations poorly correlated with measures of impairment. In particular, they found that blood and oral fluid concentrations around legal per se limits often failed to discriminate impairment and thus per se laws may not be justified.
25. Hitchcock LN, Tracy BL, Bryan AD, Hutchison KE, Bidwell L: Acute effects of cannabis concentrate on motor control and speed: Smartphone-based mobile assessment. *Front Psychiatry* 2021, 11:1626. 10.3389/fpsy.2020.623672
26. Peng YW, Desapriya E, Chan H, Brubacher JR: Residual blood THC levels in frequent cannabis users after over four hours of abstinence: A systematic review. *Drug Alcohol Depend* 2020:108177. 10.1016/j.drugalcdep.2020.108177
27. Ogourtsova T, Kalaba M, Gelinis I, Korner-Bitensky N, Ware MA: Cannabis use and driving-related performance in young recreational users: A within-subject randomized clinical trial. *CMAJ Open* 2018, 6:E453–E462. 10.9778/cmajo.20180164

28. Tank A, Tietz T, Daldrup T, Schwender H, Hellen F, Ritz-Timme S, Hartung B: On the impact of cannabis consumption on traffic safety: A driving simulator study with habitual cannabis consumers. *Int J Legal Med* 2019, 133:1411–1420. 10.1007/s00414-019-02006-3 [PubMed: 30701315]
29. Brown T, McConnell M, Rupp G, Meghdadi A, Richard C, Schmitt R, Gaffney G, Milavetz G, Berka C: Correlation of EEG biomarkers of cannabis with measured driving impairment. *Traffic Inj Prev* 2019, 20:S148–S151. 10.1080/15389588.2019.1662256 [PubMed: 31674856] \* This driving simulator study examined the association between THC and driving performance. With biological THC concentrations poorly correlated with measures of impairment, the innovation of this study was to collect electroencephalogram (EEG) biomarkers from a wireless headset combined with neurobehavioral tests. The findings were promising for being able to discriminate dose-dependent impairment in driving through noninvasive methods.
30. Karoly HC, Milburn MA, Brooks-Russell A, Brown M, Streufert J, Bryan AD, Lovrich NP, DeJong W, Bidwell LC: Effects of high-potency cannabis on psychomotor performance in frequent cannabis users. *Cannabis Cannabinoid Res* 2020. 10.1089/can.2020.0048
31. Porath AJ, Beirness DJ: Predicting categories of drugs used by suspected drug-impaired drivers using the Drug Evaluation and Classification Program tests. *Traffic Inj Prev* 2019, 20:255–263. 10.1080/15389588.2018.1562178 [PubMed: 30946603]
32. Colizzi M, Bhattacharyya S: Cannabis use and the development of tolerance: A systematic review of human evidence. *Neurosci Biobehav Rev* 2018, 93:1–25. 10.1016/j.neubiorev.2018.07.014 [PubMed: 30056176]
33. Ramaekers JG, Mason NL, Theunissen EL: Blunted highs: Pharmacodynamic and behavioral models of cannabis tolerance. *Eur Neuropsychopharmacol* 2020, 36:191–205. 10.1016/j.euroneuro.2020.01.006 [PubMed: 32014378]
34. Ciano PD, Matamoros A, Matheson J, Fares A, Hamilton HA, Wickens CM, Watson TM, Mann RE, Foll BL, Byrne PA, et al.: Effects of therapeutic cannabis on simulated driving: A pilot study. *J Conc Disord* 2020, 2:3–13. \*\* The innovation of this driving simulator study examining the effects of THC on driving performance is in the target population of therapeutic cannabis users. It is the first study to focus on this population, which is more likely to develop tolerance from frequent, daily cannabis use. The study found that cannabis consumption among this population still acutely altered driving behavior in meaningful ways.
35. Neavyn MJ, Blohm E, Babu KM, Bird SB: Medical marijuana and driving: A review. *J Med Toxicol* 2014, 10:269–279. 10.1007/s13181-014-0393-4 [PubMed: 24648180]
36. Bonar EE, Cranford JA, Arterberry BJ, Walton MA, Bohnert KM, Ilgen MA: Driving under the influence of cannabis among medical cannabis patients with chronic pain. *Drug Alcohol Depend* 2019, 195:193–197. [PubMed: 30638777]
37. Pennypacker SD, Romero-Sandoval EA: CBD and THC: Do they complement each other like yin and yang? *Pharmacotherapy* 2020, 40:1152–1165. 10.1002/phar.2469 [PubMed: 33080058]
38. Freeman AM, Petrilli K, Lees R, Hindocha C, Mokrysz C, Curran HV, Saunders R, Freeman TP: How does cannabidiol (CBD) influence the acute effects of delta-9-tetrahydrocannabinol (THC) in humans? A systematic review. *Neurosci Biobehav Rev* 2019, 107:696–712. 10.1016/j.neubiorev.2019.09.036 [PubMed: 31580839]
39. Arkell TR, Vinckenbosch F, Kevin RC, Theunissen EL, McGregor IS, Ramaekers JG: Effect of cannabidiol and 89-tetrahydrocannabinol on driving performance: A randomized clinical trial. *JAMA* 2020, 324:2177–2186. 10.1001/jama.2020.21218 [PubMed: 33258890]
40. Arkell TR, Lintzeris N, Kevin RC, Ramaekers JG, Vandrey R, Irwin C, Haber PS, McGregor IS: Cannabidiol (CBD) content in vaporized cannabis does not prevent tetrahydrocannabinol (THC)-induced impairment of driving and cognition. *Psychopharmacology* 2019, 236:2713–2724. 10.1007/s00213-019-05246-8 [PubMed: 31044290] \*\* This experimntal study examined the effects of different THC:CBD ratios on cognitive outcomes and driving performance. Results showed that CBD did not ameliorate the effects of THC on cognition and driving ability. In fact, in some tests CBD actually exacerbated THC-induced impairment.
41. Spindle TR, Cone EJ, Goffi E, Weerts EM, Mitchell JM, Winecker RE, Bigelow GE, Flegel RR, Vandrey R: Pharmacodynamic effects of vaporized and oral cannabidiol (CBD) and vaporized



CBD-dominant cannabis in infrequent cannabis users. *Drug Alcohol Depend* 2020, 211:107937. 10.1016/j.drugalcdep.2020.107937

42. Celius EG, Vila C: The influence of THC:CBD oromucosal spray on driving ability in patients with multiple sclerosis-related spasticity. *Brain Behav* 2018, 8. 10.1002/brb3.962\* This systematic review of the research examined literature published from 2000–2017 to determine the effects of Sativex, a THC:CBD-equivalent oromucosal spray, on driving performance in multiple sclerosis patients. There is little evidence that this treatment impairs driving performance. In fact, many patients reported improved driving behaviors, which was attributed to reduced spasticity and improved cognition.
43. Harvey PD: Domains of cognition and their assessment. *Dialogues Clin Neurosci* 2019, 21:227. [PubMed: 31749647]
44. Hammond D: Communicating THC levels and ‘dose’ to consumers: Implications for product labelling and packaging of cannabis products in regulated markets. *International Journal of Drug Policy* In Press:102509.