



The Challenge of Cannabis-Related Driving Impairment

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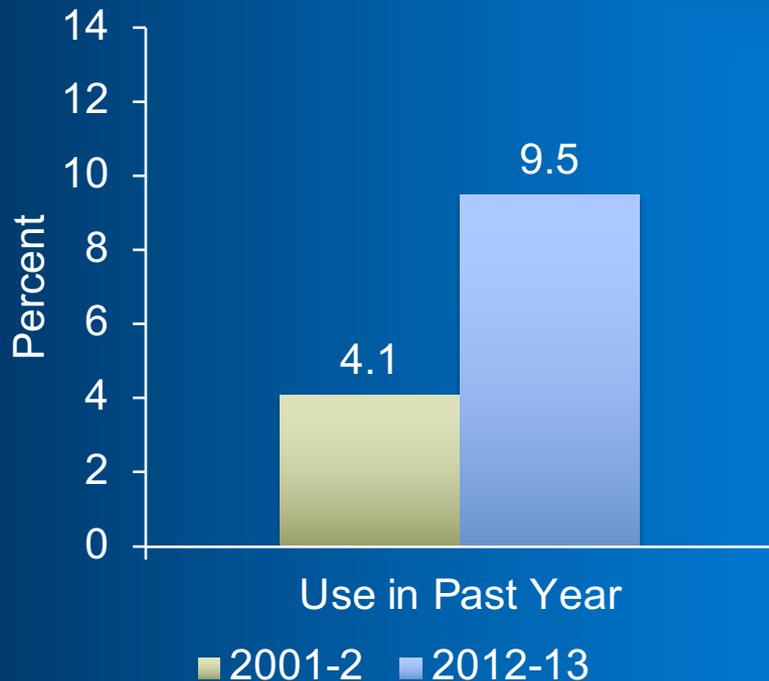
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Prevalence of Cannabis Use

22.2 million (8.3% of the population) Americans ≥ 12 yo used cannabis in the past month (2015 National Survey on Drug Use and Health)

National Epidemiologic Survey on Alcohol and Related Conditions Use in Past Year (Hasin et al., 2015)

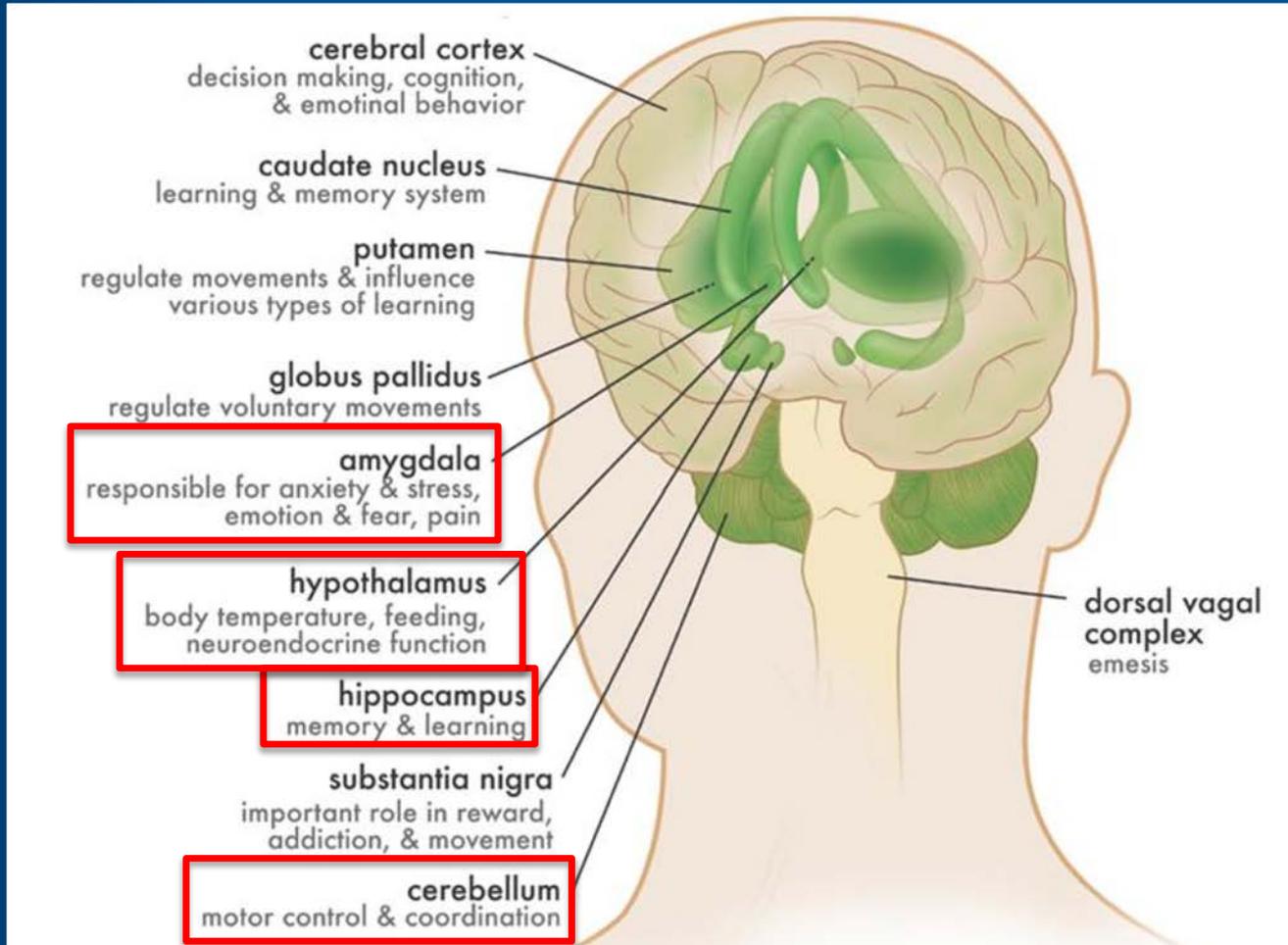


Age	2001-2	2012-13
18-29	10.5%	21.2%
30-34	4.1%	10.1%
45-64	1.6%	5.9%
<65	0.0%	1.3%

Increases across all sex, race/ethnicities, educational levels, income levels, urbanicity, geographic regions

Distribution of CB1 Receptors in the Brain

Acute Effects



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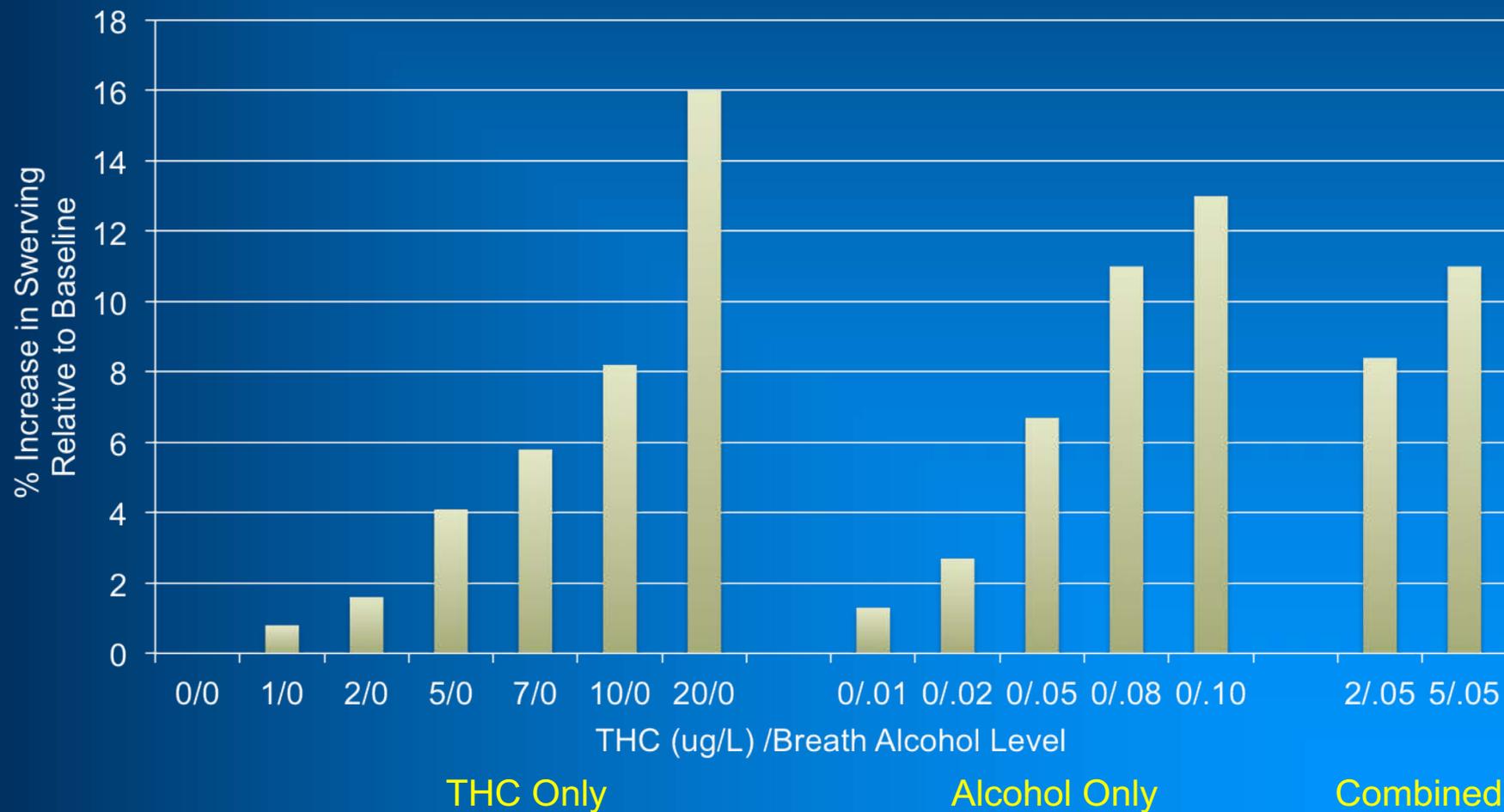
Cannabis and driving

