Webinar

Key Information for DUIC Policy

Professor Nicholas Ward

Director, Center for Health and Safety Culture

DUIC Key Information Webinar, November 6th.

Purpose

- Provide an accessible report that **integrates** evidence about cannabis and traffic safety.
- Provide **tools** for stakeholders to discuss implications of cannabis decriminalization laws on traffic safety:
  - Report
  - Posters (Infographics)
  - Presentations (PPT)
  - Talking Points
  - Webinar

Included

- The Context: Reasons for growing **interest**.
- The Drug: **Issues** affecting measurment.
- The Logic: **Impairment** sequence of drug.
- The Risk: Interpretation of crash **risk**.
- The Law: Effect of decriminalization **laws**.

Excluded

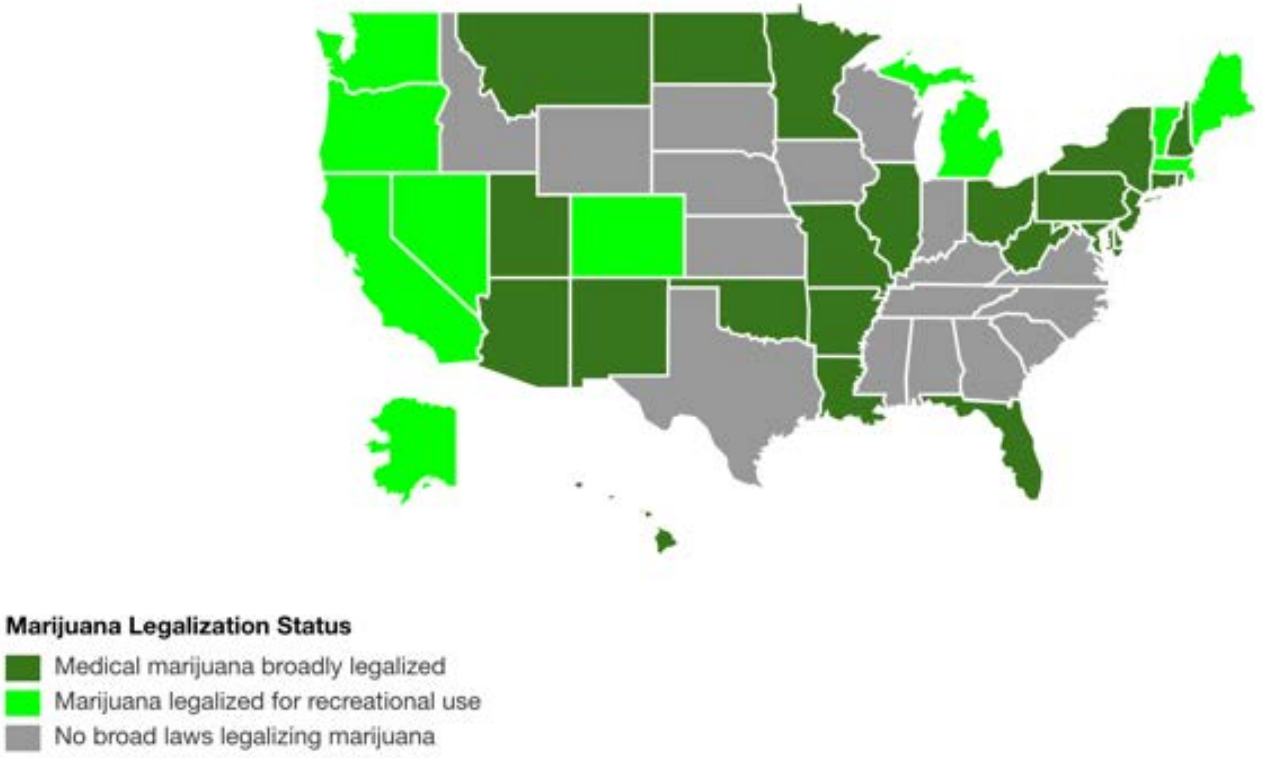
- **Ethics** of cannabis use.
- **Medical** effectiveness of cannabis.
- **Justification** for cannabis laws.
- **Policies and technology** for cannabis detection.

NOTE: We are trying to present the consensus within the research, not debate the results of individual studies.

The Context

Why is there growing interest in this topic?

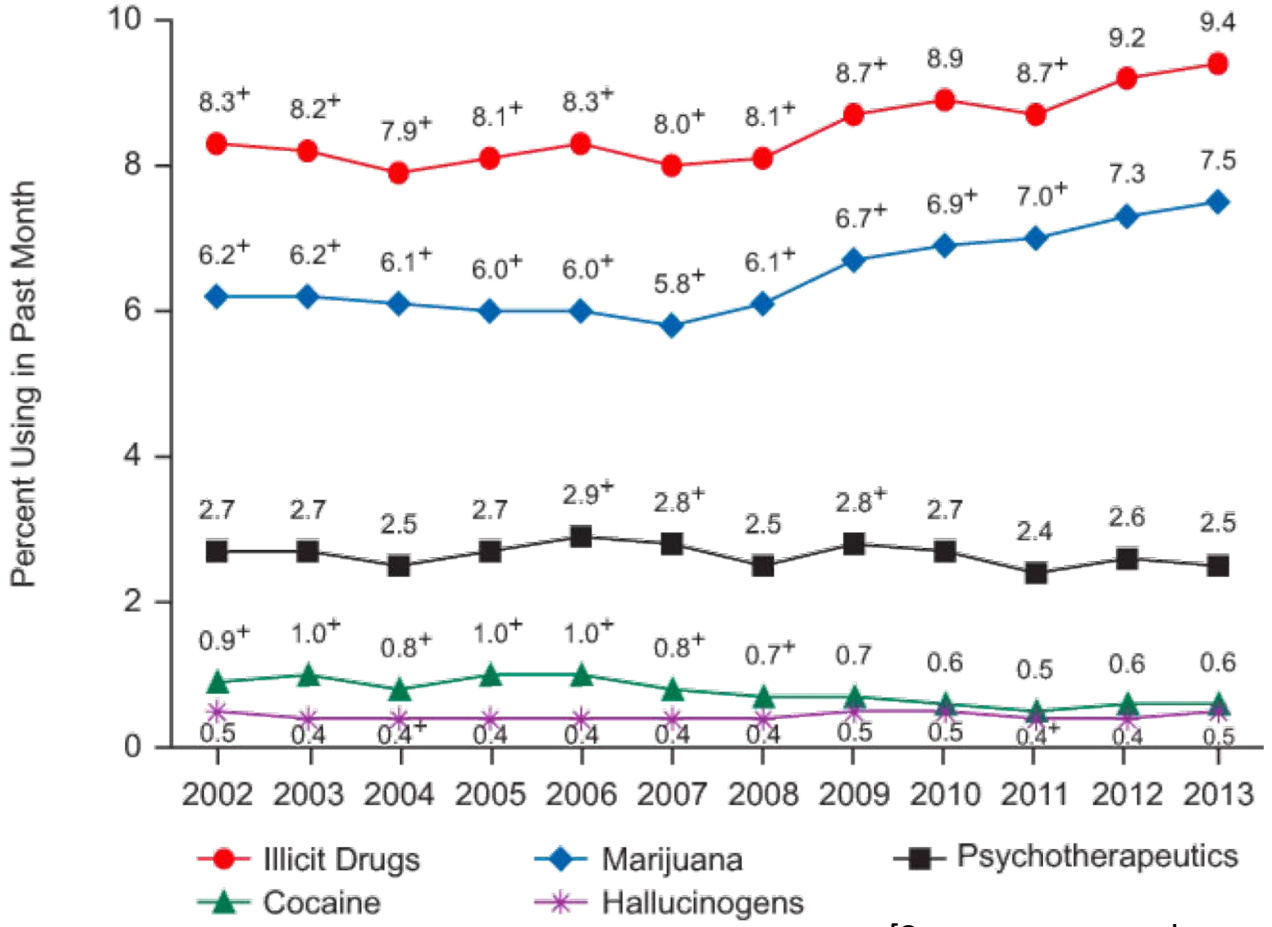
Access



Types of laws regarding cannabis use in states by end of 2018 (Source: Governing 2019).

