Association of driving with blood THC: A systematic review

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Summary

Background: Driving under the influence of cannabis increases the risk of motor vehicle collisions. In some jurisdictions, deterrence rests on the ability to detect delta-9-tetrahydrocannabinol (THC) in blood. Recent evidence suggests that there may be a nuanced relationship of blood THC to driving. The purpose of this systematic review was to summarize all published papers investigating the presence of a relationship between blood THC and driving, primarily measured by simulated driving in the lab.

Methods: The systematic review was completed according to PRISMA, and the protocol was preregistered (PROSPERO CRD42023493758). All peer-reviewed studies that measured the strength of the linear relationship between driving outcomes and blood THC, up to September 2023 were included. The studies were appraised using SIGN Methodology Checklists. The main outcomes assessed included 'weaving'/lateral control (e.g., standard deviation of lateral position (SDLP)), speed, car following (following distance; coherence), reaction time, and overall driving performance. Summary

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 Findings: Of the 4,845 records from the literature search, only 12 met the criteria. 10 of these reported no significant linear correlations between blood THC and measures of driving (8 out of 9 for 'weaving'/lateral control, 4 out of 5 for speed, 2 of 3 for car following tasks (coherence / headway maintenance task), 1/1 for reaction time, 3/3 for overall driving performance). The studies that did find an association between driving and blood THC employed complex driving situations.

Interpretation: This synthesis has important implications for road safety given driving situations can be complex due to challenging road situations and increases in potency of cannabis over the past years. Current methods of detection of impairment may be suited to some types of situations but more large-scale studies on the relationship of blood THC and driving are needed that systematically vary driving complexity and cannabis potency.

Funding: This study did not receive specific funding.

Introduction

Cannabis increases the risk of a motor vehicle collision ¹⁻⁶, and one method of deterring driving after use of cannabis rests on the ability to detect delta-9-tetrahydrocannabinol (THC) in the blood of the driver. The THC concentration in the blood at which driving is believed to be impaired varies by jurisdiction but is generally in the range of 2 to 5 ng/mL⁷. Laboratory studies provide converging evidence that cannabis increases 'weaving' (standard deviation of lateral position; SDLP) $8-19$, slows reaction time $9,11,13,20$ and produces compensatory decreases in speed ^{9,11,13,21,22} and increases in headway maintenance task ^{13,14,21}. A number of studies found that there are dose-dependent increases in SDLP ^{10,23} and speed 8,11,14,24-26, suggesting that the degree of impairment may be related to blood THC concentration. Introduction

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of cannabis rests on the ability to detect delta-4-tetrahydrocannabinol (THC) in the blood of the d

The recent relaxation of regulations for non-medical cannabis in Canada and the United States has led to an increased use in cannabis ^{27,28}. At present, this may lead to growing concerns for road safety as acute cannabis use has been shown to significantly increases the risk of vehicle collisions 1 . However, demonstration of a clear relationship between changes in driving and blood THC would provide guidance in the detection of cannabis-impaired driving.

The purpose of the present synthesis was to review all published reports that attempted to determine whether blood THC is related to driving. Particular attention was paid to studies that employed correlational or regression analyses to attempt to elucidate whether there is a linear relationship between blood THC and driving. A literature search was conducted on peer-reviewed papers published until 2023 that measured both driving (simulated or on-the-road) and blood THC. The relationship of driving variables to blood THC was assessed.

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Methods

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRSIMA) guidelines ²⁹. A protocol was pre-registered on Prospero, the international prospective register of systematic reviews (registration number CRD42023493758)

Information Sources and Search Strategy

A comprehensive search strategy (see Supplementary Material, eAppendix 1) was drafted in Ovid Medline by a Medical Librarian (RB) and refined with input from the research team. The following terms were searched broadly (THC/cannabis) AND (blood or oral fluid or substance detection) AND driving. The Medline strategy was adapted into PsycINFO, Embase, Cochrane Central, Cochrane Database of Systematic Review via Ovid platform, Web of Science's Core Collection, Ebsco's Criminal Justice Abstracts, ProQuest's Dissertations & Theses Global, and Transport Research International Documentation (TRID Database). All strategies used database specific syntax, and controlled vocabulary when translated. To increase specificity of results, an animals studies filter was used 30 ; no further limits were applied. Each database was searched from inception to September 2023. Reference lists of included articles were scanned to identify further studies meeting eligibility criteria. M[e](https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023493758)thods
This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and
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prospective

All database records were imported into Covidence for de-duplication and title and abstract screening. Endnote, a citation and reference management tool, was also used to manage records.

