Medical Cannabis and Cannabinoids

Evidence in Context – Commentary

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Cannabis Effects on Driving Performance: Clinical Considerations

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Key Points

- Driving under the influence of cannabis has been identified as a public health concern as medical and recreational cannabis availability increases in some countries.
- A recent randomized clinical trial found similar levels of acute driving impairment with THC-dominant cannabis and with a combination of THC-CBD equivalent cannabis using on-road driving tests that provided real-world conditions; however, CBD-dominant cannabis did not produce significant cognitive or psychomotor impairment compared with placebo in this trial.
- Media coverage of this study conveyed the findings as CBD-dominant cannabis not causing driving impairment while THC-dominant cannabis does, with the latter lasting up to 4 h post-dose.
- It is recommended that clinicians counsel about the risks of driving impairment when patients disclose use of cannabis products containing THC.

Keywords
Cannabis · Marijuana · Cannabidiol · Tetrahydrocannabinol · Driving · Impairment

Introduction

Driving under the influence of cannabis (DUIC) is an important public safety concern as access to medical and recreational cannabis increases in North America and internationally [1]. Following alcohol, cannabis is the most commonly detected drug in both crash-involved drivers and the general driving population [2, 3]. Medical and recreational use may differ in the cannabinoids used, however, which may differentially impact driving ability. Δ^9-tetrahydrocannabinol (THC) is the most psychoactive cannabinoid and responsible for the intoxicating "high" and impairing side effects associated with cannabis. In contrast, cannabidiol (CBD) may counteract some THC effects but can still produce effects of drowsiness [4] which may impair one's driving ability. In addition to cannabinoid content, factors such as user tolerance, product potency, dosage, and route of administration affect the onset, intensity, and duration of impairment. It should

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also be considered that cannabis may affect driving performance acutely (in the short-term) or over the long-term if a person is using sufficient quantities of cannabis for a sustained period.

Although several studies have concluded there is moderate increased crash risk associated with acute cannabis use, few studies have explored the magnitude and duration of driving impairment with varying concentrations of THC and CBD including CBD alone [1, 5–7]. A randomized clinical trial (RCT) assessing cannabis use on driving performance by Arkell et al. drew significant attention on this subject recently as the first study to examine four experimental drug conditions: (1) CBD-dominant cannabis (13.75 mg CBD), (2) THC-dominant cannabis (13.75 mg Δ^9-THC), (3) THC/CBD-equivalent cannabis (13.75 mg CBD; 13.75 mg Δ^9-THC), and (4) placebo (trace CBD, Δ^9-THC) [8]. This commentary aims to elaborate on its findings relative to past research and to provide context on how the available evidence can guide conversations on cannabis use safety and ultimately inform policymakers on public health implications.

An RCT to Examine Driving Impairment

The Arkell trial used a randomized, double-blind, within-subject, placebo-controlled, crossover design. Participants ($n = 26$ enrolled; $n = 22$ completers) received a unique vaporized cannabis dose during four sessions (1 drug condition per session, 1 week apart) and completed two on-road driving tests during each session – one at 40–100 min post-dose and one at 240–300 min post-dose. Participants were accompanied by a trained driving instructor who had dual accelerator and brake control access. Cognitive tests, biological specimen collection, and subjective drug assessments were administered at baseline and at subsequent intervals post-dose. The primary endpoint was standard deviation of lateral position (SDLP, a measure of horizontal lane weaving) at 40 and 240 min after cannabis consumption. At 40–100 min post-dose, SDLP was significantly increased after THC-dominant (2.33 cm, 95% CI, 0.08–3.86; $p < 0$ .001) and THC/CBD-equivalent cannabis (2.83 cm, 95% CI, 1.28–4.39; $p < 0.001$) administration, but not after CBD-dominant cannabis (−0.05 cm, 95% CI, −1.49–1.39; $p > 0.99$), relative to placebo. At 240–300 min post-dose, all of the active doses were similar to placebo with no impairment detected.

The within-subjects design is a key strength as it minimizes bias that may occur with a between-subjects design and offers a statistical advantage of power. However, 15% of the randomized participants ultimately did not complete the study. Additionally, the sample in this study was comprised of a younger age group (mean 23.2 years, SD 2.6), which limits generalizability. While cannabis use is most prevalent among young adults (18–25 years) [1], adults ages 50 years and older represent the largest proportion of growth in the cannabis user population [9], yet generalizability to middle-aged and older adults is lacking, a particular concern with vision declines with age. Furthermore, older adults are more likely to use multiple prescription medications and may experience further impairment when combined with cannabis [10].