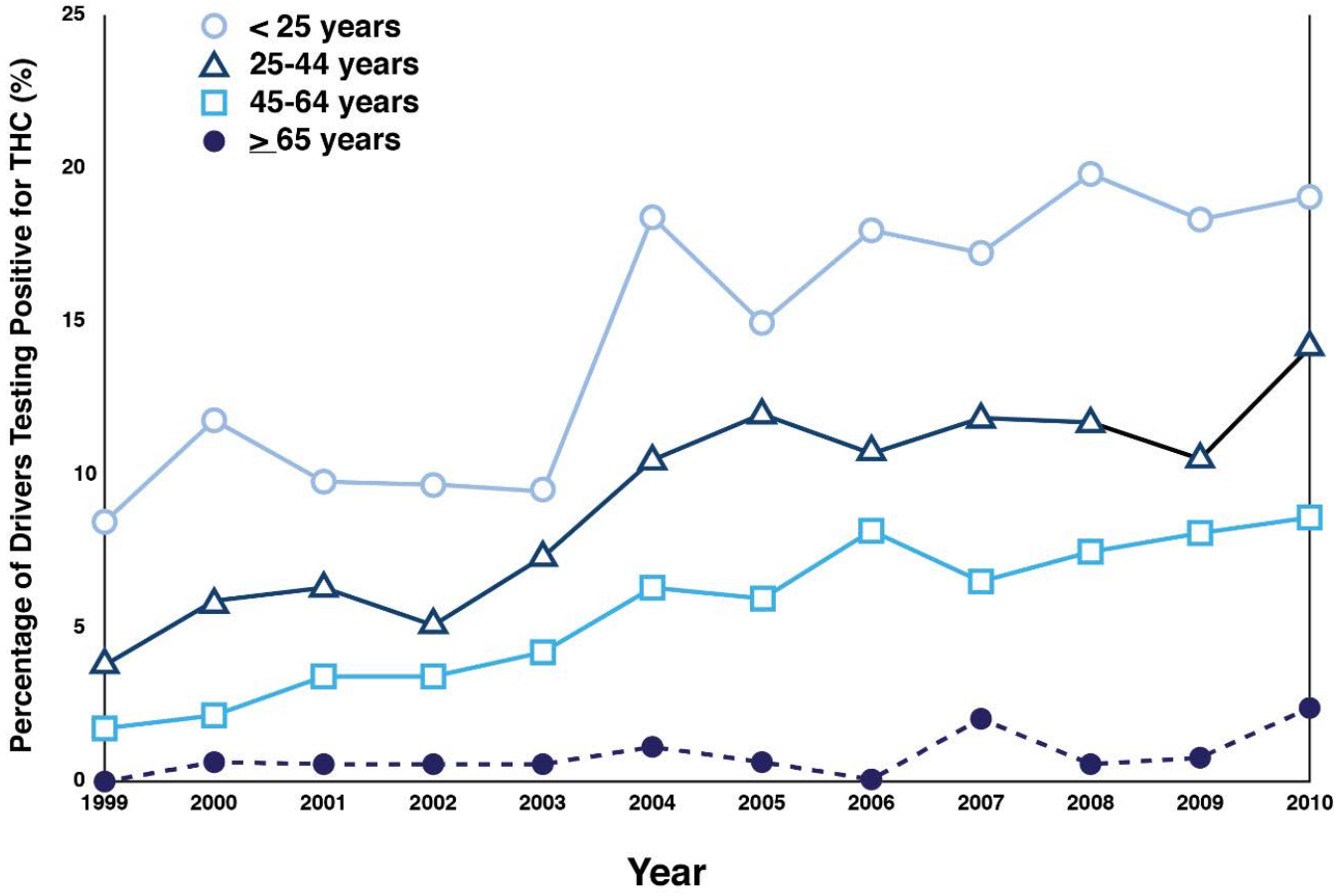
Use

Age 12 and older.
+ compare to 2013 ($p < .05$)



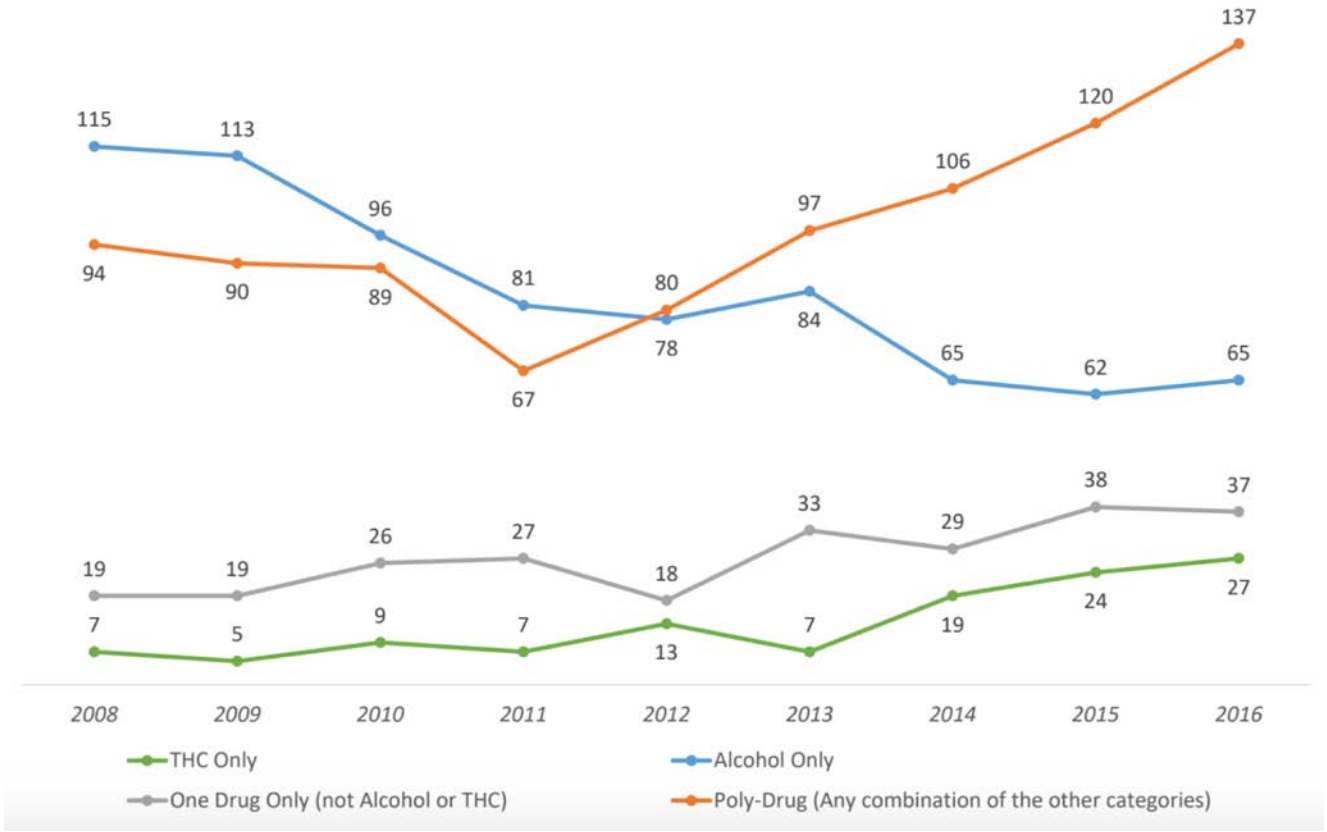
[Source: www.samhsa.gov]

Fatalities



Percentage of THC-positive drivers killed in crashes as a function of driver age (Brady and Li 2014).

Polydrug



Drugs detected in drivers involved in fatal crashes (WTSC)

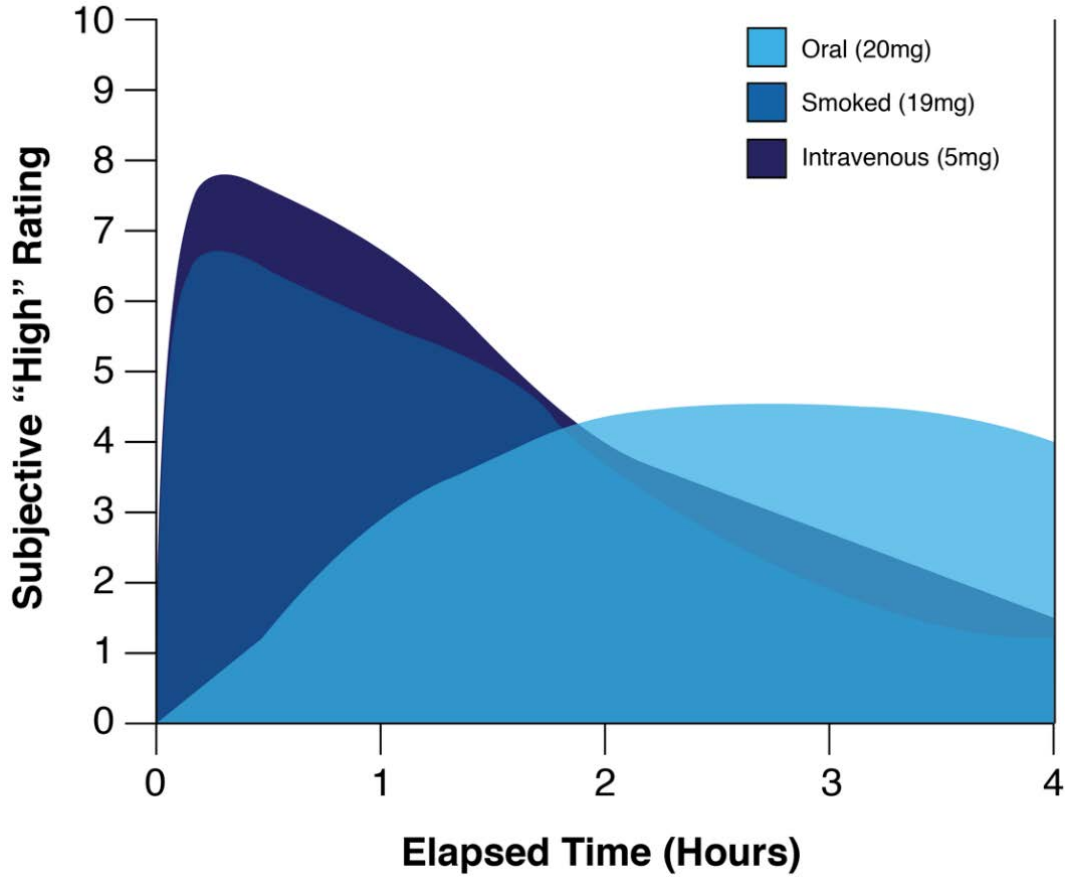
The Drug

How is cannabis different (than alcohol)?