- **Cognition:** Reduced learning, attention, processing speed, psychomotor abilities
- **Controlled on-road/simulator studies**
 - » Delayed reactions (brake latency)
 - » Poor lane tracking (standard deviation of lateral position)
 - » Reduced judgment of speed and distances
 - » Dose dependent
- **Epidemiology**
 - » Modest increased crash risk (~ two-fold)
 - » State experience unclear
- Amplified by consumption of **alcohol**
- Cannabis users judge selves to be more impaired; more cautious (allow more headway; drive more slowly; avoid passing other cars)

National Advanced Driving Simulator (NADS) University of Iowa

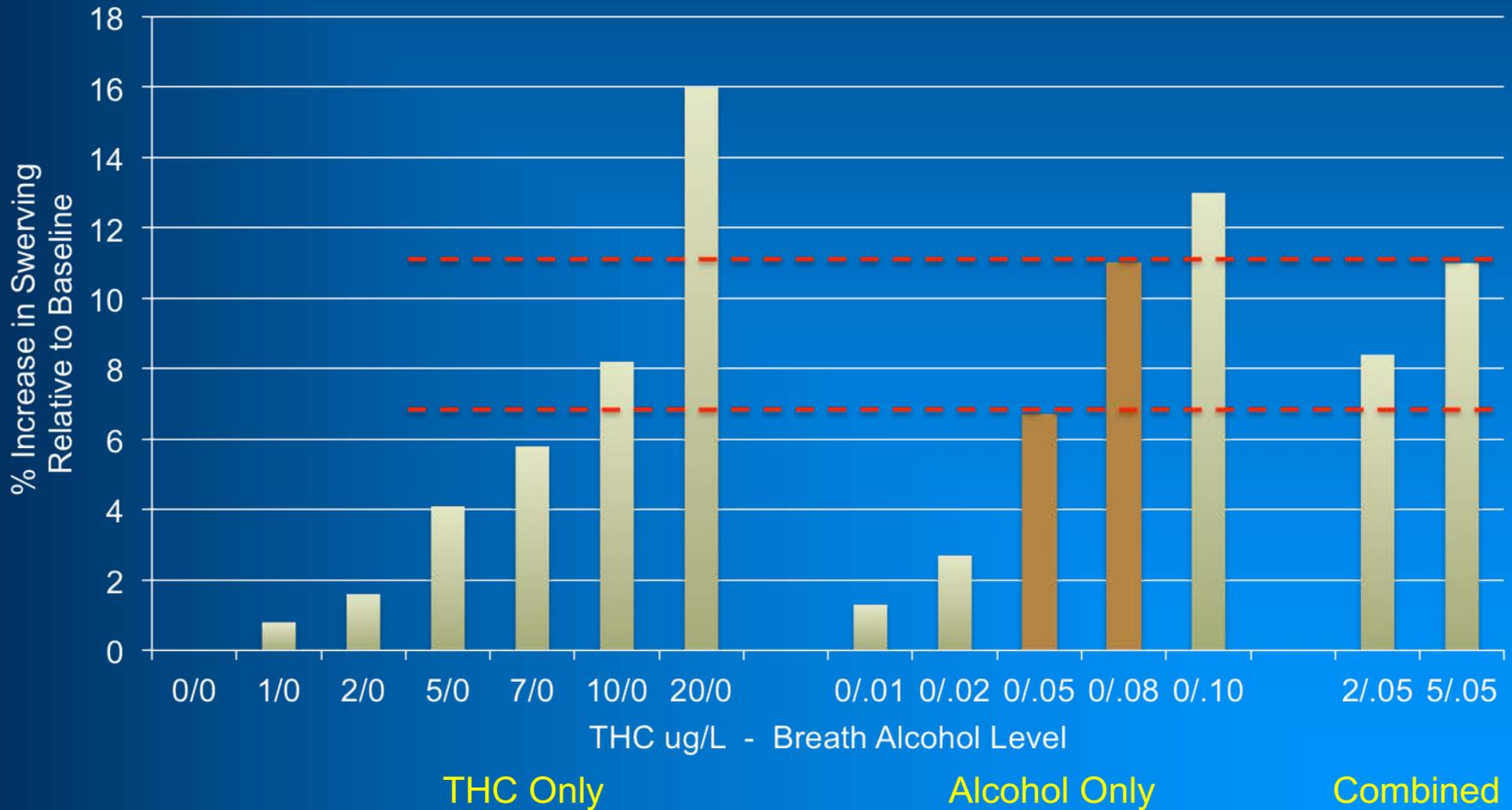


Cannabis blood levels/Breath alcohol level and simulator swerving



Hartman et al., 2015

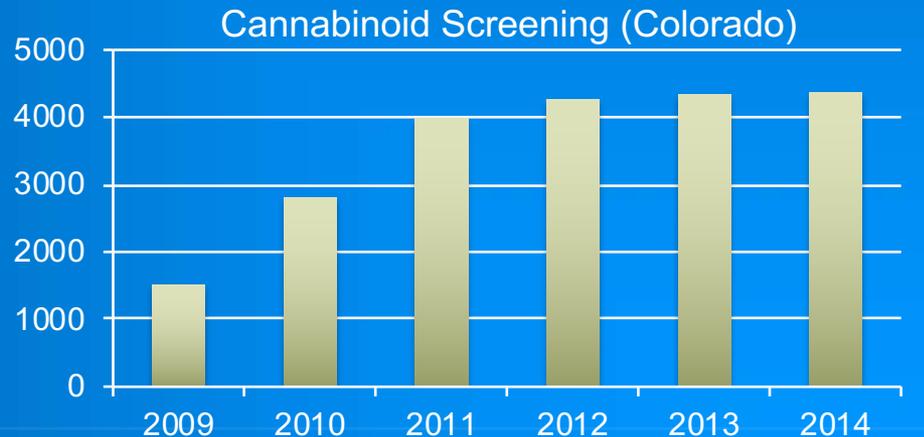
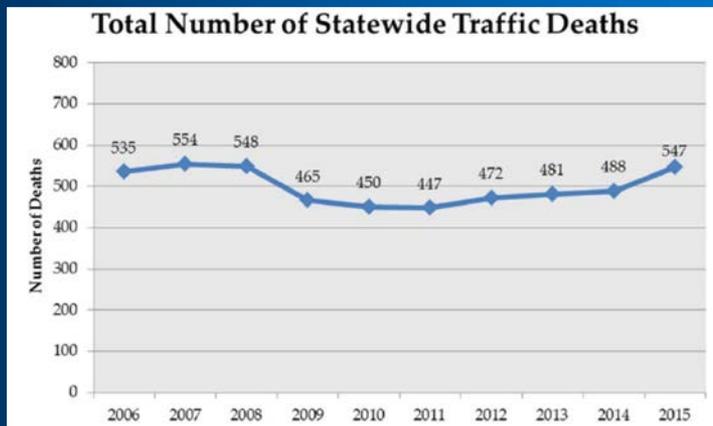
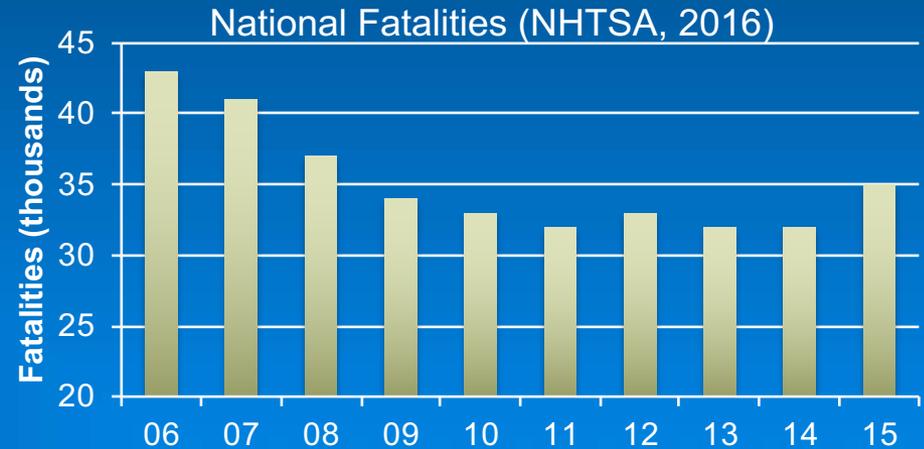
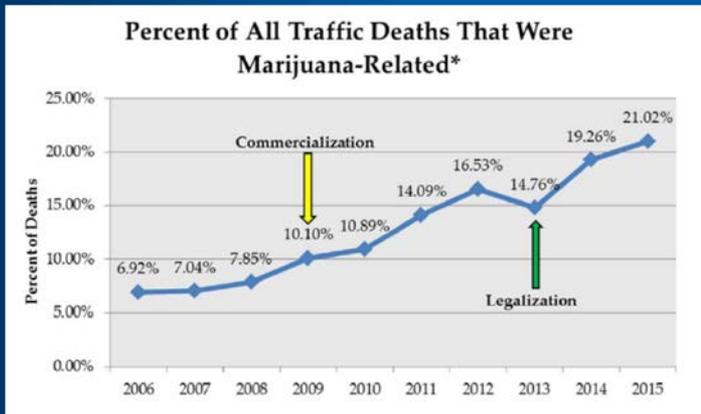
Cannabis blood levels/Breath alcohol level and simulator swerving



Hartman et al., 2015

Impact of Legalization in Colorado

- Marijuana-related traffic deaths (marijuana “mentioned”; includes other substances) increased 48% (2013-15) compared to 2010-2012; All traffic deaths only increased 11%.



RMHIDTA, 2015

Collision Claim Increases in Legal Recreational States (Highway Loss Data Institute, 2017)

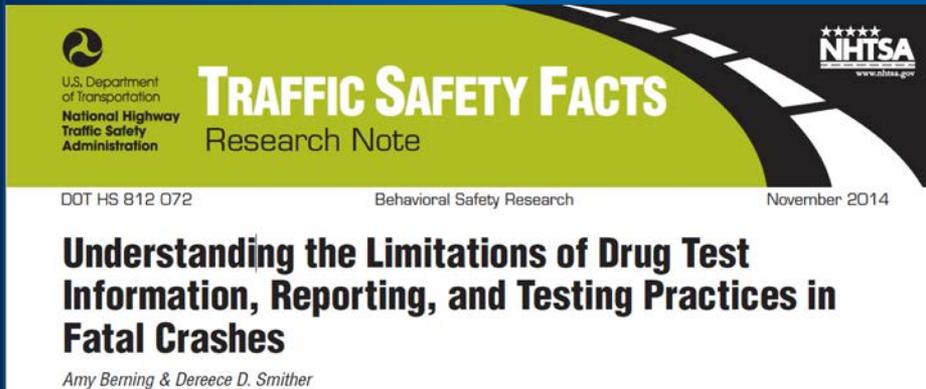
- Colorado (first to legalize), Washington, Oregon
- Collision coverage/claims: Physical damage to driver's vehicle (object or other vehicle); generally at fault
- Compared to nearby states
- Combined, 3% greater increase in claims than would be expected without legalization

Laboratory vs. Real World Findings

Why is there a disconnect between controlled studies vs. real-world findings?

- » **Epidemiologic findings based upon imperfect data**
 - **Incomplete reporting [e.g., toxicology], delayed blood collection**
- » **Large numbers of THC+ unimpaired drivers may statistically mask the effects of impaired drivers**
- » **Confounding by concurrent use of other substances**
- » **Compensatory behaviors**
- » **Magnitude of the effects seen in the laboratory may not be sufficient to substantially increase real world risks in all users**

Limitations of the Fatality Analysis Reporting System (FARS)