The study was conducted in the Netherlands and therefore, international differences in both driver education and the requirements to obtain a driver's license should be considered. Similarly, differences in societal acceptance of cannabis vary by country, which may translate to differences in how law enforcement decides to adopt policies to assess or pursue suspected impairment, such as zero tolerance or effect-based "per se limit" approaches. The authors also acknowledge that the CBD dosage used was lower than that used in approved prescription products for epilepsy, but is more similar to CBD doses in recreational and medical cannabis products. While the CBD dosage in this study may have been on the low end, a recent RCT that tested a range of acute CBD doses (0–1,500 mg) found simulated driving was not significantly impairing or intoxicating, which supports findings in the Arkell et al. study [11]. Still, we cannot conclude that CBD does not cause any degree of impairment given strong sedation has been demonstrated in clinical trials of high-dose prescription products [4, 12].

The RCT Findings as Compared with Other Literature

In comparison to recent experimental studies in which cannabis was administered on-site (see Table 1 for a summary of relevant studies), there appears to be consistency in findings that THC, whether alone or in combination with CBD, adversely affects some conventional driving measures (i.e., SDLP [13] and mean speed [14]) but not all (i.e., simple processing-speed tasks [15]) [7]. Despite differences in strengths of cannabis, routes of administration, and use of a placebo group, some experimental studies appear to support a dose-dependent relationship between THC and driving ability impairment [14, 16]. Two trials demonstrated that peak plasma THC concentrations play a role in magnitude of impairment, in chronic

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Table 1. Summary of recent experimental studies on the effects of cannabis on driving performance when cannabis was administered on-site