Cannabis

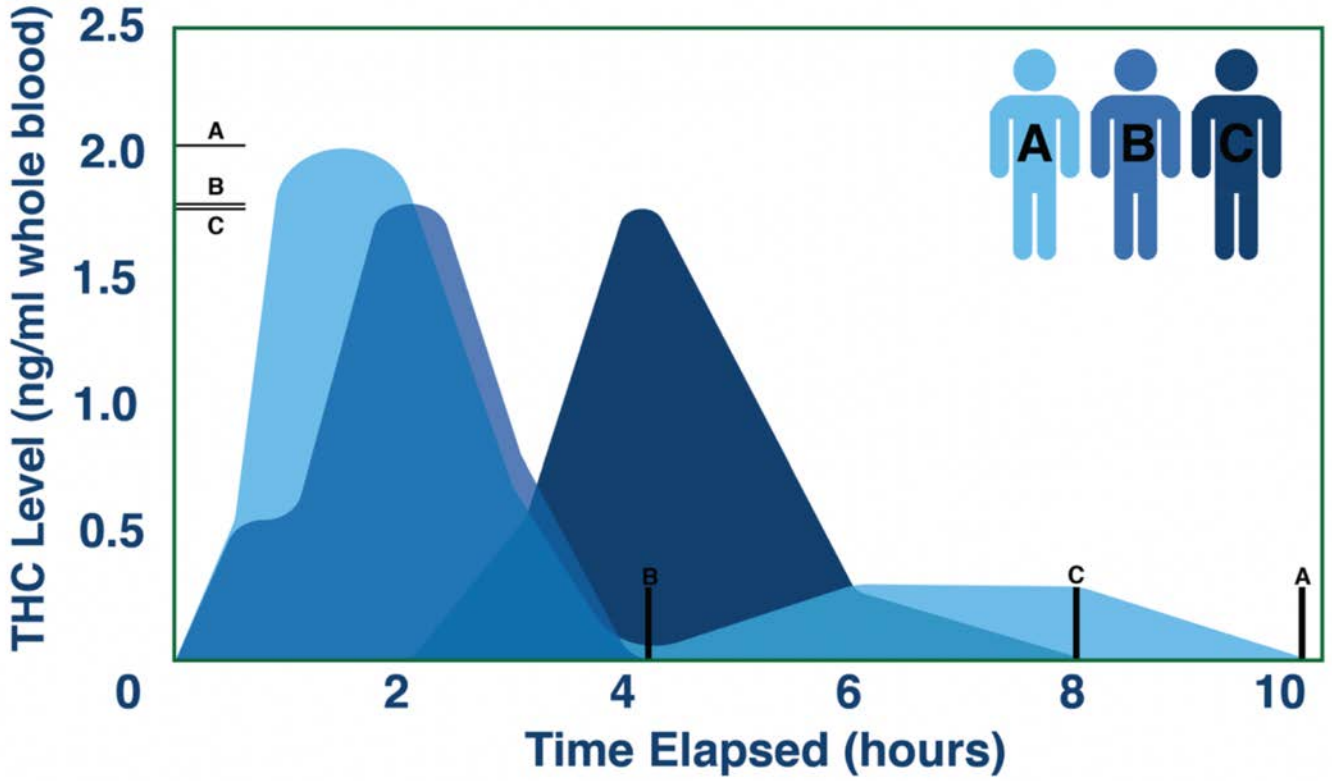
	Cannabis	Alcohol
Source	Plant	Fermentation
Active Ingredients	66 (THC, CBD, CBC, CBG)	1 (ethanol)
Method	Smoke, eat, oral	Oral
Effect	Inhibit endocannabinoid system (CB1)	Inhibits neurotransmitters (GABA)
Absorption	Fat	Water

Consumption



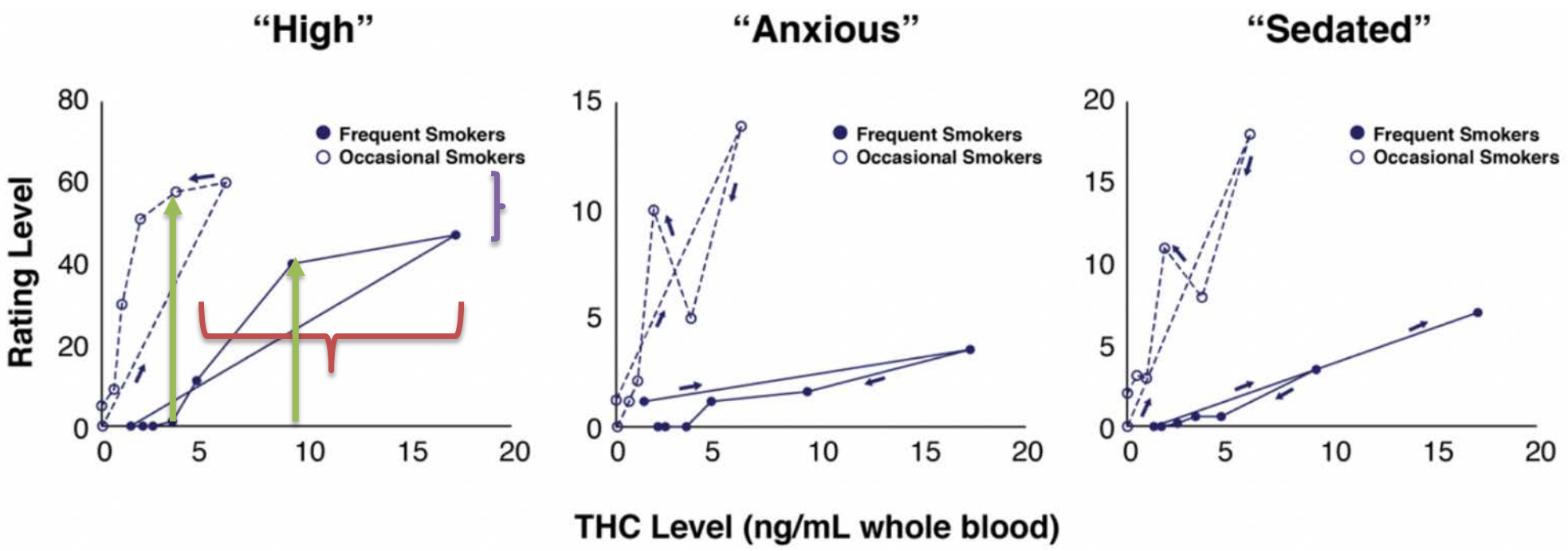
Subjective "high" over time as a function of THC dose method of use (Grotenhermen, 2003).

Time



Example of individual differences in THC levels (whole blood) from standard oral dose (Grotenhermen, 2003).

Frequency



Subjective experience of THC as a function of absorption and elimination phases (Desrosiers et al. 2015).

Tolerance

- We do not fully understand the **conditions** by which tolerance is developed. Indeed, evidence of tolerance can often be attributed to **poor experimental designs**:
  - "Cognitive function of daily or near daily cannabis users can be **substantially impaired** from repeated cannabis use, during and beyond the initial phase of intoxication. As a consequence, frequent cannabis use can be expected to interfere with cognitive performance in many daily environments such as school, work or **traffic**.

(Ramaekers et. al. 2016, 7)

Measurement

- Test method (sensitivity).
- Testing policy (reliability).
- Test criterion (validity).
  - Units (whole blood, blood serum)
  - Time (fatty tissue, elimination)
  - Postmortem redistribution (time, location)

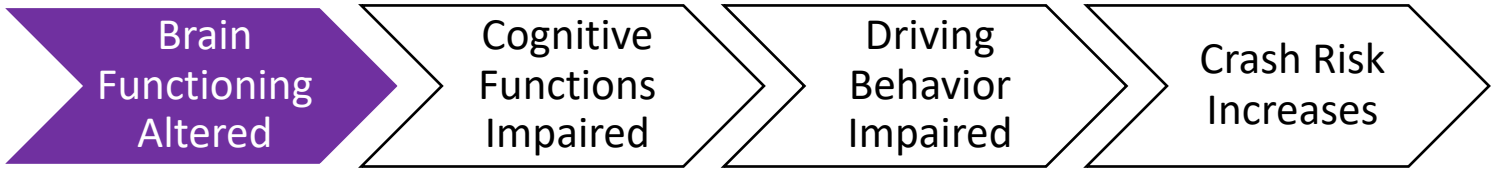
The Logic

How can cannabis impairment influence crash risk?