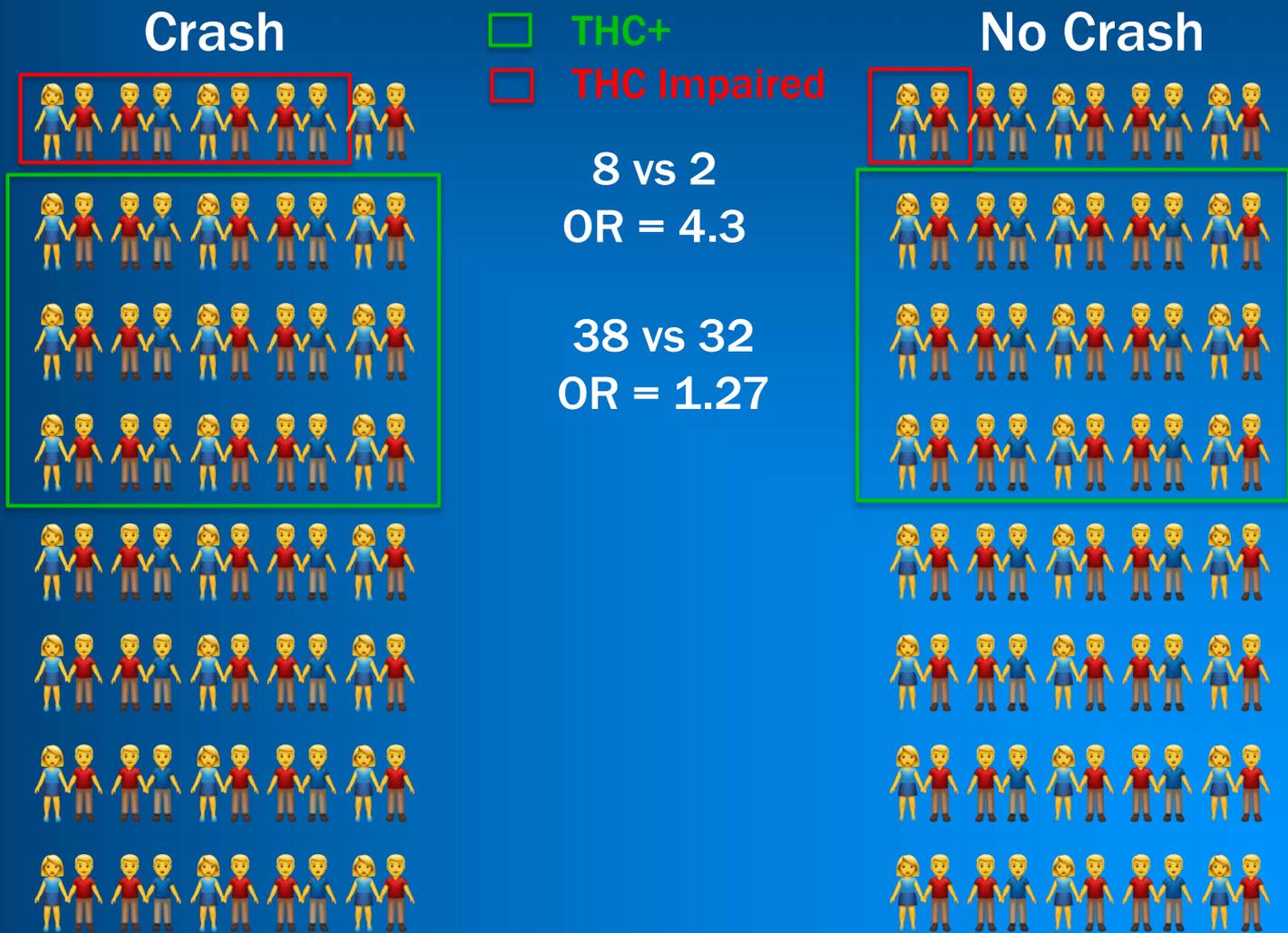


- Inconsistent testing methods (who, which drugs, when, cutpoints, equipment, bodily fluid)
- Some test only: fatally injured drivers, all drivers in a fatal crash, no drivers
- Often no drug testing if alcohol present
- Inconsistency in performing screening, and confirmatory, tests
- Limit to reporting 3 drugs
- **Presence ≠ impairment**

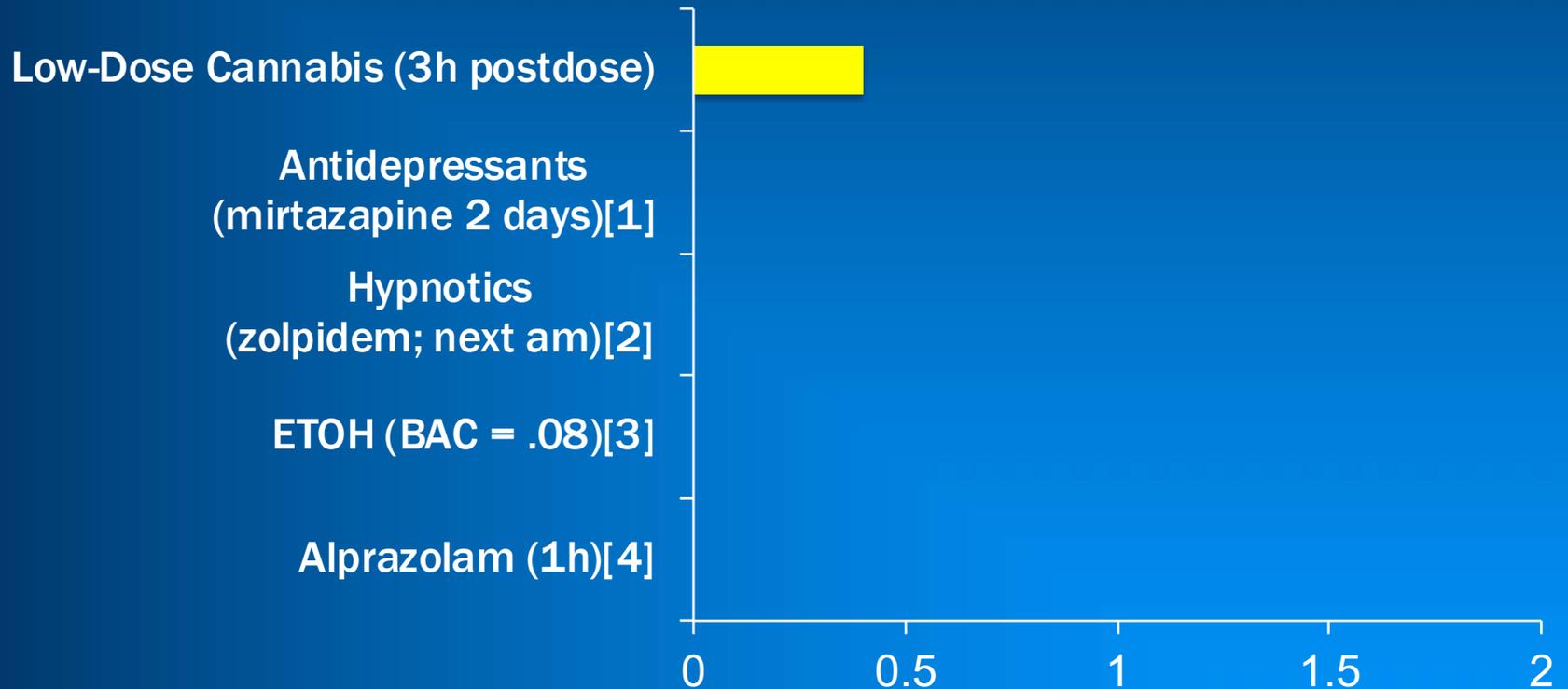
“Currently, the data in FARS is insufficient to allow comparisons of drug use across years, or across States.”

“... it is also not possible to make inferences about impairment, crash causation, or comparisons to alcohol from this limited data.”

Effects of Prolonged Presence of THC in Detecting Crash Risks (hypothetical example)