Inclusion Criteria

The primary focus of this synthesis was to evaluate studies that conducted a correlational analysis between blood THC and driving (on-the-road or simulated). However, understanding that this may not capture the breadth of knowledge and literature on the topic, similar measures of association such as linear regression or general linear model (GLM) regressions were also included. Only studies in English were included, due to lack of personnel available to translate and complete the full text extraction and risk of bias assessment.

Only peer-reviewed published articles of the following types were included: randomized controlled trials, before-and-after studies, cohort, case-control, cross-sectional, and longitudinal studies. Only studies of human participants were included that focused on the effects of acute cannabis (i.e. in the hours after administration). Moreover, this review only included studies of the effects of THCdominant cannabis, and not cannabidiol (CBD). Driving measures of interest included but were not limited to standard deviation of lateral position (SDLP; 'weaving'), reaction time, mean speed, maximum speed, collisions and for car following tasks (coherence / headway maintenance task - the ability to consistently follow the lead vehicle). Inelusion Criteria

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Exclusion Criteria

The review excluded the following study designs: meta-analyses / reviews, case studies, and qualitative studies. Conference abstracts and posters and grey literature were also excluded.

Selection and Data Collection Process

All the articles from the literature search were transferred into Covidence, which automatically removed the majority of duplicates. Two authors (DB, SZ) then independently completed the title / abstract screening, and full text review. This was followed by data extraction, which was also completed independently by two authors (DB, SZ). The full text data extraction form is available in eTable 1 in the Supplementary, and includes general characteristics, such as: author(s), journal, year of publication, study location, and study design. Population characteristics were also included: sample size (n), age range / mean, and percent or number of females. Furthermore, the following study characteristics were documented: objectives, inclusion / exclusion criteria, how outcomes were assessed, and results / outcome point estimates. Given the nature of the study, the amount of THC/cannabis administered was also recorded. Any disagreement or conflict during these processes was addressed through discussion, and a third reviewer (PDC) was consulted on differences that could not be resolved. Selection and Data Collection Process

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Risk of Bias

Following full text extraction, two authors (D.B., S.Z.) utilized the Scottish Intercollegiate Guidelines Networks (SIGN) methodology checklists to individually assess the risk of bias for the included studies. Any disagreement or conflict was addressed through discussion, and a third reviewer (P.D.C.) was consulted for a final decision on differences that could not be resolved. The SIGN methodology checklists assess risk of bias through the following characteristics: study design, randomization, concealment, blinding, allocation, treatment vs control group differences, outcome assessment method, attrition, and confounding. These categories collectively determine the overall assessment of the study, which is coded as high quality – low risk of bias; acceptable quality – medium risk of bias; low quality –

high risk of bias; or unacceptable – study to be omitted from review. This provides a method to rank the degree of bias present in the study, and a categorical measure of the confidence in a study's results.

As per the protocol, correlational analysis on oral-fluid THC and driving measures was also observed. However, given the limited literature available, there is not sufficient data to be presented as part of the 'results' synthesis, but is discussed in eAppendix 2 of the Supplementary. Night risk of biss; or unscend baller -study to be annitred from review. This provides a method to rank the
degree of biss present in the study, and a categorical measure of the confidence in a study's results.
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There was no specific funding source for this study.

Results

The selection process is visualized from the PRISMA Flow Diagram attached as Figure 1. The literature search resulted in 4,845 records. After the literature search, another two studies relevant to the review were published and were also included. Overall, a total of 1,648 duplicates were removed, leaving 3,199 unique articles to be screened. From these, 3,102 were excluded during the title and abstract screening. Of the remaining 97 articles, 96 underwent full-text screening, as one study could not be retrieved. Of the 96 articles screened, 12 were included in the review. An overall breakdown of the reasons for study exclusion is provided in Figure 1. Overall, the included studies date from 1998 to 2024.