The Logic


Cannabis Access
Cannabis Use
Brain Functioning Altered
Cognitive Functions Impaired
Driving Behavior Impaired
Crash Risk Increases

The Logic


Brain Functioning Altered
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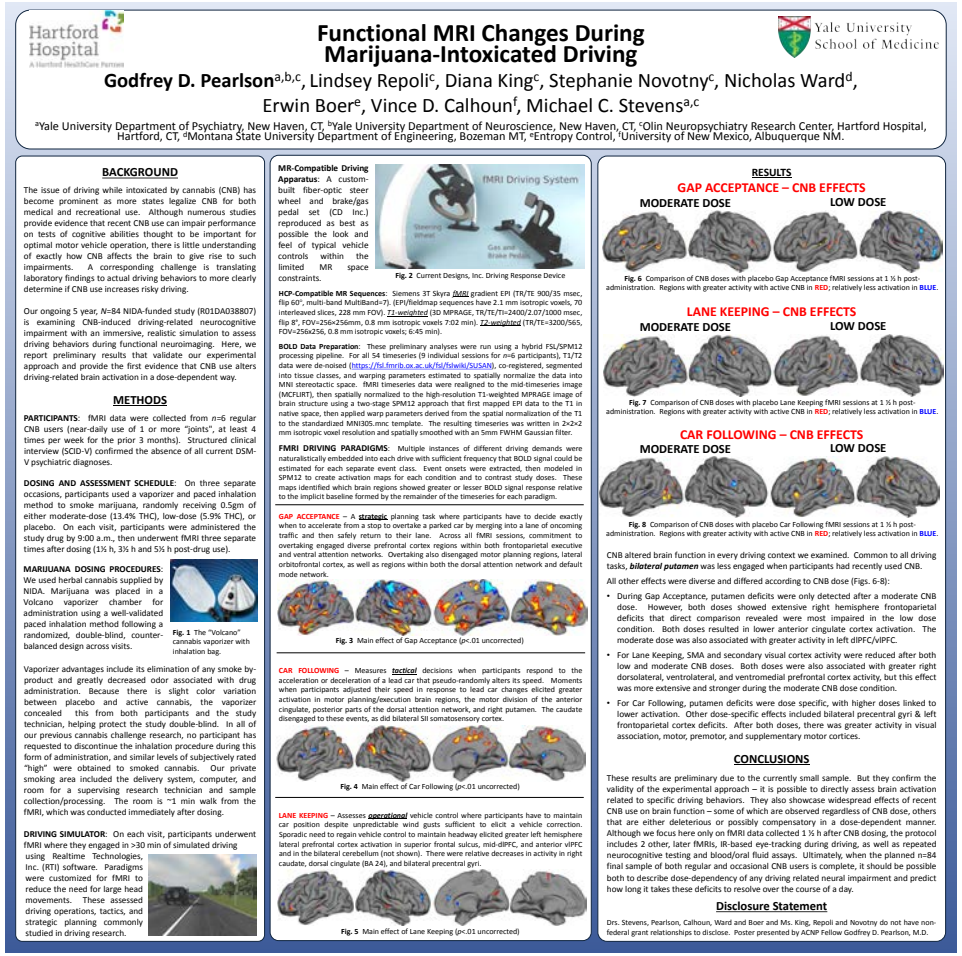
Functioning



Hartford Hospital
A Hartford HealthCare Partner

Functional MRI Changes During Marijuana-Intoxicated Driving

Yale University School of Medicine

Godfrey D. Pearlson[a,b,c], Lindsey Repoli[c], Diana King[c], Stephanie Novotny[c], Nicholas Ward[d], Erwin Boer[e], Vince D. Calhoun[f], Michael C. Stevens[a,c]

[a]Yale University Department of Psychiatry, New Haven, CT, [b]Yale University Department of Neuroscience, New Haven, CT, [c]Olin Neuropsychiatry Research Center, Hartford Hospital, Hartford, CT, [d]Montana State University Department of Engineering, Bozeman MT, [e]Entropy Control, [f]University of New Mexico, Albuquerque NM.

BACKGROUND

The issue of driving while intoxicated by cannabis (CNB) has become prominent as more states legalize CNB for both medical and recreational use. Although numerous studies provide evidence that recent CNB use can impair performance on tests of cognitive abilities thought to be important for optimal motor vehicle operation, there is little understanding of exactly how CNB affects the brain to give rise to such impairments. A corresponding challenge is translating laboratory findings to actual driving behaviors to more clearly determine if CNB use increases risky driving.

Our ongoing 5 year, N=84 NIDA-funded study (R01DA038807) is examining CNB-induced driving-related neurocognitive impairment with an immersive, realistic simulation to assess driving behaviors during functional neuroimaging. Here, we report preliminary results that validate our experimental approach and provide the first evidence that CNB use alters driving-related brain activation in a dose-dependent way.

METHODS

PARTICIPANTS: fMRI data were collected from *n*=6 regular CNB users (near-daily use of 1 or more "joints", at least 4 times per week for the prior 3 months). Structured clinical interview (SCID-V) confirmed the absence of all current DSM-V psychiatric diagnoses.

DOSING AND ASSESSMENT SCHEDULE: On three separate occasions, participants used a vaporizer and paced inhalation method to smoke marijuana, randomly receiving 0.5gm of either moderate-dose (13.4% THC), low-dose (5.9% THC), or placebo. On each visit, participants were administered the study drug by 9:00 a.m., then underwent fMRI three separate times after dosing (1½ h, 3½ h and 5½ h post-drug use).

MARIJUANA DOSING PROCEDURES: We used herbal cannabis supplied by NIDA. Marijuana was placed in a Volcano vaporizer chamber for administration using a well-validated paced inhalation method following a randomized, double-blind, counter-balanced design across visits.

Fig. 1 The "Volcano" cannabis vaporizer with inhalation bag.

Vaporizer advantages include its elimination of any smoke by-product and greatly decreased odor associated with drug administration. Because there is slight color variation between placebo and active cannabis, the vaporizer concealed this from both participants and the study technician, helping protect the study double-blind. In all of our previous cannabis challenge research, no participant has requested to discontinue the inhalation procedure during this form of administration, and similar levels of subjectively rated "high" were obtained to smoked cannabis. Our private smoking area included the delivery system, computer, and room for a supervising research technician and sample collection/processing. The room is ~1 min walk from the fMRI, which was conducted immediately after dosing.

DRIVING SIMULATOR: On each visit, participants underwent fMRI where they engaged in >30 min of simulated driving using Realtime Technologies, Inc. (RTI) software. Paradigms were customized for fMRI to reduce the need for large head movements. These assessed driving operations, tactics, and strategic planning commonly studied in driving research.

MR-Compatible Driving Apparatus: A custom-built fiber-optic steer wheel and brake/gas pedal set (CD Inc.) reproduced as best as possible the look and feel of typical vehicle controls within the limited MR space constraints.

Fig. 2 Current Designs, Inc. Driving Response Device

HCP-Compatible MR Sequences: Siemens 3T Skyra *fMRI* gradient EPI (TR/TE 900/35 msec, flip 60°, multi-band MultiBand=7). (EPI/fieldmap sequences have 2.1 mm isotropic voxels, 70 interleaved slices, 228 mm FOV). *T1-weighted* (3D MPRAGE, TR/TE/TI=2400/2.07/1000 msec, flip 8°, FOV=256×256×256mm, 0.8 mm isotropic voxels 7:02 min). *T2-weighted* (TR/TE=3200/565, FOV=256x256, 0.8 mm isotropic voxels; 6:45 min).

BOLD Data Preparation: These preliminary analyses were run using a hybrid FSL/SPM12 processing pipeline. For all 54 timeseries (9 individual sessions for *n*=6 participants), T1/T2 data were de-noised (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/SUSAN), co-registered, segmented into tissue classes, and warping parameters estimated to spatially normalize the data into MNI stereotactic space. fMRI timeseries data were realigned to the mid-timeseries image (MCFLIRT), then spatially normalized to the high-resolution T1-weighted MPRAGE image of brain structure using a two-stage SPM12 approach that first mapped EPI data to the T1 in native space, then applied warp parameters derived from the spatial normalization of the T1 to the standardized MNI305.mnc template. The resulting timeseries was written in 2×2×2 mm isotropic voxel resolution and spatially smoothed with an 5mm FWHM Gaussian filter.

FMRI DRIVING PARADIGMS: Multiple instances of different driving demands were naturalistically embedded into each drive with sufficient frequency that BOLD signal could be estimated for each separate event class. Event onsets were extracted, then modeled in SPM12 to create activation maps for each condition and to contrast study doses. These maps identified which brain regions showed greater or lesser BOLD signal response relative to the implicit baseline formed by the remainder of the timeseries for each paradigm.

GAP ACCEPTANCE – A ***strategic*** planning task where participants have to decide exactly when to accelerate from a stop to overtake a parked car by merging into a lane of oncoming traffic and then safely return to their lane. Across all fMRI sessions, commitment to overtaking engaged diverse prefrontal cortex regions within both frontoparietal executive and ventral attention networks. Overtaking also disengaged motor planning regions, lateral orbitofrontal cortex, as well as regions within both the dorsal attention network and default mode network.