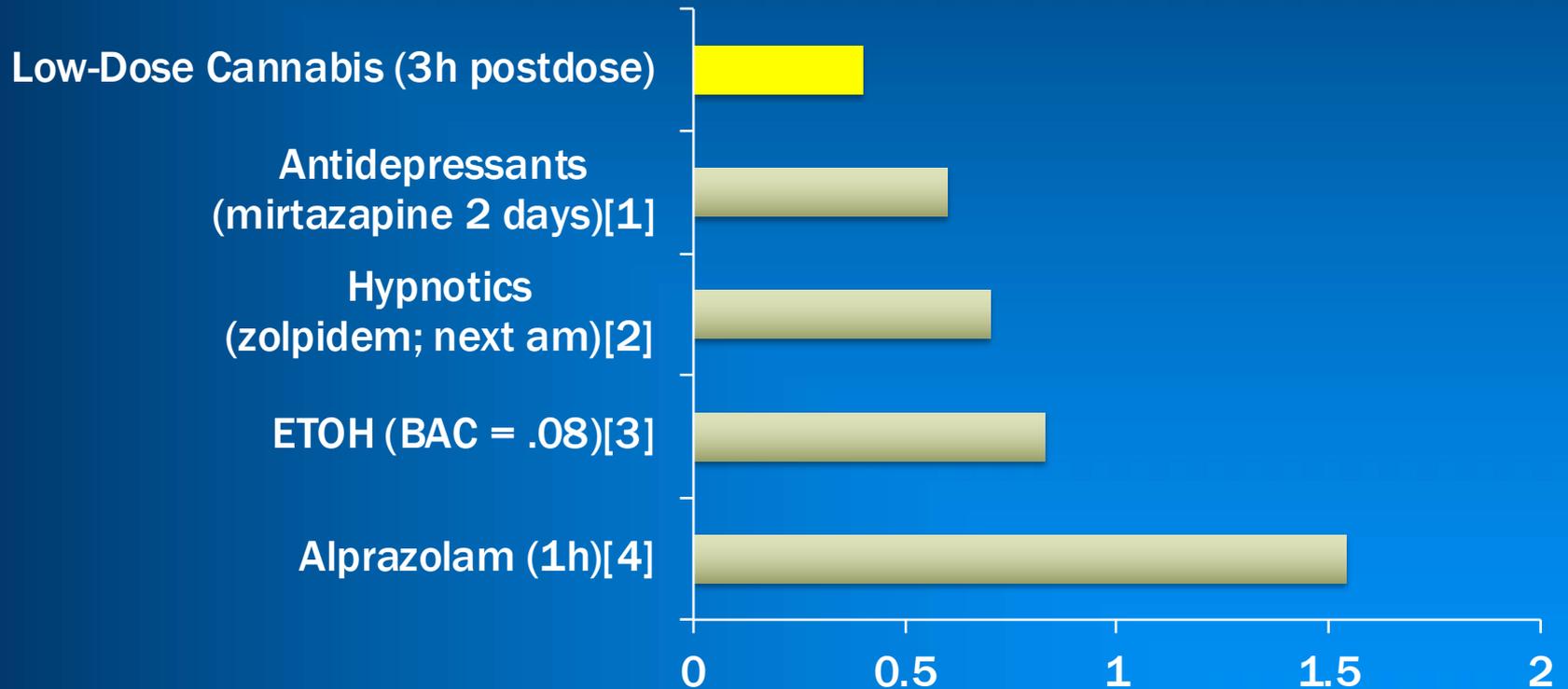


SDLP (“swerving”) Effect Sizes for Prescription Medications



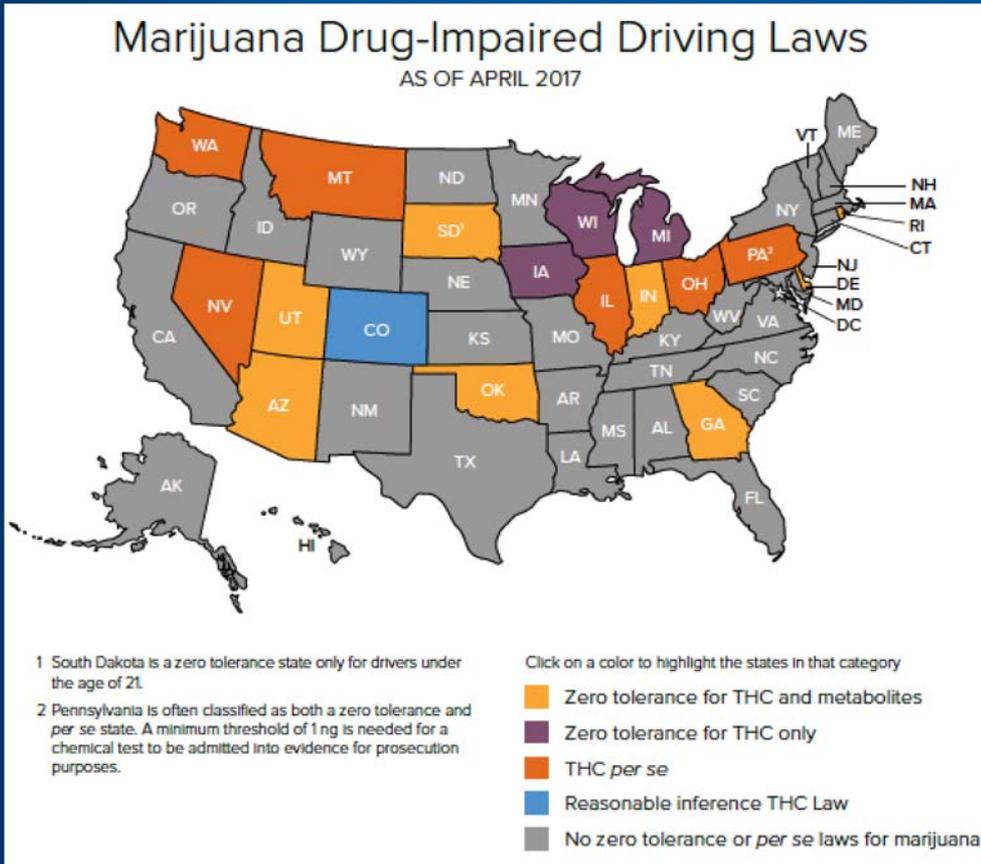
- [1] Sasada et al. (2013) *Human psychopharmacology*; Wingen M, et al. (2005) *J Clin Psychiatry*;
[2] Bocca et al. (2011) *Psychopharmacology (Berl)*; [3] Mets et al. (2011) *Human psychopharmacology*;
[4] Verster et al. (2002) *Neuropsychopharmacology*

SDLP (“swerving”) Effect Sizes for Prescription Medications



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THC levels and *per se* Laws



18 States with zero tolerance on non-zero *per se* laws