Study (year), design, and country	Study participants and cannabis use history	Type(s) of cannabis and route of administration (vaporized/smoked/oral)	Type of driving test and assessment	Primary driving outcome and result
Marcotte et al. (2022) [27] Randomized, double-blind, placebo-controlled parallel trial USA	Regular cannabis users, (*N* = 191) Mean age: 29.9 (SD 8.3) years Regular use defined**:** self-reported cannabis use ≥4 times in the past month	5.9% THC-dominant versus 13.4% THC-dominant versus placebo (0.02% THC) Route: smoked	Simulated driving test, 25 min, 4 total Tests of simulated driving occurred pre-dose and 30 min, 1 h 30 min, 3 h 30 min, and 4 h 30 min post-dose First task: at a specified distance, modification of the Surrogate Reference task completed, requiring participants to maintain their lane position and speed in a straight roadway, while responding to a divided attention task on an iPad to the side of the dashboard Second task: at another distance, car following required participants to adjust their speed to a lead car that speeds up and slows down according to a sinusoidal wave	Crashes and change in Composite Drive Score (CDS)[1] from baseline (pre-dose) Crashes ⇔ no significant differences between the 3 groups at any time point CDS ↑ THC groups had a significant decline in CDS performance ⇔ no significant differences between the 2 THC groups in change over time (groups combined for subsequent analyses**)** CDS at 30 min post-dose (relative to placebo) ↑ THC group performed significantly worse CDS at 1 h 30 min post-dose (relative to placebo) ↑ THC group performed significantly worse CDS at 3 h 30 min post-dose (relative to placebo) ⇔ no significant differences CDS at 4 h 30 min post-dose (relative to placebo) ⇔ no significant differences
Arkell et al. (2020) [8] Randomized, double-blind, placebo-controlled, within-subjects, crossover trial The Netherlands	Healthy occasional cannabis users, (*N* = 26) Mean age 23.2 (SD 2.6) years Occasional use defined**:** self-reported cannabis use ≤2 times/week in the past 12 months and ≥10 lifetime exposures	13.75 mg THC-dominant (THC 22% and CBD <1%) versus 13.75 mg CBD-dominant (THC <1% and CBD 9%) versus 13.75 mg THC/CBD equivalent versus placebo (<0.2% total cannabinoid content) Route: vaporized	On-road driving test, 60 min each, 8 total Licensed driving instructor with dual access to accelerator and brake present Participants drove a specially instrumented vehicle over a 100-km highway circuit while maintaining a constant speed (95 km/h [59 mph]) and a steady lateral position in the right (lower) lane	Mean SDLP[2] At 40–100 min post-dose (relative to placebo) ↑ THC alone increased SDLP ↑ THC/CBD equivalent increased SDLP ⇔ CBD alone did not alter SDLP At 240–300 min post-dose (relative to placebo) ⇔ THC alone did not alter SDLP ⇔ THC/CBD equivalent did not alter SDLP ⇔ CBD alone did not alter SDLP
Arkell et al. (2019) [13] Randomized, double-blind, placebo-controlled, within-subjects, crossover trial Australia	Healthy infrequent cannabis users, (*N* = 14) Mean age 27.5 (SD 4.5) years Infrequent use defined**:** self-reported cannabis consumption ≤ 2 times/week in the previous 3 months and ≥10 lifetime exposures	125 mg THC-dominant (11% THC, <1% CBD) versus 125 mg THC/CBD equivalent (11% THC, 11% CBD) versus placebo (<1% THC, <1% CBD) Route: vaporized	Simulated driving test, 30 min each, 6 total Tests of simulated driving began 30 min (T1) and 210 min (T2) post-dose First task: 5-min car-following task in which participants were required to follow and maintain a constant distance (headway) to a lead vehicle Second task: 25-min drive consisting of highway and rural segments, participants were instructed to follow spoken GPS directions and drive as they normally would	First task: SDLP, mean headway (distance to the lead vehicle), and standard deviation (SD) of headway Second task: SDLP, mean speed (MSP), and standard deviation of speed (SDSP) First task (relative to placebo) ↑ THC alone increased SDLP at T1 and T2 ↑ THC/CBD equivalent increased at T1 and T2 ⇔ THC alone did not alter mean headway at T1 and T2 ⇔ THC/CBD equivalent did not alter mean headway at T1 and T2 ⇔ THC alone did not alter SD headway at T1 and T2 ⇔ THC/CBD equivalent did not alter SD headway at T1 ↑ THC/CBD equivalent increased SD headway at T2 Second task (relative to placebo) ⇔ THC alone did not alter SDLP, MSP, or SDSP at T1 and T2 ⇔ THC/CBD equivalent did not alter SDLP, MSP, or SDSP at T1 and T2
Brands et al. (2019) [14] Randomized, double-blind, placebo-controlled, parallel-group trial Canada	Healthy young adults, regular cannabis users, (*N* = 91) Mean age 21.9 (2.2) years for placebo group 22.2 (1.8) for low THC group; and 22.3 (2.0) for high THC group Regular use defined: 1–4 days/week and evidence of recent use by qualitative urine THC-COOH determination	93.75 mg active cannabis* (cigarette with approximately 93.75 mg of 12.5% THC) versus placebo (0.07 mg THC) Cannabis cigarette smoked ad libitum *f*or 10 min *Active cannabis users split into High THC and low THC group**s**, based on a median split at 7.3 ng/mL blood THC concentration at +30 min (the beginning of the driving trials) Route: smoked	Simulated driving test, 3 total, at baseline (pre-consumption) and at 30 min, 24 h, and 48 h post-dose Single task condition: participants were instructed to drive as they normally would on a straightaway (i.e., straight stretch of road without any traffic control signals or other moving vehicles) with 80 km/h speed limit Dual-task condition: participants counted backward from a number between 700 and 999 × 3's while driving	Mean speed and lateral control[3] Single task condition, 30-min post-dose ↑ Mean speed differed between high THC, low THC, and placebo groups ⇔ High THC and low THC groups decreased their speed relative to placebo ⇔ High THC or low THC did not alter lateral control ⇔ No group differences at 24 h and 48 h post-dose Dual-task condition, 30-min post-dose ⇔ Mean speed and lateral control differed between high THC and low THC groups differed from placebo but not from one another ⇔ o group differences at 24 h and 48 h post-dose

Table 1 (continued)