Fig. 3 Main effect of Gap Acceptance ($p<.01$ uncorrected)

CAR FOLLOWING – Measures ***tactical*** decisions when participants respond to the acceleration or deceleration of a lead car that pseudo-randomly alters its speed. Moments when participants adjusted their speed in response to lead car changes elicited greater activation in motor planning/execution brain regions, the motor division of the anterior cingulate, posterior parts of the dorsal attention network, and right putamen. The caudate disengaged to these events, as did bilateral SII somatosensory cortex.

Fig. 4 Main effect of Car Following ($p<.01$ uncorrected)

LANE KEEPING – Assesses ***operational*** vehicle control where participants have to maintain car position despite unpredictable wind gusts sufficient to elicit a vehicle correction. Sporadic need to regain vehicle control to maintain headway elicited greater left hemisphere lateral prefrontal cortex activation in superior frontal sulcus, mid-dlPFC, and anterior vlPFC and in the bilateral cerebellum (not shown). There were relative decreases in activity in right caudate, dorsal cingulate (BA 24), and bilateral precentral gyri.

Fig. 5 Main effect of Lane Keeping ($p<.01$ uncorrected)

RESULTS

GAP ACCEPTANCE – CNB EFFECTS

Fig. 6 Comparison of CNB doses with placebo Gap Acceptance fMRI sessions at 1 ½ h post-administration. Regions with greater activity with active CNB in RED; relatively less activation in BLUE.

LANE KEEPING – CNB EFFECTS

Fig. 7 Comparison of CNB doses with placebo Lane Keeping fMRI sessions at 1 ½ h post-administration. Regions with greater activity with active CNB in RED; relatively less activation in BLUE.

CAR FOLLOWING – CNB EFFECTS

Fig. 8 Comparison of CNB doses with placebo Car Following fMRI sessions at 1 ½ h post-administration. Regions with greater activity with active CNB in RED; relatively less activation in BLUE.

CNB altered brain function in every driving context we examined. Common to all driving tasks, ***bilateral putamen*** was less engaged when participants had recently used CNB.

All other effects were diverse and differed according to CNB dose (Figs. 6-8):

- During Gap Acceptance, putamen deficits were only detected after a moderate CNB dose. However, both doses showed extensive right hemisphere frontoparietal deficits that direct comparison revealed were most impaired in the low dose condition. Both doses resulted in lower anterior cingulate cortex activation. The moderate dose was also associated with greater activity in left dlPFC/vlPFC.
- For Lane Keeping, SMA and secondary visual cortex activity were reduced after both low and moderate CNB doses. Both doses were also associated with greater right dorsolateral, ventrolateral, and ventromedial prefrontal cortex activity, but this effect was more extensive and stronger during the moderate CNB dose condition.
- For Car Following, putamen deficits were dose specific, with higher doses linked to lower activation. Other dose-specific effects included bilateral precentral gyri & left frontoparietal cortex deficits. After both doses, there was greater activity in visual association, motor, premotor, and supplementary motor cortices.

CONCLUSIONS

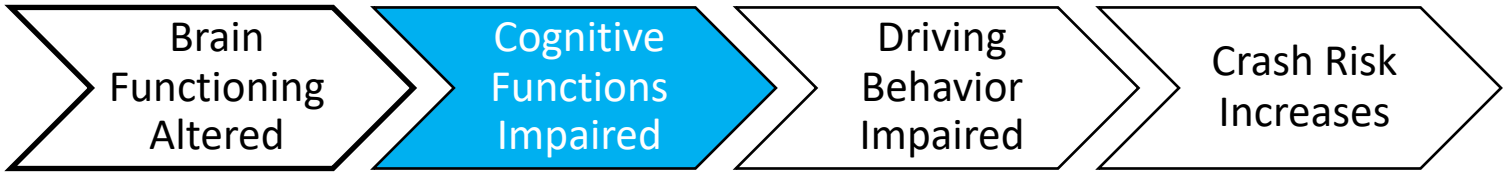
These results are preliminary due to the currently small sample. But they confirm the validity of the experimental approach – it is possible to directly assess brain activation related to specific driving behaviors. They also showcase widespread effects of recent CNB use on brain function – some of which are observed regardless of CNB dose, others that are either deleterious or possibly compensatory in a dose-dependent manner. Although we focus here only on fMRI data collected 1 ½ h after CNB dosing, the protocol includes 2 other, later fMRIs, IR-based eye-tracking during driving, as well as repeated neurocognitive testing and blood/oral fluid assays. Ultimately, when the planned n=84 final sample of both regular and occasional CNB users is complete, it should be possible both to describe dose-dependency of any driving related neural impairment and predict how long it takes these deficits to resolve over the course of a day.

Disclosure Statement

Drs. Stevens, Pearlson, Calhoun, Ward and Boer and Ms. King, Repoli and Novotny do not have non-federal grant relationships to disclose. Poster presented by ACNP Fellow Godfrey D. Pearlson, M.D.

- Region deactivation
  - Relevant to driving
  - Visual processing
  - Time estimation
- Networking disruption
- Functional adaptation

The Logic


Brain Functioning Altered
Cognitive Functions Impaired
Driving Behavior Impaired
Crash Risk Increases

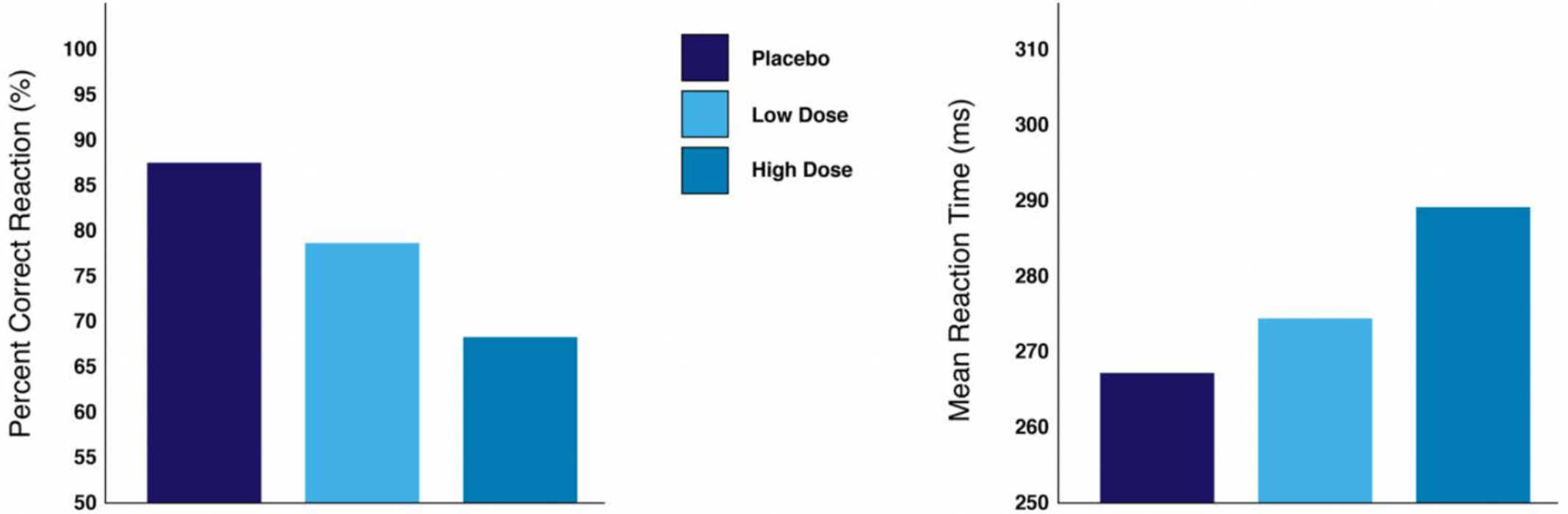
Cognitive Functions

Consistency of Evidence for THC Impairment of Core and Executive Cognitive Functions (Broyd et al. 2016).

Cognitive Domain	Acute	Chronic	Persistence
Attention	+ + +	+ + +	+ –
Memory	+ + +	+ + +	+ –
Psychomotor Control	+ + +	+	+
Executive Functions	+ –	+ –	+ –

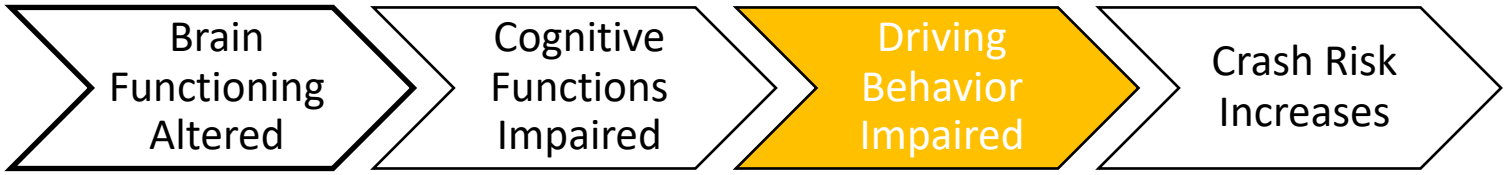
Note: + + +, strong and largely consistent evidence for impairment; + +, moderate evidence for impairment; +, weak evidence for impairment, being based on only a small number of studies; + –, mixed evidence.