Zero tolerance (THC/metabolite)
AZ, DE, GA, IN, OK, RI, SD, UT

Zero tolerance (THC)
IA, MI, WI

Per se

1 ng (PA), 2 ng (NV, OH), 5 ng (IL, MT, WA); non-zero metabolites (NV, OH, PA)

Reasonable inference

5 ng (CO)

Governors Highway Safety Administration (GHSA) (2017)

THC levels in blood and *per se* laws

- DREs determined driver was impaired due to cannabis
- 602 cases

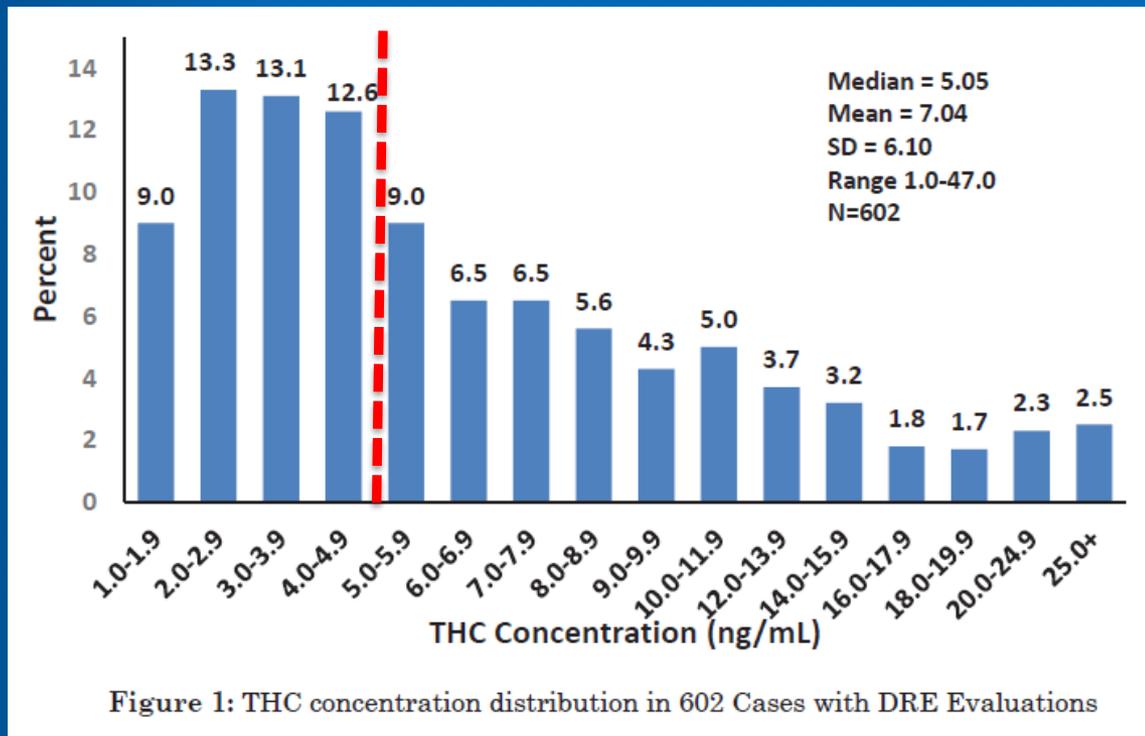


Figure 1: THC concentration distribution in 602 Cases with DRE Evaluations



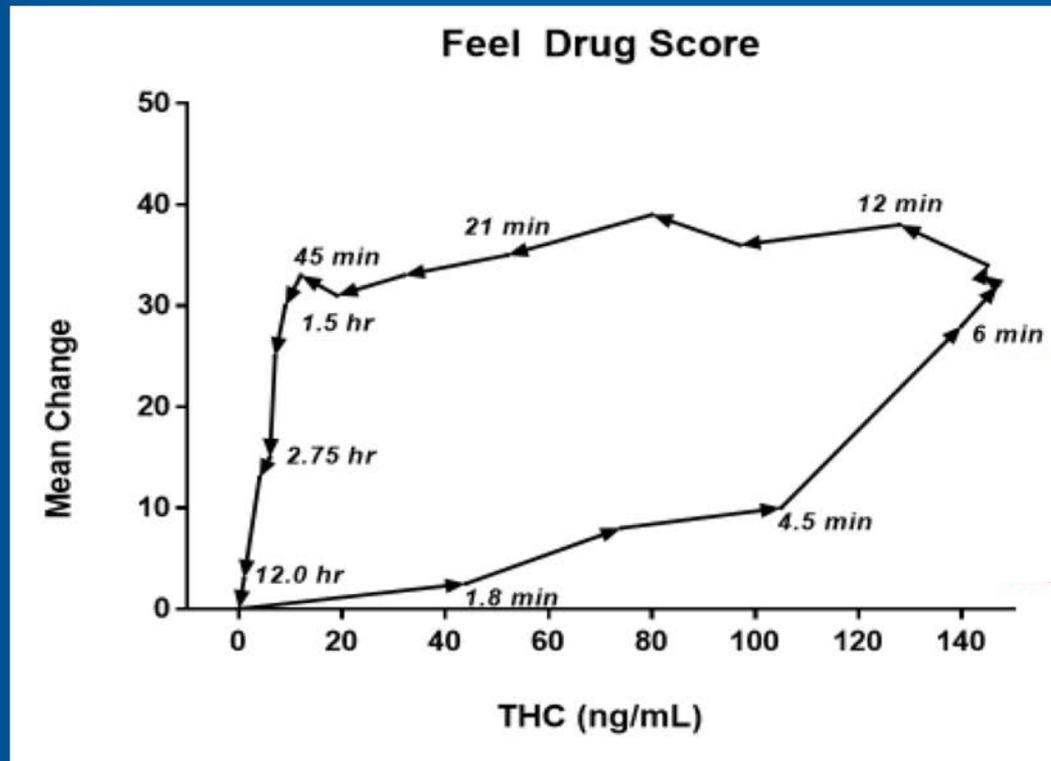
THC is Detectable in Blood in Frequent Users Days after Smoking