Of the 12 papers included, eleven used inhaled (smoked/vaped) routes and one used edibles (Table 1). Only two papers studied oral fluid (eAppendix3 in Supplementary Material).

Nine articles included data on blood THC and SDLP or other measures of lateral control; 8 found no relationship and 1 found a relationship. Zhao et al. ²² was the sole study to use edibles and participants consumed an average of 7.30 mg THC, and Pearson r correlations revealed no significant correlation between blood THC and SDLP (single task: $r = -0.202$, $p = 0.366$; dual task: $r = -0.096$, $p = 0.671$). In Arkell et al. ³¹ participants vaped 13.75 mg THC and upon conducting Kendall's tau-b correlation, found that blood THC was not significantly correlated (T_b = -0.11, p = 0.90) with SDLP. For Robbe et al. ²³ participants smoked 20.8 mg THC on average and reached the same conclusion, that there was no significant correlation between blood THC and SDLP or mean lateral position. In Hartley et al. 32 participants smoked doses up to 30 mg THC and used linear regression to determine that there was no significant association between blood THC pharmacokinetic parameters (Cmax, Tmax, and AUC) and Results

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SDLP. In Di Ciano et al. ⁸ participants smoked an average of 56.93 mg THC, and there was no significant correlation (Pearson's r) between blood THC and SDLP (single task $r = 0.147$, $p = 0.43$; dual-task: $r =$ 0.027, $p = 0.89$). For Brands et al. ²⁴ participants smoked 93.75 mg THC and using bivariate correlations discovered that there was no significant correlation (single task $r = -0.16$, $p = 0.21$; dual task $r = 0.16$, $p =$ 0.22) between blood THC and change in lateral control. In Di Ciano et al. 33 participants smoked 94 mg THC and upon conducting Spearman's correlations, also found that blood THC did not significantly correlate (r = 0.201) with SDLP. In Fitzgerald et al. 34 participants similarly smoked doses up to \sim 94 mg THC and using Spearman's correlations discovered that blood THC was not significantly correlated (r = −0.02, padj = 0.89) with SDLP. SOIP. In Dictions cent. ^{it} participants smoked an average of 56.93 mg THC, and there was no significant
correlation (Pearson's r) between blood THC and SOIP (single trak $r = 0.147$, $p = 0.48$, disal trak it $r =$
0.022,

Hartman et al. ¹⁷, was the only study that found a significant relationship of blood THC to SDLP. Their participants inhaled up to \sim 33.5 mg THC and conducted general linear model (GLM) regression models, finding a significant association ($b = 0.26$, $p = 0.0004$) between blood THC and SDLP. The data from the model indicated that for every 1 µg/L increase in blood THC, there was a 0.26 cm increase in SDLP. However, there was no association between blood THC and standard deviation of the steering wheel (curvy and straight routes), lane departures / min, or maximum lateral acceleration (sharp and non-sharp events).

Five of the included studies included measures of blood THC and speed, 4 of these studies found no relationship of blood THC to speed. Zhao et al. ²² found no significant correlation between blood THC and mean speed (single task: $r = 0.151$, $p = 0.503$; dual task: $r = 0.139$, $p = 0.536$). Robbe et al. ²³ conducted correlational analysis and found no significant correlation between blood THC and maintenance of constant speed or standard deviation of speed. Di Ciano et al. ⁸ also found no significant correlation between blood THC and mean speed (single task: $r = 0.206$, $p = 0.27$; dual-task: $r = 0.056$, $p =$ 0.76). Brands et al. ²⁴ conducted Pearson r correlations and found no significant correlation (single task r $= -0.18$, $p = 0.15$; dual task $r = -0.083$, $p = 0.53$) between blood THC and change in mean speed.