Psychomotor Control



Dose effects of THC on basic psychomotor performance (Boggs, Surti, and Gupta 2018).

The Logic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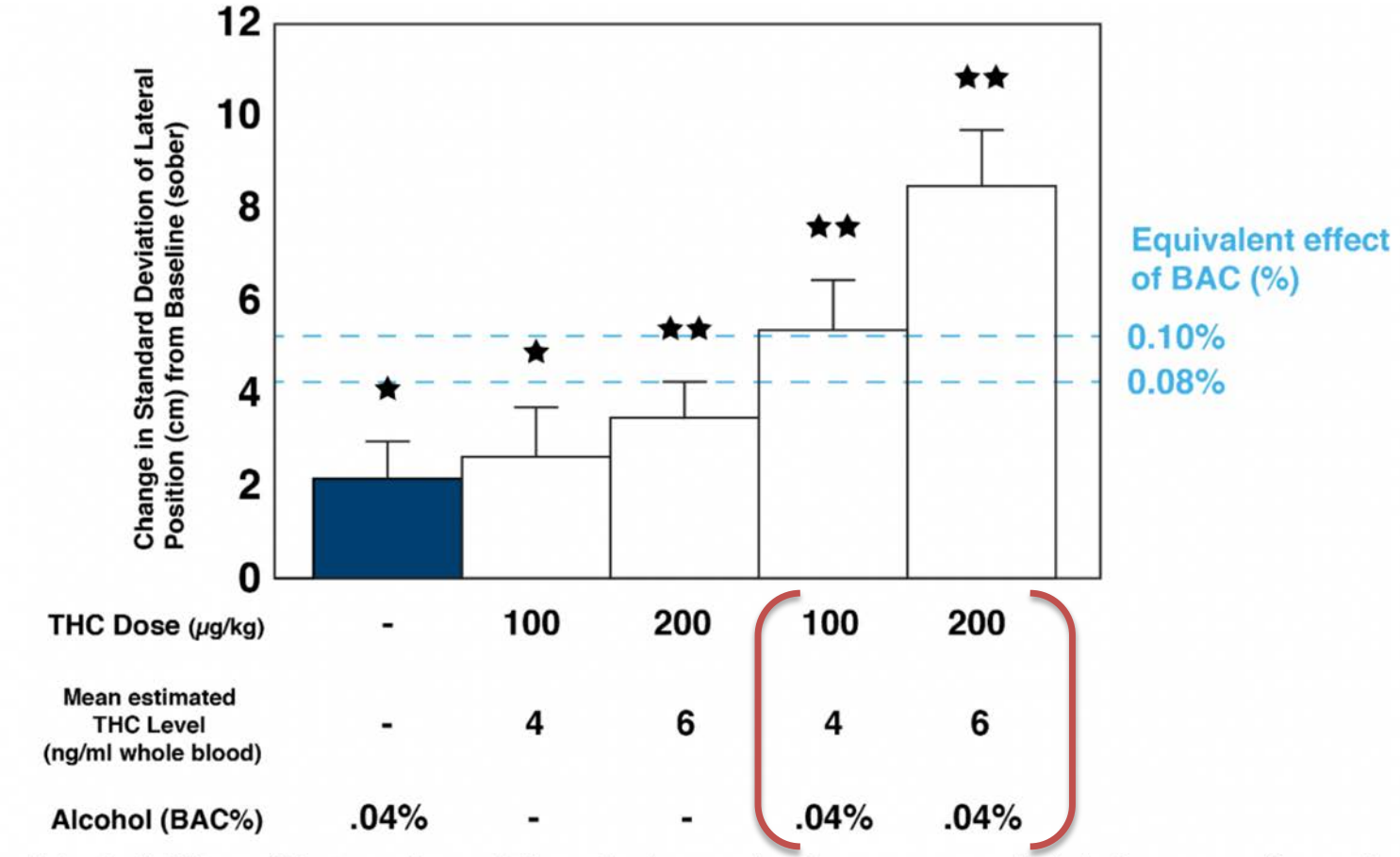
Driving Behavior



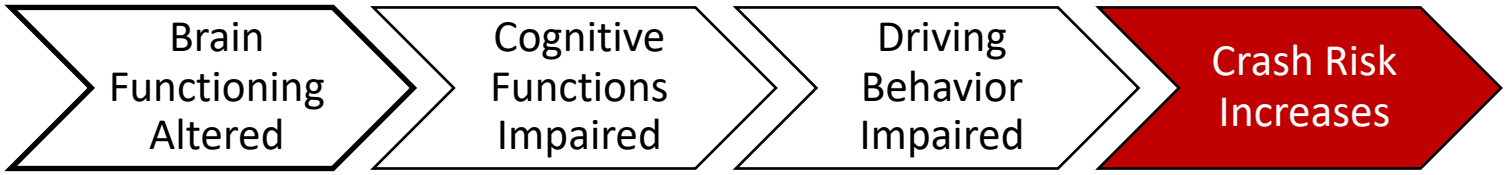
Variability of lateral position in lane during on-road driving as a function of THC dose, alcohol level (Ramaekers, Robbe, and O'Hanlon 2000) and estimated THC level (whole blood) (Ramaekers 2019).

Compensation

"Drivers certainly do try to **compensate**, but they do not always succeed. In my view the compensation strategy is often **misquoted**. Virtually all studies demonstrate that drivers are **not able to fully compensate** for their impairments. There is compensation on some parameters, but there is **none on others**."

(Ramaekers 2019)

The Logic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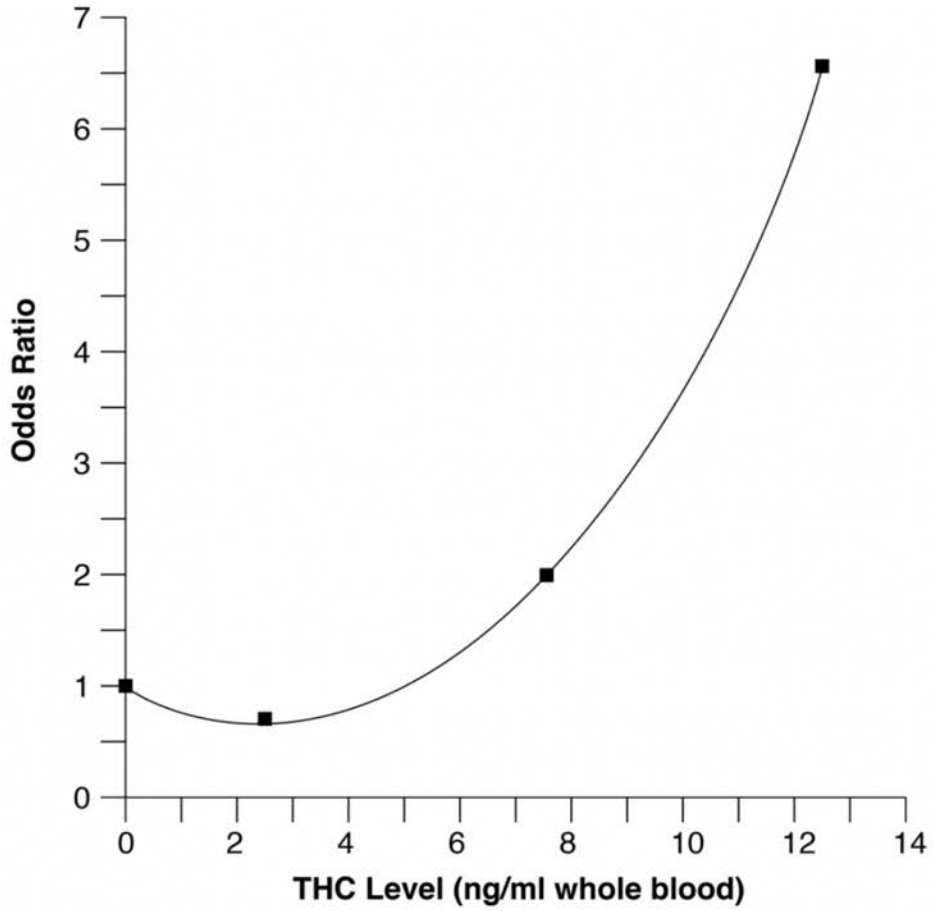
Unsafe Acts

Predicted Odds of a Driver Committing an Unsafe Act in a Fatal Crash as a Function of THC and BAC Level (Dubois et al. 2015).

BAC	Predicted Odds	
	THC absent	THC present
0.00	1.07	1.25
0.01	1.19	1.37
0.02	1.32	1.50
0.03	1.46	1.64
0.04	1.61	1.79
0.05	1.78	1.94
0.06	1.95	2.10
0.07	2.13	2.27
0.08	2.32	2.44

1.17
1.15
1.14
1.12
1.11
1.09
1.08
1.07
1.05

Culpability



Estimated relationship of crash culpability (odds ratio) as a function of THC level (whole blood) (Sewell, Poling, and Sofouglu 2009).