Chronic users (>5 days/week); ~30 participants

Day	% detect	Median	Max
Admit	90%	1.4ng	6.3ng
1	68%	1.8	2.9
2	80%	1.2	2.2
3	79%	1.3	2.6
4	79%	1.1	2.3
5	77%	1.0	1.9
6	72%	1.0	2.2
7	79%	0.9	2.0

Bergamaschi et al., 2013

Poor correlation of being “high” and blood concentrations of THC

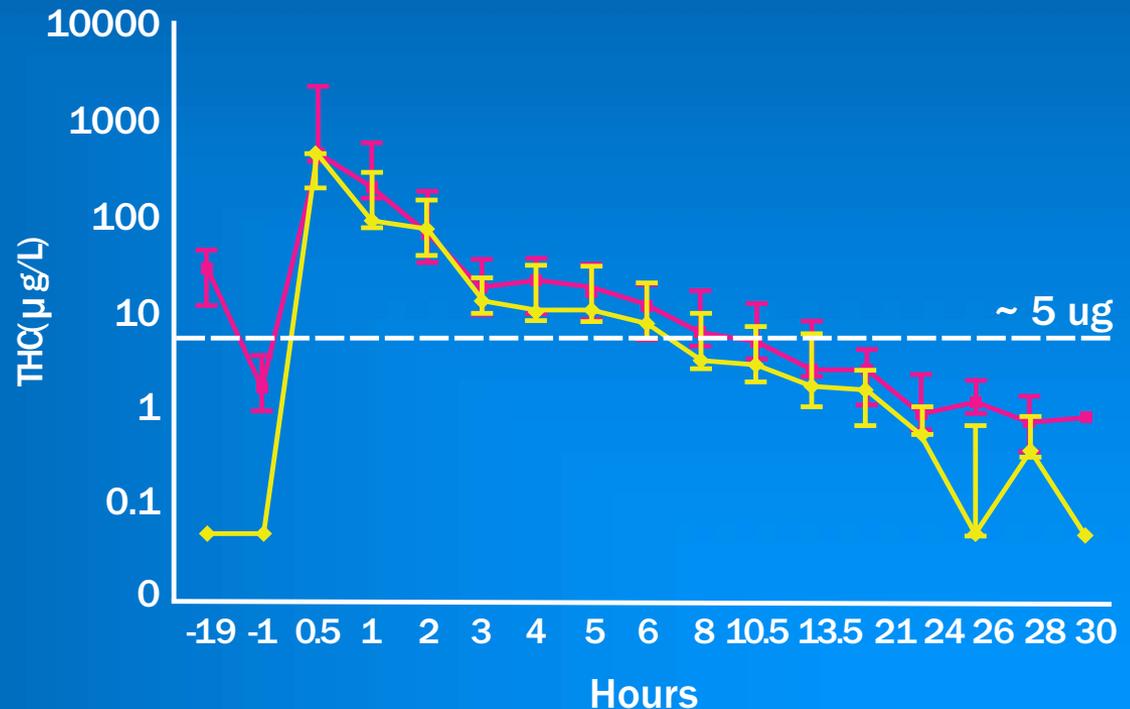


Counter-clockwise Hysteresis (M. Huestis)

Oral fluid – Detection of THC

THC concentrations (median, IQR)
in frequent and occasional users
(after 6.8% cigarette)

- Potential screening tool
- Easy to administer
- Minimally invasive
- Many studies suggest it may reflect recent drug use
- But some individuals may yield values > 5ng many hours after smoking



Anizin et al, 2013

Questions to Ask Regarding Biological Assays

- **Is the approach reliable?**
 - » Do you get the same values if you repeat the test under the same circumstances?
 - » Do you get the same results under different circumstances (e.g., environmental)?
- **Can the results be masked (e.g., by alcohol, other substances)?**
- **Do the assays work with different modes of ingestion (smoke, edible, dabs, etc.)?**
- **What do the results mean?**
 - » **Time since use?**
 - » **Impairment?**

Drug Recognition Expert (DRE)

- **Drug Evaluation and Classification (DEC) Program**
 - » **Current Gold Standard; 152 hours training**
 - » **Systematic, standardized 12-step evaluation of physical, mental, and medical components of substance use**
- **Hartman et al. (2016) – 302 THC-only and 302 un-impaired individuals**
 - » **Best predictors: Finger-to-nose, Modified Romberg (eyelid tremors), One-leg stand (sway), Walk and turn; Requiring $\geq 2/4$ (96.9% efficiency)**
- **Declues (2016; 2018) – 363 THC only/116 with DRE**
 - » **WAT most sensitive (other studies show OLS); Modified Romberg (time) not sensitive**
 - » **Multiple tests is best approach**

SFST/DRE Evaluations

■ Limitations

- » **Controls not well matched to cases**
- » **Tested under different conditions**
- » **Often report only “true positives” (cases correctly identified as THC only)**
 - **Inform which of the components most strongly predicted the overall conclusion ; no external standard**
 - **Miss (1) false positives (those who didn't do well, and did not have THC), (2) false negatives (those with THC, but passed the tests)**

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**Assessing
Cannabis-Related Driving Impairment**

Program of Research

Aims

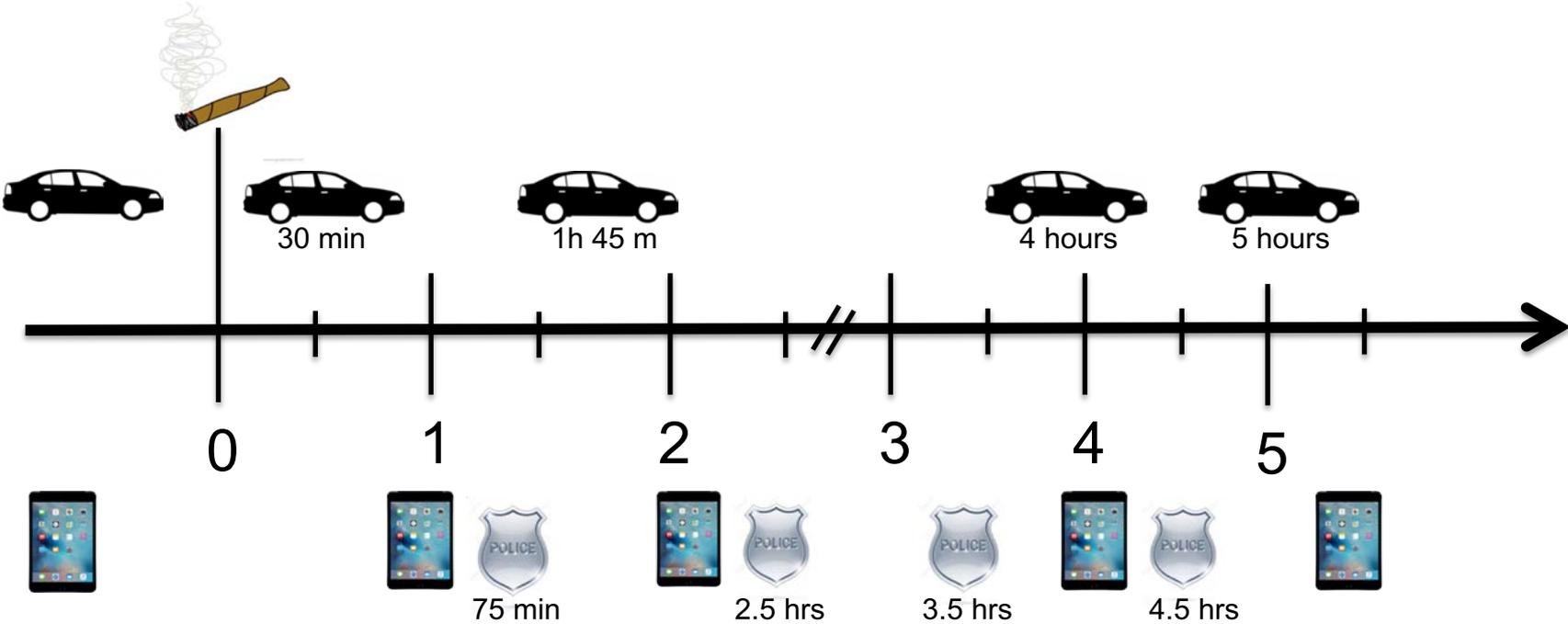
Assessing Cannabis-Related Driving Impairment