Hartman et al. ²¹ conducted GLM regression models and found significant associations between blood THC and mean speed relative to the speed limit ($b = 0.11$, $p = 0.0001$) and percent speed low [percent of time spent >10% below the speed limit] (b = 0.07, p = <0.0001). Essentially, higher blood THC was associated with decreased mean speed and increased time spent at low speeds. However, they also found that blood THC was not associated with standard deviation of speed, percent speed high, maximum longitudinal acceleration and minimum longitudinal acceleration. 0.76). Romain et al. ²⁴ conducted Peurson r correlations and found molegatism teameless per restates (with the state of the stat

Three studies conducted car following tasks, with 1 finding a significant correlation. Robbe et al. ²³ conducted a car-following test and found no significant correlation with blood THC. Fitzgerald et al. ³⁴ observed the association between coherence and blood THC, and upon using Spearman's correlations, found no significant correlation ($r = -0.102$, $p = 0.46$) between the two.

Hartman et al. ²¹ conducted GLM regression models and found significant associations between blood THC and headway maintenance [mean following distance] (b = 2.18, p = 0.0139). Essentially, higher blood THC was associated with increased following distance.

Hartley et al. ³² was the only study to analyse reaction time and found no significant association between blood THC pharmacokinetic parameters (Cmax, Tmax, and AUC) and mean reciprocal reaction time (mRRT) using linear regression.

Three studies focused on correlating blood THC with overall driving performance, and none found a significant correlation. Robbe et al. ²³ conducted the Royal Dutch Tourist Association's Driving Proficiency Test and found no significant correlation with blood THC. Tank et al. ³⁵ gave their participants

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300 ug THC / kg bodyweight per cigarette with a 3-cigarette allowance, resulting in blood THC concentration ranging from 2.4 to 42.9 ng/mL. They found no significant correlation between blood THC and overall driving performance (which included measures such as collisions, roadway deviation and traffic lights). In a study conducted by Marcotte et al. 36 , participants smoked doses going up to \sim 94 mg THC; using Spearman's correlations, no significant correlation (r *=* 0.025, p = 0.78) between blood THC and the composite drive score (incorporates lane tracking and car following) was found. Hence, both articles are in agreement that there is no correlation between blood THC and composite measures of overall driving performance. 360 ug THC / kg bodyweight per réprette with a 3 cigarette allowance, resulting in blood THC
concentration ranging from 2.4 to 4.2 9 ng/ml . They found no significant correlation between blood THC
and overall driving perfo

Quality of Studies

Using the SIGN methodology checklists, all twelve studies were assessed for bias. Nine of the included studies were randomized controlled trial (RCT) studies, all of which were assessed to be of high quality 17,21,23,24,31-34,36. The two cohort studies were assessed to be of high quality 8,22. The exception was Tank et al. ³⁵, a controlled trial which was assessed using the RCT checklist and determined to be of acceptable quality. A summary of the risk of bias assessment is available in eTable 2 in the Supplementary Material.

Discussion

The purpose of the present synthesis was to evaluate the peer-reviewed papers published on the relationship between driving and blood THC levels. Of the 12 papers included in the present review, ten found no correlation between blood THC and any measure of driving 8,22-24,31-36, including SDLP, speed, car following, reaction time, or overall driving performance. The two papers that did find a significant association were from the same study and found significant relationship with blood THC and SDLP¹⁷, speed and following distance ²¹.

The consensus is that there is no linear relationship of blood THC to driving. This is surprising given that blood THC is used to detect cannabis-impaired driving. However, roadside detection is based on cut offs, which vary by jurisdiction ⁷. In this regard, one paper found that SDLP was significantly higher in people whose blood THC was above the legal cut off than those who were below 33. Similarly, when a median split was conducted based on levels of blood THC, there were more changes in driving in those who were above the legal limits 24 . In these same studies 24,33,37 , there were no correlations between blood THC and driving. Thus, there may be limits above which driving is impaired, which may explain why the one study with high doses found significant correlations between driving and blood THC.