Risk (fatal)

Odd ratios (Unadjusted) for 2007 U.S. fatal crashes for different drug types (Li, Brady, and Chen 2013).

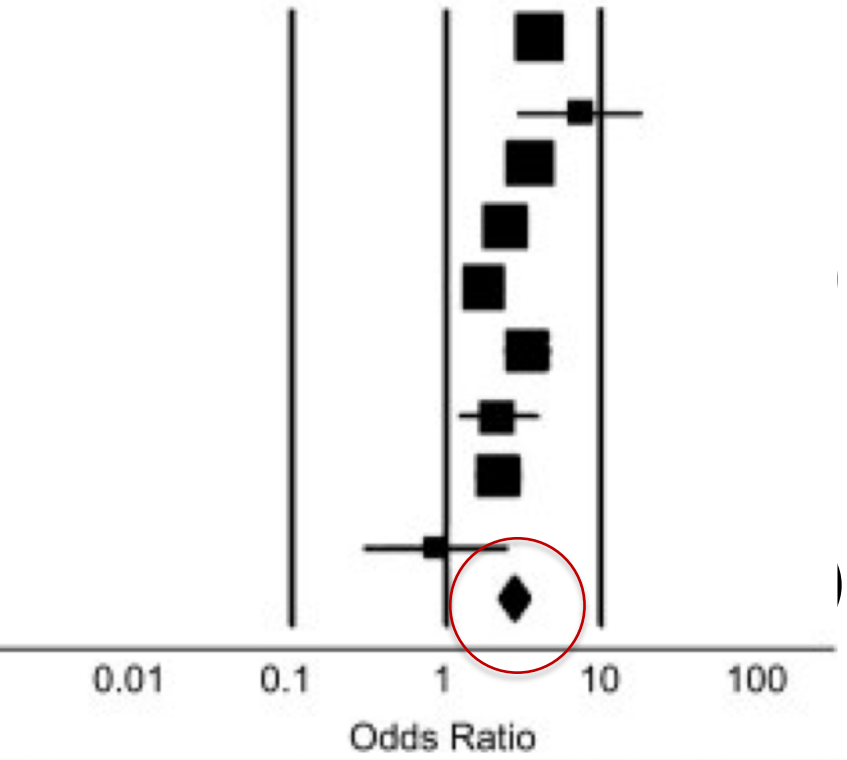
Drug Type	Odds Ratio	95th Confidence Interval
Cannabis	1.83	1.39 – 2.39
Narcotics	3.03	2.00 – 4.48
Stimulants	3.57	2.63 – 4.76
Depressants	4.83	3.18 – 7.21
Any drug (average)	2.22	1.68 – 2.92
Polydrug	3.41	2.43 – 4.73
Alcohol	13.64	11.12 – 16.72
Alcohol + Drug	23.24	17.79 – 30.28

The Risk

What does the risk data really mean?

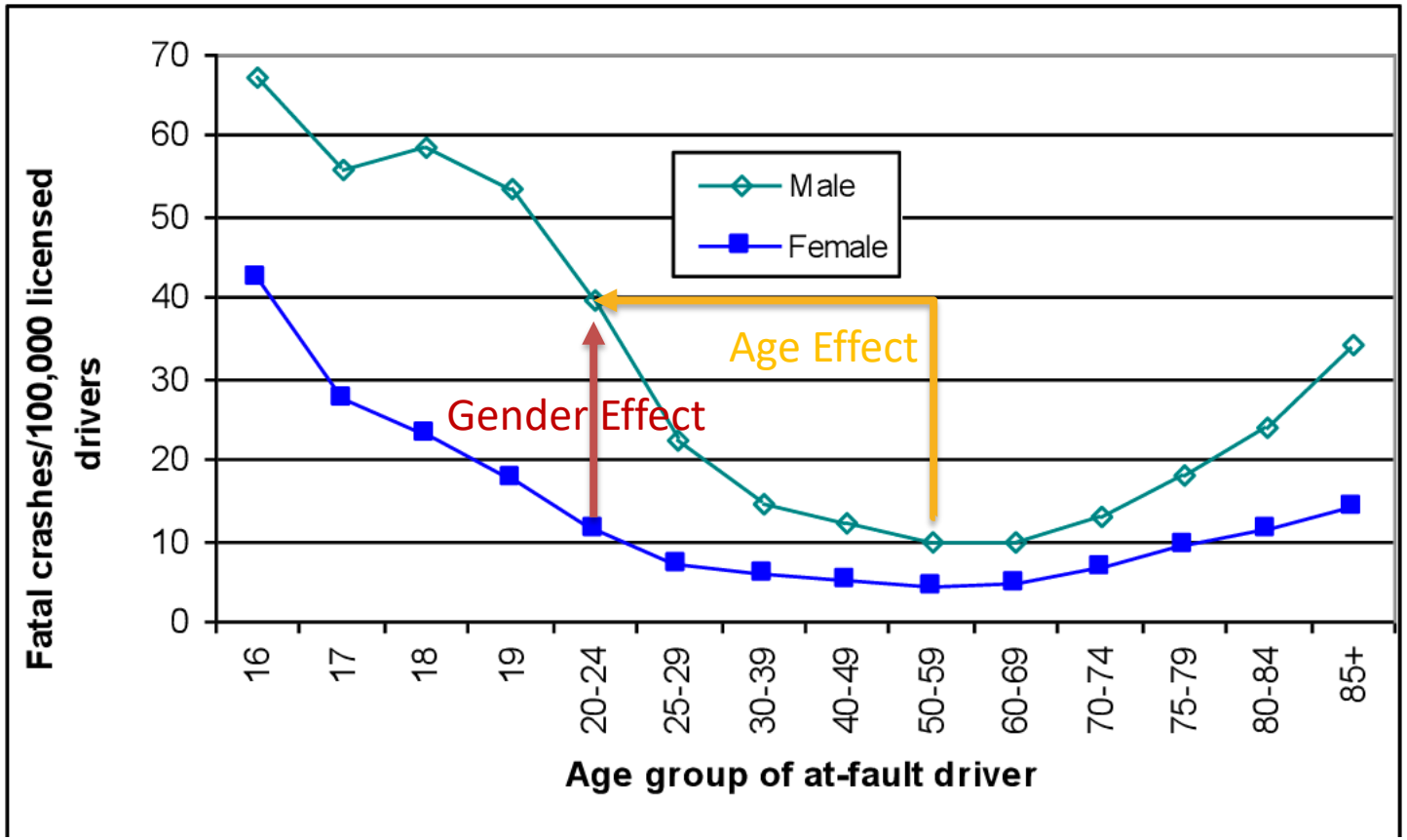
Odds

First Author, Year (Reference No.)	Odds Ratio	95% CI	% Weight
	Statistics for Each Study		
Asbridge, 2005 (66)	3.88	3.17, 4.75	15.16
Blows, 2005 (64)	7.16	2.77, 18.52	4.88
Brault, 2004 (68)	3.43	2.69, 4.36	14.55
Fergusson, 2001 (70)	2.37	1.98, 2.84	15.44
Gerberich, 2003 (69)	1.70	1.25, 2.32	13.40
Mann, 2010 (62)	3.28	2.29, 4.71	12.42
Movig, 2004 (63)	2.10	1.10, 4.01	7.88
Mura, 2003 (67)	2.11	1.46, 3.06	12.26
Woratanarat, 2009 (65)	0.85	0.29, 2.50	4.01
Overall (random-effects model)	2.66	2.07, 3.41	100.00