Study (year), design, and country	Study participants and cannabis use history	Type(s) of cannabis and route of administration (vaporized/smoked/oral)	Type of driving test and assessment	Primary driving outcome and result
Hartley et al. (2019) [16] Randomized, double-blind, crossover trial France	Healthy chronic cannabis (CC) users, (n = 15) and occasional cannabis (OC) users (n = 30) Mean age 21.5 (3.26) Chronic (CC) use defined: 1–2 joints/day Occasional (OC) use defined: 1–2 joints/week Hair sampling was performed to confirm declarative OC or CC consumption	10 mg or 30 mg THC cannabis-containing cigarette (9.8% THC mixed with 1 g of tobacco and textile-grade hemp) Route: smoked	Simulated driving test, 30-min each, 7 total A monotonous 4-lane highway, with occasional passing vehicles, speed limit signs that the participants were encouraged to observe, and gusts of wind pushing the car and requiring corrective maneuvers	To examine the relationship between the dose and concentration of inhaled THC, reaction time, and driving ability Whole blood peak THC was 2 times higher in CC than in OC for a same dose and occurred 5 min after the end of consumption. THC remained detectable only in CC after 24 h, but CC consumed more than OC**.** Maximal effect for reaction time was dose- and group-dependent and only group-dependent for driving performance, both being decreased and more marked in OC than in CC. Delayed decrease in vigilance and driving performance, more pronounced and lasting longer in OC than in CC**.**
Ogourtsova et al. (2018) [15] Randomized, within-subjects trial (assessors blinded to time since cannabis use, participants blinded to randomization sequence) Canada	Young adult recreational cannabis users, (N = 45) Mean age 20.6 (1.3) years Recreational use defined: current use at least once within past 3 months and ≤4 days/week	100 mg THC cannabis (12.5% THC) Route: smoked	Simulated driving test ? duration not stated, 4 total Four randomized sequences of driving tests: (1) no cannabis (2) 1 h post-dose (3) 3 h post-dose (4) 5 h post-dose	Performance on three Useful Field of View (UFOV) measures UFOV-1: a simple processing-speed task UFOV-2: a complex divided-attention task UFOV-3: a complex selective-attention task Up to 5 h post-dose ⇔ No effect on simple driving-related tasks (UFOV-1) ↑ Significant impairment on complex tasks (UFOV-2, UFOV-3) ⇔ Lower self-perceived driving ability and safety
Micallef et al. (2018) [28] Randomized, placebo-controlled, double-blind, crossover trial France	Moderate tobacco smokers and occasional cannabis users Simulated driving (n = 15 completed) Real driving (n = 11 completed) Occasional use defined**:** self-reported smoking THC <1 time/month	20 mg THC (8% THC) and tobacco total, cannabis-containing cigarette versus Placebo cigarette (contained strong tobacco) Cigarette smoked as completely as possible (~20 min) Route: smoked	Simulated driving test, 2 h, 2 total versus Real (on-road) driving test, 2 h, 2 total Professional driving instructor with dual access to accelerator and brake present for real driving	Inappropriate line crossings (ILC) and SDLP Simulated driving condition ↑ THC impaired driving stability ↑ THC increased ILC Real driving condition ↑ THC impaired driving stability ⇔ THC did not significantly alter ILC Simulated driving was proven to be more sensitive for demonstrating THC-induced effects on driving performances
Bosker et al. (2012) [29] Randomized, placebo-controlled, double-blind, three-way crossover trial The Netherlands	Occasional cannabis users (n = 12) and heavy cannabis users (n = 12) Occasional use defined 5–36 times/year Heavy use defined**:** >160 times/year	10 mg dronabinol versus 20 mg of dronabinol versus Placebo Dronabinol and placebo were given only when occasional users tested negative and heavy users positive on THC and negative on other drugs (alcohol breath test and urine drug screen) Route: oral	On-road driving test, 3 total, between 2 and 4 h post-dose Road-tracking test (1 h): subjects had to maintain a constant speed of 95 km/h (60 miles/hr) and drive as straight as possible on the right-hand lane of a primary highway Car-following test (25 min): subjects drove behind a leading vehicle on a primary highway maintaining a constant distance between vehicles during a series of speed decelerations/acceleration initiated by the experimenter in the leading vehicle	SDLP, time to speed adaptation (TSA), and performance on Standard Field Sobriety Test (SFST) Road-tracking ↑ Dronabinol increased SDLP in occasional users (relative to heavy users) Car-following ⇔ Dronabinol did not significantly increase TSA in occasional users (relative to heavy users) SFST ⇔ No significant effects of dronabinol or cannabis use history

1. A composite of standard deviation of lateral position (SDLP), standard deviation of speed, number of correct divided attention stimuli identified while driving (first task); and coherence between the participant and lead car, a correlation ranging from 0 to 1 (second task). 2. Standard deviation of lateral position (SDLP) is a measure of lane weaving. 3. Lateral control operationalized as the standard deviation of the absolute distance between the center of the simulated vehicle and the center of the lane in which the participant was driving. * Peak plasma concentrations and ranges of blood concentrations were reported inconsistently in reviewed studies and so are excluded from this summary.

users compared with occasional users [16], as well as with THC/CBD equivalent (11% THC, 11% CBD) cannabis suggesting a potential pharmacokinetic (or potentially pharmacodynamic) interaction [13].

This aligns with findings from prospective observational studies of chronic cannabis users. A prospective cross-sectional study by Dahlgren et al. [17] found significant driving impairment among chronic, heavy, recreational cannabis users compared with healthy controls with the cannabis users abstaining at least 12 h prior to a simulated driving test. A similarly designed study by Doroudgar et al. [18] found significant differences between chronic cannabis users and nonusers in failed standardized field sobriety tests and slower visual reaction times, although they deviated less in speed. Limitations of these studies are differences in THC detection (Dahlgren et al. used plasma and oral samples; Doroudgar et al. used urinary samples). Additionally, Dahlgren et al. note that impulsivity personality traits may be an important confounder as an impulsive style of driving performance was observed among non-intoxicated cannabis users, characterized by increased accidents, speeding, lateral movement, and decreased rule-following [17].