1. Effect of **dose** of THC on driving performance
2. **Time course** of driving impairment (hours since use)
3. Utility of **saliva or exhaled air (breath)** to inform regarding time since use, or impairment
4. Determine whether **standardized, tablet-based measures** can augment the standard field sobriety test

Study Design

- **Parallel design with healthy participants (each person sees one treatment)**
 - » **Minimize practice effects**
 - » **Maximize retention in study**
- **Smoke**
 - » **0% THC (n = 60)**
 - » **5.9% THC (n = 60)**
 - » **13.4% THC (n = 60)**
- **Assess throughout the day**
 - » **Driving Performance – simulations**
 - » **Standardized Field Sobriety Test/DRE assessment**
 - » **Tablet-based (iPad) cognitive/motor performance**
 - » **Fluids (cannabinoids, metabolites) – Blood, Saliva, Breath**

Study Schedule



	Simulation
	iPad
	DRE

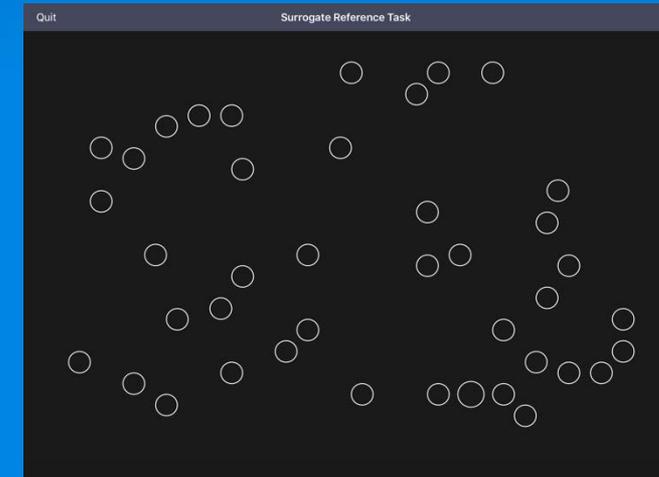
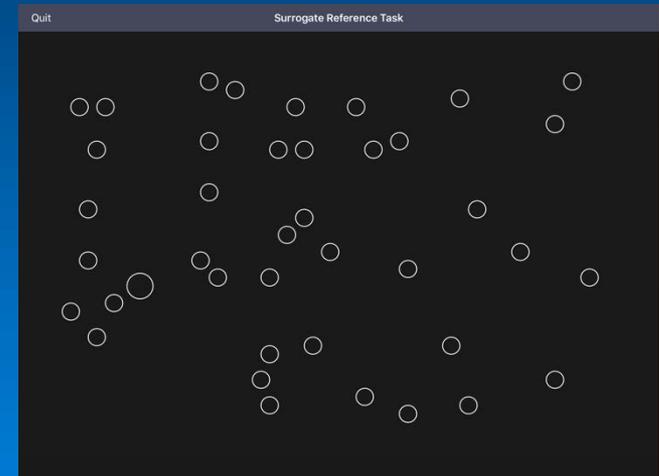
30 min	Driving Simulation	200	DRE
60	iPad	230	Driving Simulation
75	DRE	260	iPad
105	Driving Simulation	275	DRE
135	iPad	300	Driving Simulation
150	DRE	330	iPad

Driving simulator

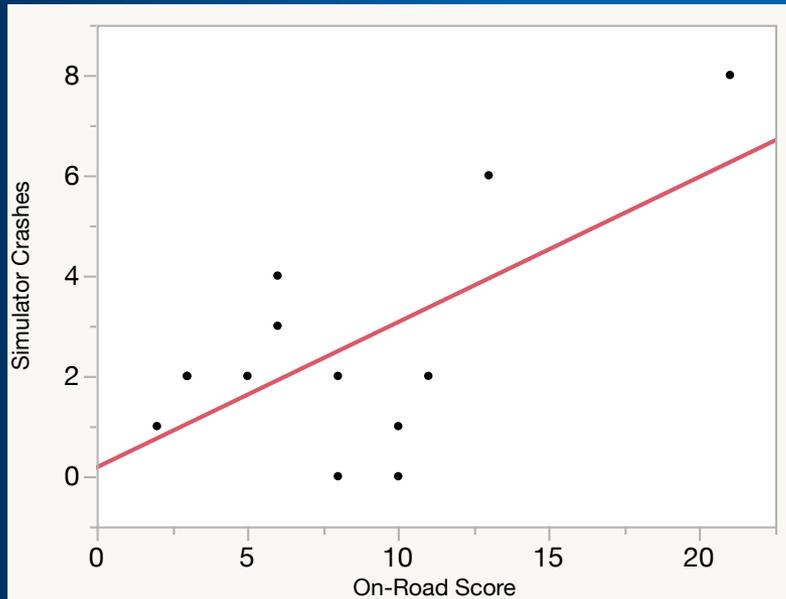


Driving Simulation Scenarios – Distracted Driving/Multi-tasking

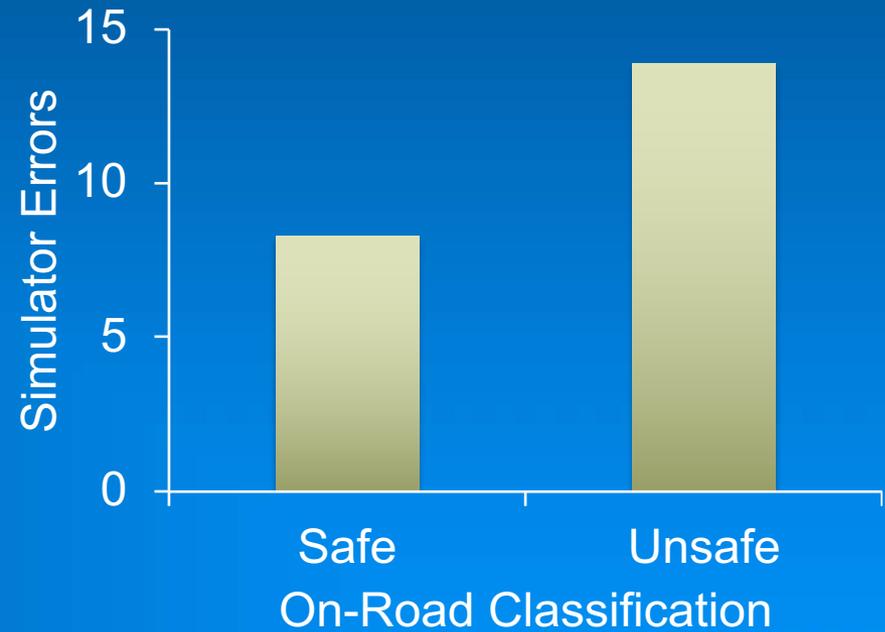
- Identify circle that is different than others
- Two levels of difficulty
- Response time and accuracy
- Driving performance prior to/during task
 - Standard deviation of lateral position (SDLP) – swerving
 - Speed deviation