The two Hartman et al.^{17,21} papers that came from the same study and found significant relationships between blood THC and driving, used complex driving situations that consisted of a combination of rural, urban and interstate roads. By comparison, the other studies used either rural roads 8,22-24,32,33 or urban ³⁵ situations. Only a few studies combined the use of two types of drives within a single scenario^{23,31,34,36}. Additionally, the Hartman et al.^{17,21} simulated drives were more complex as they included distractors such as deer emerging in rural areas, car doors opening into traffic and kids on bicycles. They also conducted the drives under dual task conditions, which only a few of the other studies 8,22,24,36 integrated. The dual tasks place additional cognitive load on participants and required divided attention as they involved watching lights in the rear-view mirror and selecting a specific CD title. Thus, the only two studies which combined more than two types of drives, had complex distractors and observed dual task conditions, found significant correlations between blood THC and driving. Thus, scenario and task complexity may be an important variable in revealing an association between blood THC and driving. Future studies will need to vary the task demands of the drive to unravel the complex relationship of blood THC to driving. The conversas is that there is no linear relationship of blood THC to driving. This is surprising
given that blood THC is used to detect completion paired driving. However, roadside detection is joined
on cut offs, which

One variable which may have influenced the results is the potency of cannabis used and method of administration. An abstract submitted (unpublished; LeFoll et al., 2024) by the present authors, suggests dose related effects of THC on measures of driving. In this study, the highest dose condition provided participants with 22% THC or up to 165 mg THC in a procedure that involved a fixed dose administration. Both SDLP (slope=0.01, SE=0.001, p<0.001) and reaction time (slope=0.01, SE=0.003, p<0.001) showed significant positive associations with blood THC. This indicates that for each 1 ng/mL increase in blood THC, SDLP increased by 1 cm, and reaction time increased by 10 milliseconds. It was noted that minimal differences were observed in the low (6.25%/up to 47 mg THC) and medium dose $(12.5\%/$ up to 94 mg THC), but consistent and significant differences were present in the high dose 38 . It is known that the potencies of cannabis on the legal market are increasing ³⁹, and thus it can be inferred that people are using higher doses of THC than those used in most existing studies. In addition, the fixed dose procedure used in part of this study may have influenced the results ⁴⁰. Ad libitum dosing studies may lead to increased variability in the data with little distinction between doses 34,36, as people can titrate to their desired effect. Orderly relationships between blood THC and driving may be evident only with discrete increments in dosing. Future studies will need to include more realistic higher potency cannabis, and vary the dosing method, because it is possible that blood THC may have orderly relationships to higher potency cannabis use. One variable which may have influenced the matrix si the patency of cannobis used and method
of administration. An abstract submitted (unpublished; LeFoll et al., 2024) by the present authors,
suggests dose related effect

Limitations

This synthesis is not without limitations. First, all but one 22 of the included studies investigated the inhaled (smoked, vaped) route of administration. The use of edibles is on the rise ^{27,41,42} and edibles have a different pharmacokinetic relationship than the inhaled route $43-49$, which suggests that the relationship of cannabis edibles to blood THC may be different. Further, only two studies used

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naturalistic designs 8,22. With legalization, it is now possible, in some jurisdictions, to study a user's preferred legal source cannabis in the lab. In addition to the considerations around the potency of cannabis and method of administration, future studies should vary task complexity with a variety of routes of administration, both controlled and naturalistic.

Conclusions

The present synthesis suggests that driving after the use of cannabis may be difficult to detect through blood THC, except in situations where there is a high task complexity; there is some evidence for a relationship when potencies of cannabis are high. Driving can involve a number of challenging situations and future studies will need to explore the relationship of THC to driving after a number of different task situations and cannabis potencies. maturalistic designs ⁶². With legalization, it is now possible, in some jurisdictions, to study a user's
preferred legal source consider in the lab. In addition to the considerations anound the potency of
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Panel: **Research in context**

Evidence before this study

The psychoactive component of cannabis is THC, and has been shown to have impairing effects on driving. Research on THC and driving has shown that it leads to increased weaving, decreased reaction time, and a decreased ability to follow a lead vehicle. To regulate cannabis use during driving, blood THC is often used to assess impairment. Current research indicates that there may be a more complex relationship between blood THC and driving. However, to date, there is no published synthesis of data, on whether these is a correlational relationship between blood THC and driving outcomes. Therefore, a search of numerous databases from inception to September 2023 was conducted, to find published articles that measured the relationship between blood THC and driving outcomes, using correlations, linear regressions and general linear mixed models.