What the totality of the research thus far lacks, as summarized well by the National Academy of Science, Engineering, and Medicine's report, are important methodological limitations of "DUIC" not necessarily referring to acute intoxication but satisfied by recent use; and a lack of definitive causal evidence for the association of THC levels in blood with either acute intoxication or driving impairment, which has inhibited determining a clear dose at which driving becomes sufficiently unsafe as to increase motor vehicle accident (MVA) risk [1]. Epidemiological studies generally support that there is a moderate risk with cannabis use and being involved in or responsible for a MVA [7]. A meta-analysis by Rogeberg and Elvik of 21 case-control or culpability studies, found that DUIC (by self-reported cannabis use or the presence of THC metabolites in urine or blood) was associated with 20–30% higher odds of an MVA [6]. However, simulated driving studies were not included and the authors described the magnitude of the association as low to moderate [6].

Clinical Considerations

It should be noted by clinicians that self-reported use and presence of a THC metabolite in screening tests (e.g., urine and blood tests) do not necessarily equate to acute impairment. Blood tests for THC are challenging to administer in a timely fashion immediately after an accident or concerning traffic event, which limits the utility of existing tests as enforcement tools. In a follow-up study in 2019, Rogeberg showed that culpability studies tend to misinterpret effect estimates and substantially exaggerate risk associated with cannabis [5], likely in part due to the lack of acuity in distinguishing impairment from recent exposure. A US National Highway Traffic Safety Administration report on marijuana-impaired driving concurs with exercising caution in the interpretation of risks obtained from culpability studies [19]. Another recent review concluded that there is evidence of significant correlation between high THC plasma concentration (≥3 ng/mL) and risk but not for lower levels of THC (1–2 ng/mL), though establishing a clear cut-off value remains elusive practically speaking [20]. Numerous factors affect THC blood concentrations including route of administration, regular cannabis use, and time-lapse between exposure and measurement, in addition to variability in collection, storage, and analytic methods. Yet, THC blood level cut-off are already recommended as per se limits by experts and policymakers in some USA, Canada, European countries, and other jurisdictions [20]. Overall, the breadth of the cannabis crash risk literature demonstrates that acute cannabis intoxication can impair driving-related skills and neurobehavioral skills (e.g., impaired executive function which increases reaction time, such as stopping at a red light) [7, 19, 21, 22]. Still, high-quality data sources for tracking cannabis use and monitoring DUIC are critically needed for public health research and policymaking [23].

The current evidence base begs two unanswered questions for DUIC: (1) how, or to what extent, do cannabis and its many constituents impair an individual's ability to drive? and (2) is association between cannabinoid levels and the extent of impairing effects accurate and reliable? Scenarios not addressed in the Arkell study highlight questions that warrant more research including: tolerance by regular users (i.e., medical cannabis users); varying modes of administration (e.g., edibles have lower bioavailability but a delayed onset of action leading to longer lasting impairment [24]); impairment when cannabis is combined with other substances; and variability of cannabis products at the local, national, and global level. A conservative approach is to exercise caution following administration of, and up to at least 5 h after [7], THC-containing cannabis products before operating a vehicle. Canada's "Lower Risk Cannabis Use Guidelines" may be considered as a starting point for clinical recommendations [25].

Conclusion

In the absence of standard and universal thresholds indicating impairment for DUIC, as well as lack of cannabis packaging warnings, it is recommended that clinicians counsel their patients on driving safety and risks, particularly if it is known that the patient is using THC-containing cannabis products. Counseling in a broad sense could communicate risks of impairment for at least 5 h after using a THC-containing cannabis product alone and longer if concomitant with alcohol or other substances; or complete abstention from driving after cannabis use for a significant period (e.g., at least 12 h), particularly if residing in a jurisdiction with zero-tolerance laws. However, the type, dosage, and frequency of cannabis product use should be considered by the clinician when tailoring communication for their patient's needs.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Brianna Costales and Amie J. Goodin conceptualized and drafted the work. Shanna L. Babalonis and Joshua D. Brown drafted and revised. All approved the final version.

Editor's Note

Evidence in Context is part of the outreach effort of the Consortium for Medical Marijuana Clinical Outcomes Research to examine and discuss implications of research into cannabis and cannabinoids for clinical practice, thus providing a translational approach to these studies to make clear, concise, and actionable evidence available for clinicians and patients.

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