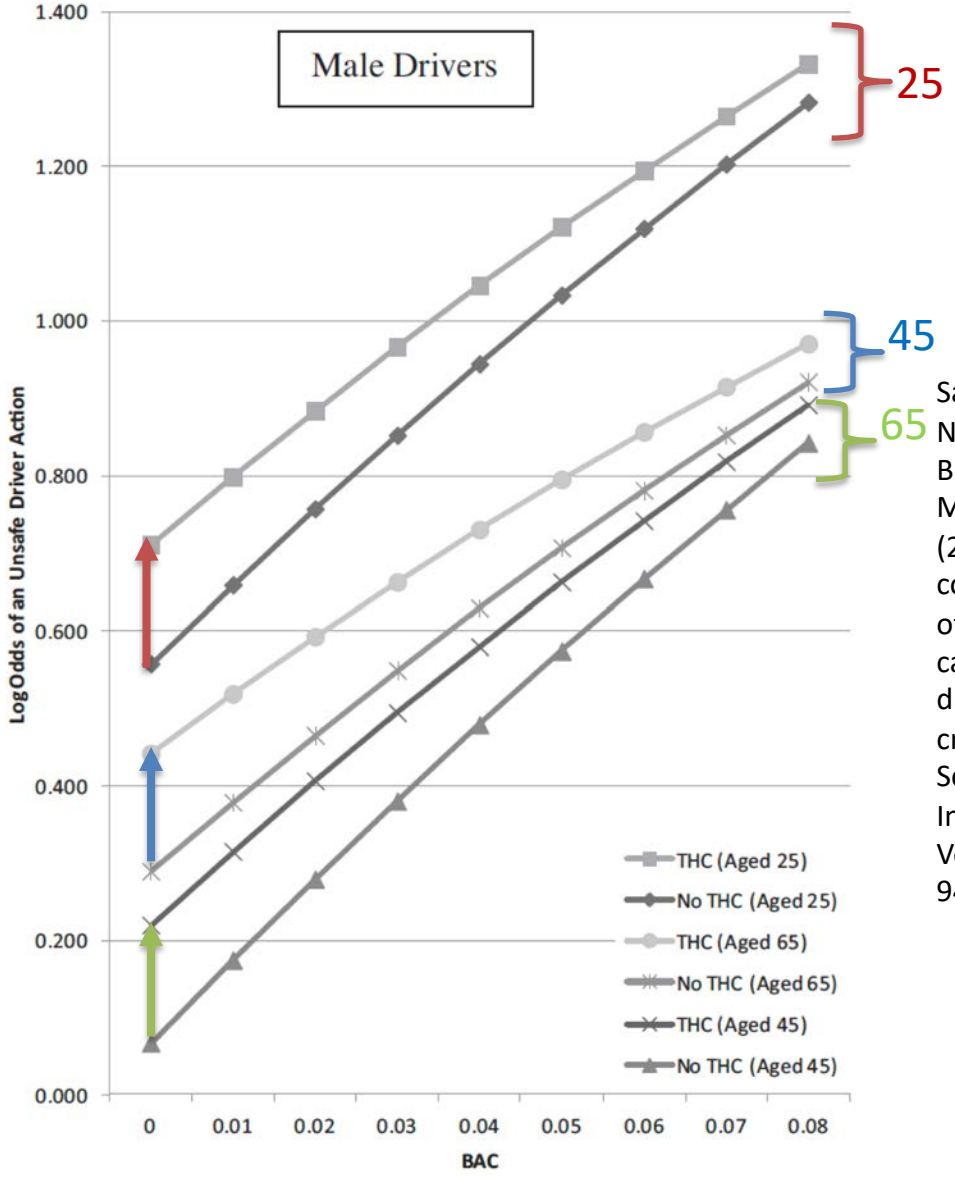
Li, M. C., Brady, J. E., DiMaggio, C. J., Lusardi, A. R., Tzong, K. Y., & Li, G. (2012). Marijuana use and motor vehicle crashes. *Epidemiologic reviews*, *34*(1), 65–72.

Adjust



Eustace, D., & Wei, H. (2010). The Role of Driver Age and Gender in Motor Vehicle Fatal Crashes. Journal of Transportation Safety and Security, 2, online.

Log odds of an unsafe driver action by age, sex, BAC level, and THC status.



Sacha Dubois, Nadia Mullen, Bruce Weaver, Michel Bédard (2015). The combined effects of alcohol and cannabis on driving: Impact on crash risk. Forensic Science International, Volume 248, Pages 94-100.

Random-effects Summary Odds Ratios and 95% Confidence Intervals of Crash Involvement Associated With Marijuana Use, by Study Characteristics

Study Characteristic	OR	95% CI
Study design		
Case-control	2.63	1.87, 3.71
Cohort	2.04	1.36, 3.07
Cross-sectional	3.61	2.37, 5.49
Type of drug assessment		
Self-report	2.93	2.07, 4.17
Blood or urine test	2.26	1.46, 3.49
Study time period		
Before 2000	2.82	1.77, 4.50
2000 and after	2.58	1.89, 3.53
Study location		
North America	2.97	2.13, 4.14
Other	2.31	1.59, 3.35
Age of study subjects		
<25 years	3.03	1.83, 5.01
All ages	2.50	1.81, 3.46

Abbreviations: CI, confidence interval; OR, odds ratio.

Li, M. C., Brady, J. E., DiMaggio, C. J., Lusardi, A. R., Tzong, K. Y., & Li, G. (2012). Marijuana use and motor vehicle crashes. *Epidemiologic reviews*, *34*(1), 65–72.

Harm

Odd ratios (Unadjusted) for 2007 U.S. fatal crashes for different drug types (Li, Brady, and Chen 2013).

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Alcohol	13.64	11.12 – 16.72
Alcohol + Drug	23.24	17.79 – 30.28

The odds ratios for depressants was 2.6 times greater than for cannabis, but there were nearly **twice** as many fatally injured **THC-positive drivers** (Li et al., 2013)

The Logic


Brain Functioning Altered
Cognitive Functions Impaired
Driving Behavior Impaired
Crash Risk Increases

The Law

What are the effects of decriminalization laws?

Best Practice

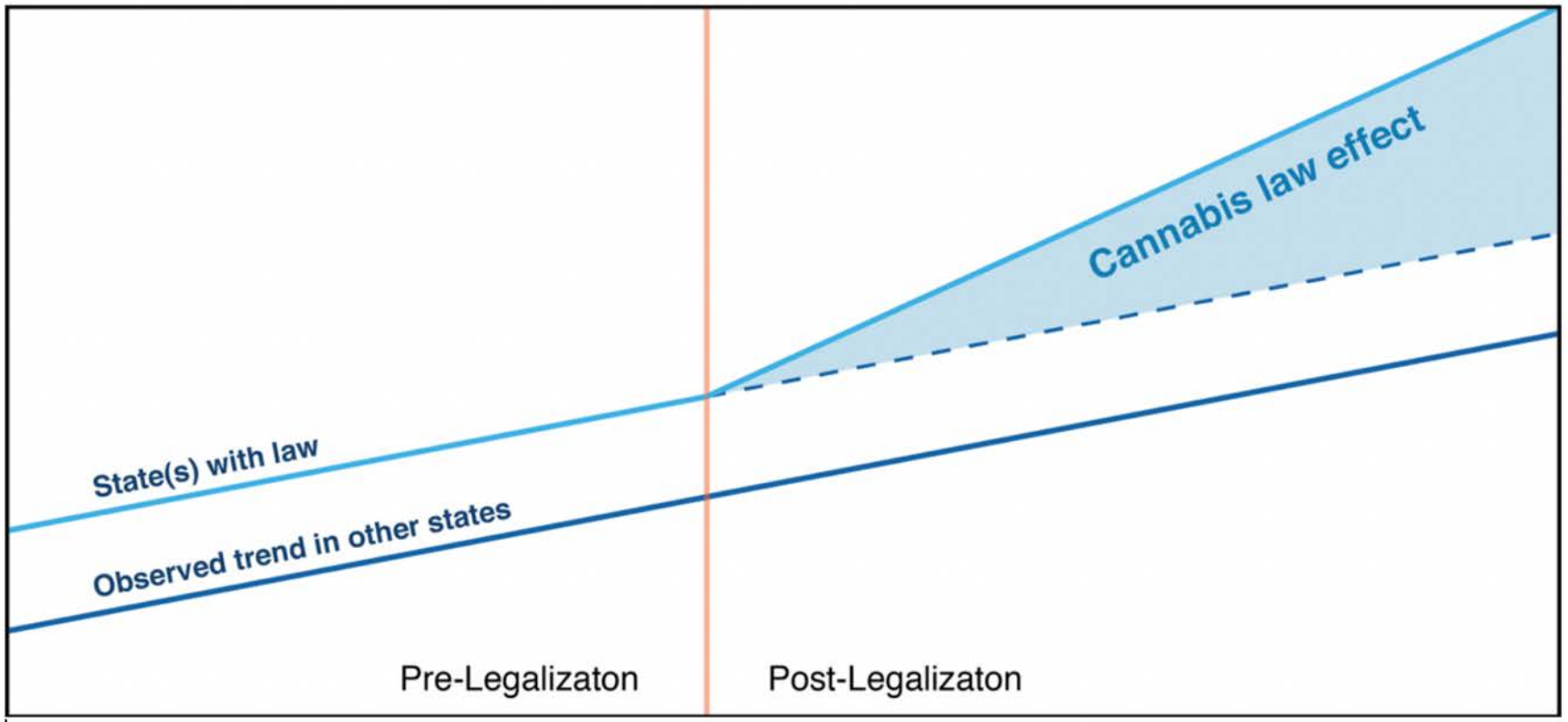

Illustration of "difference in difference estimator" method to isolate effect of cannabis legislation on traffic safety (Coyle 2018).

Social Effects

Survey Response to Interpretation of Legalization of Cannabis in Washington State.

Regardless of whether you consume alcohol or cannabis, how much do you agree or disagree with the following statements? "The legalization of cannabis implied that it is safe to drive under the influence of cannabis."

N	Strongly Disagree	Disagree	Somewhat Disagree	Neither Agree nor Disagree	Somewhat Agree	Agree	Strongly Agree
868	43.1%	18.1%	8.2%	12.2%	3.6%	7.1%	7.7%

1.47 times (0.98 to 2.18)

Thank you!

Contact Us

Web: www.chsculture.org
Email: mail@chsculture.org
Phone: (406) 994-7873

#CHSCulture

Project website:
https://www.mdt.mt.gov/research/projects/trafficsafety-duic.shtml