Added value of this study

The systematic review was composed of 12 published articles, the majority (10 studies) of which found no clear linear relationship between blood THC and driving. The papers that did find a relationship, found that increased blood THC was associated with increased weaving, decreased mean speed, and increased following distance of the car ahead. However, these studies used comparatively more complex driving scenarios than the other studies. These results provide the first synthesis of data for the correlational / linear association between blood THC and driving and indicate that generally no such relationship exists. Through the use of cut-offs, the current method of detecting roadside cannabis impairment through blood THC may still be suitable for some types of impairments, but it is not all encompassing. Panel: Research in context

Coldence before this study

The psychosctive component of cannabis is THC, and has been shown to have impairing effects on

driving Research on THC and driving has shown that it leads to increas

Implications of all the available evidence

Given that the results were not unanimous, and the two studies that did differ, did so under distinct conditions, indicates the need for further research into the subject. Future studies should look to vary task complexity and road challenges to better stimulate real-world driving. Additionally, with rising popularity of new forms of cannabis and higher potency of cannabis, researchers should look to evaluate THC across different routes of administration and greater THC concentrations. Moreover, from a policy perspective regarding road safety, there may be a need to evaluate and introduce new methods of assessing roadside cannabis impairment, or further changes in regulations, such as blood THC cutoffs. Implications of all the available endence

Olven that the results were not unanimous, and the two studies that did differ, did so under distinct

conditions, indicates the need for further research into the subject. Future

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Competing Interests:

Dr. Bernard Le Foll has obtained funding from Indivior for a clinical trial sponsored by Indivior. Dr. Le Foll has in-kind donations of placebo edibles from Indivia. Dr. Le Foll has obtained industry funding from Canopy Growth Corporation (through research grants handled by the Centre for Addiction and Mental Health and the University of Toronto). Competing Interests:

Dr. Le roll has included and and any form individual for a dinical trail is ponsoned by individual

Dr. Le rich has invisind constants of placebo eddeled from individual b. It. Le rich lass obtained

He has participated in a session of a National Advisory Board Meeting (Emerging Trends BUP-XR) for Indivior Canada and is part of Steering Board for a clinical trial for Indivior. He has been consultant for Shinogi and ThirdBridge.

He got travel support to attend an event by Bioprojet. He is supported by CAMH, Waypoint Centre for Mental Health Care, a clinician-scientist award from the department of Family and Community Medicine of the University of Toronto and a Chair in Addiction Psychiatry from the department of Psychiatry of University of Toronto.

No other authors have any conflicts to declare

Table 1: General Characteristics of Included Articles									
Authors, year	Study Design	Sample Size (% female)	Age range \prime mean	Cannabis Administration	THC Dose	Driving Assessment Scenario	Driving Measures	Method of Assessing Association	Significant Associatio n
Studies using inhaled routes for cannabis, that found a relationship between blood THC and driving									
Hartman et al., 2015 17	Randomize Controlled Trail (RCT)	18 (27.8%)	$21 -$ 37 Mean \equiv 26.1	- Vaped - Ad libitum	Placebo 2.9% THC $(^{\sim}14.5)$ mg THC) 6.7% THC $(^{\sim}33.5)$ mg THC)	Driving Simulator - Urban (two lane city roadway; 40-72 km/h with signal $-$ controlled / uncontrolled intersections) - Interstate (four lane expressway; $113 km/h$) - Rural (two lane undivided road with curves, a gravel portion, and 10 min timed straightaway)	SDLP - dual task Standard deviation of steering wheel (curvy and straight routes) - dual task Lane departures / min - dual task Maximum lateral acceleration (sharp and non-sharp events) - dual task	General Linear Model (GLM) regression models	Yes
Hartman et al., 2016 21	RCT	18 (27.8%)	$21 -$ 37 Mean \equiv 26.1	- Vaped - Ad libitum	Placebo 2.9% THC $($ ~ 14.5 mg THC) 6.7% THC $(^{\sim}33.5)$ mg THC)	Driving Simulator - Urban (two lane city roadway; 40-72 km/h with signal $-$ controlled / uncontrolled intersections) - Interstate (four lane	Mean speed - dual task Standard deviation of speed - dual task Percent speed high	GLM regression models	Yes

Table 1: General Characteristics of Included Articles