Simulator performance predicts on-road driving



Healthy Adults

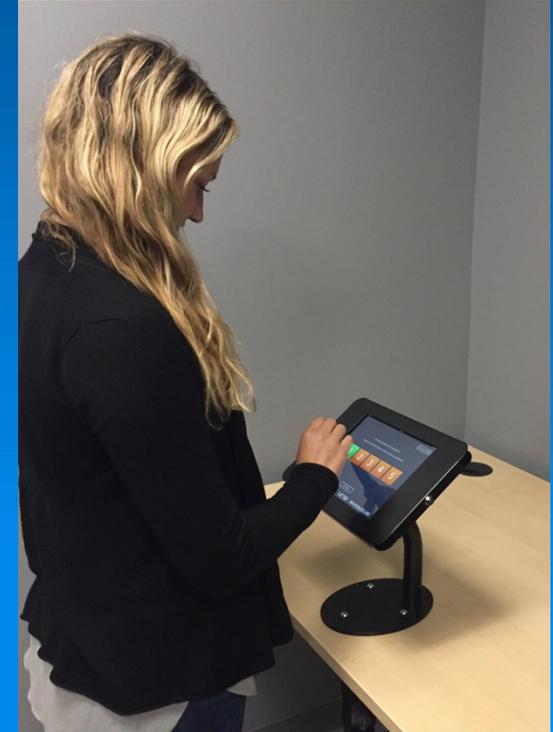


HIV+ and HIV- Adults

Performance-based field sobriety tests

Approximately 2 minutes each

- **Divided attention:** Ability to track a moving target object while simultaneously attending to another
 - Divided attention, executive functioning (shifting), psychomotor coordination, staying on task
- **Lane tracking:** Ability to keep object between two lines as the lines shift (psychomotor coordination, sustained attention)



BrainBaseline®

Performance-based field sobriety tests

Approximately 2 minutes each

- **Time Estimation:** Ability to estimate passage of time (must simultaneously perform other simple task in order to minimize subvocal counting)
- **Learning/Memory:** Memorize abstract figures and locations
- **Balance:** Lightweight Bluetooth device syncs with iPad; uses data from accelerometer, magnetoscope, and gyroscope to determine movement and sway



BrainBaseline®

DRE Evaluations for the Current Project

- California DRE Instructors (Sgt. Glen Glaser, State Coordinator)
- Double-blind, placebo controlled; randomized assignment
- All participants examined under the same circumstances
- DRE Evaluations
 - Finger to Nose (FTN)
 - Modified Romberg Balance (MRB)
 - One Leg Stand (OLS)
 - Walk and Turn (WAT)
 - Lack of Convergence (LOC)

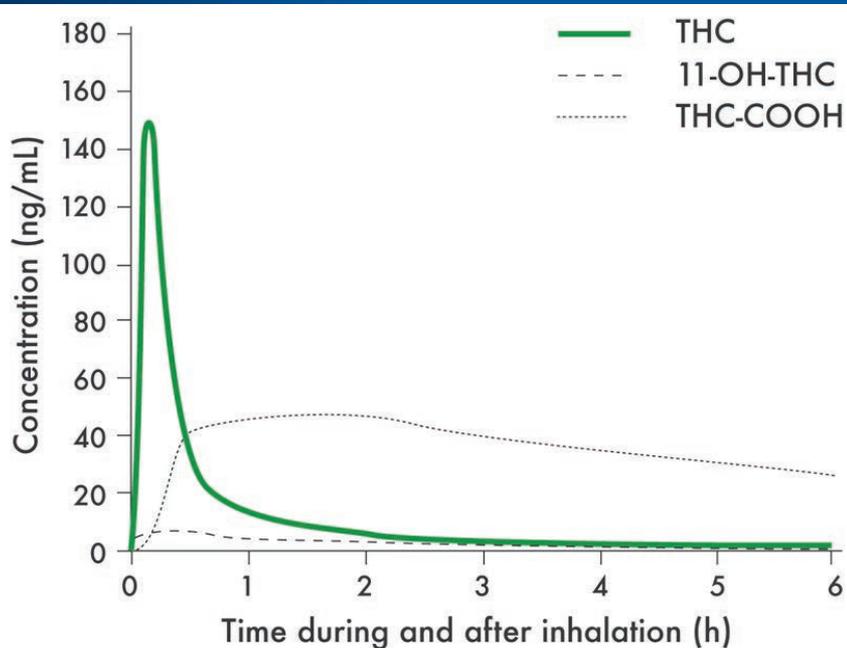
Edibles

- THC-infused food (baked goods [cookies, brownies], chocolates, gummies)
- After passing through the liver (first-pass metabolism), THC is transformed to **11-hydroxy-THC** (readily crosses the blood-brain barrier; more potent than THC)
- Hour to 1.5 hours to feel full effect
- Often absorbed better with food

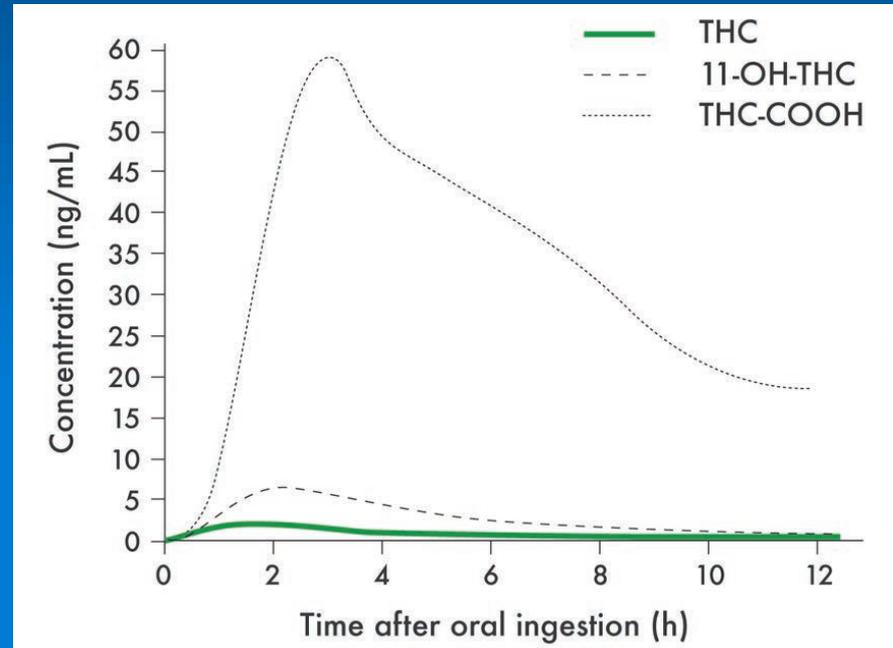


Plasma THC Levels – Smoked vs. Oral

inhaled cannabis ~34mg THC



15mg oral THC (dronabinol)



Mean plasma concentrations of Δ^9 -tetrahydrocannabinol (THC), 11-hydroxy-THC (11-OH-THC) and 11-nor-9-carboxy-THC (THC-COOH) following administration smoked cannabis vs. oral dronabinol.

Source: Grotenhermen, et al. 2003. *Clin Pharmacokinet* 2003; 42 (4): 327-360.

Cannabis and Driving

- Identifying individuals whose driving is impaired due to cannabis remains a challenge
- **Per se laws** are most effective when there is a robust correlation between fluid levels and impairment; not yet true for THC/driving
- Impact of other **administration methods**: Vape pens, dabbing, edibles, transdermal, salves, topicals, lip balm, sublingual, suppository
- Impact of **concentrates** (up to 90% THC; Wax, shatter, budder, dabs) on driving
- Do regular cannabis users develop **tolerance** to the driver impairing aspects of cannabis?
- What are the effects of cannabis combined with **alcohol, other drugs, including prescription medications**?
- **Synthetic THC**: Spice, K2, etc.
- Impact in **older users**

Research Team

UCSD

- Igor Grant, MD – CMCR Director
- Thomas Marcotte, PhD
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- Robert Fitzgerald, PhD
- David Grelotti, MD
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- Kamaron Sardar
- Jayson Siller
- Travis Easter
- Richard Horrocks
- Ryan Orloff
- Gary Martens
- Kerry Comphele
- Kevin Craig
- Billy Phu
- Eric Stayer
- Bryan Duncan
- Helena Williams



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