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# Cannabis and Cognition

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**James MacKillop, PhD**

**Peter Boris Chair in Addictions Research**

**Director, Peter Boris Centre for Addictions Research**

**Director, Michael G. DeGroote Centre for Medicinal Cannabis Research**

**Professor, Department of Psychiatry and Behavioural Neurosciences**


**St. Joseph's**  
Healthcare  Hamilton



Peter Boris Centre  
FOR ADDICTIONS RESEARCH



Michael G. DeGroote  
CENTRE FOR MEDICINAL  
CANNABIS RESEARCH

McMaster  
University   
PSYCHIATRY AND  
BEHAVIOURAL NEUROSCIENCES

# Disclosures

James MacKillop, PhD

Unrestricted research funding from:  
Peter Boris Chair in Addictions Research  
Boris Family Foundation  
Michael G. DeGroot Centre for Medicinal Cannabis  
Research  
Canadian Institutes of Health Research,  
National Institute on Alcohol Abuse and Alcoholism  
National Institute on Drug Abuse  
Correctional Service of Canada

Principal in BEAM Diagnostics, Inc.

No consultancies to or ownership in commercial cannabis  
entities.

**The central operating funding for the Michael G. DeGroot Centre for  
Medicinal Cannabis Research is from a philanthropic gift to the Michael G.  
DeGroot Initiative for Innovation in Healthcare.**

# Overview

- Cannabis fundamentals and evolving landscape
- Cannabis and cognition:
  - Acute effects
  - Residual/chronic effects
  - Neuroanatomical localization
- Practical recommendations
- Conclusions

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# Cannabis Fundamentals

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# Cannabis Fundamentals

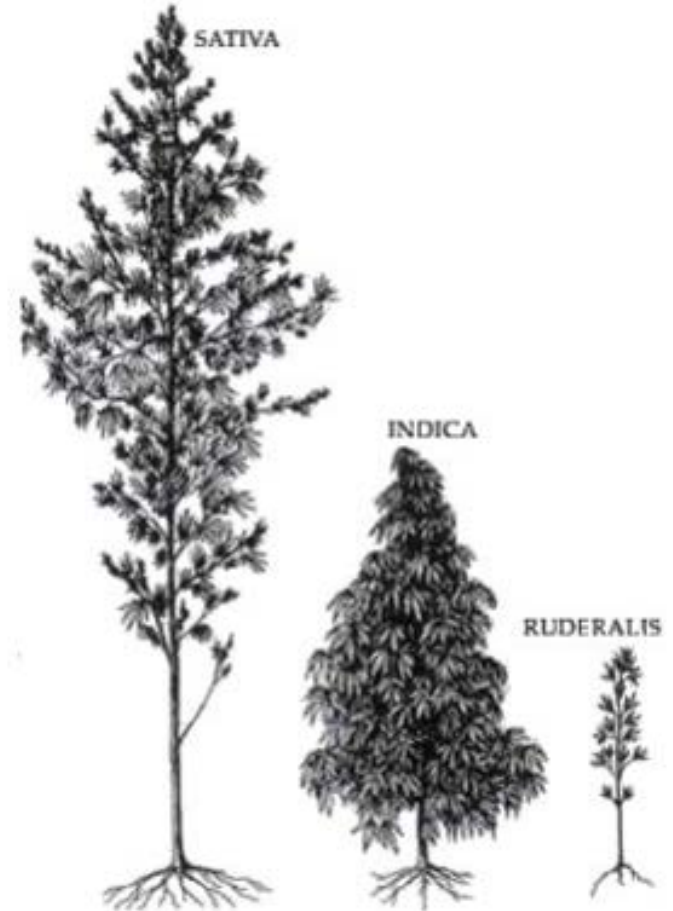
Sativa



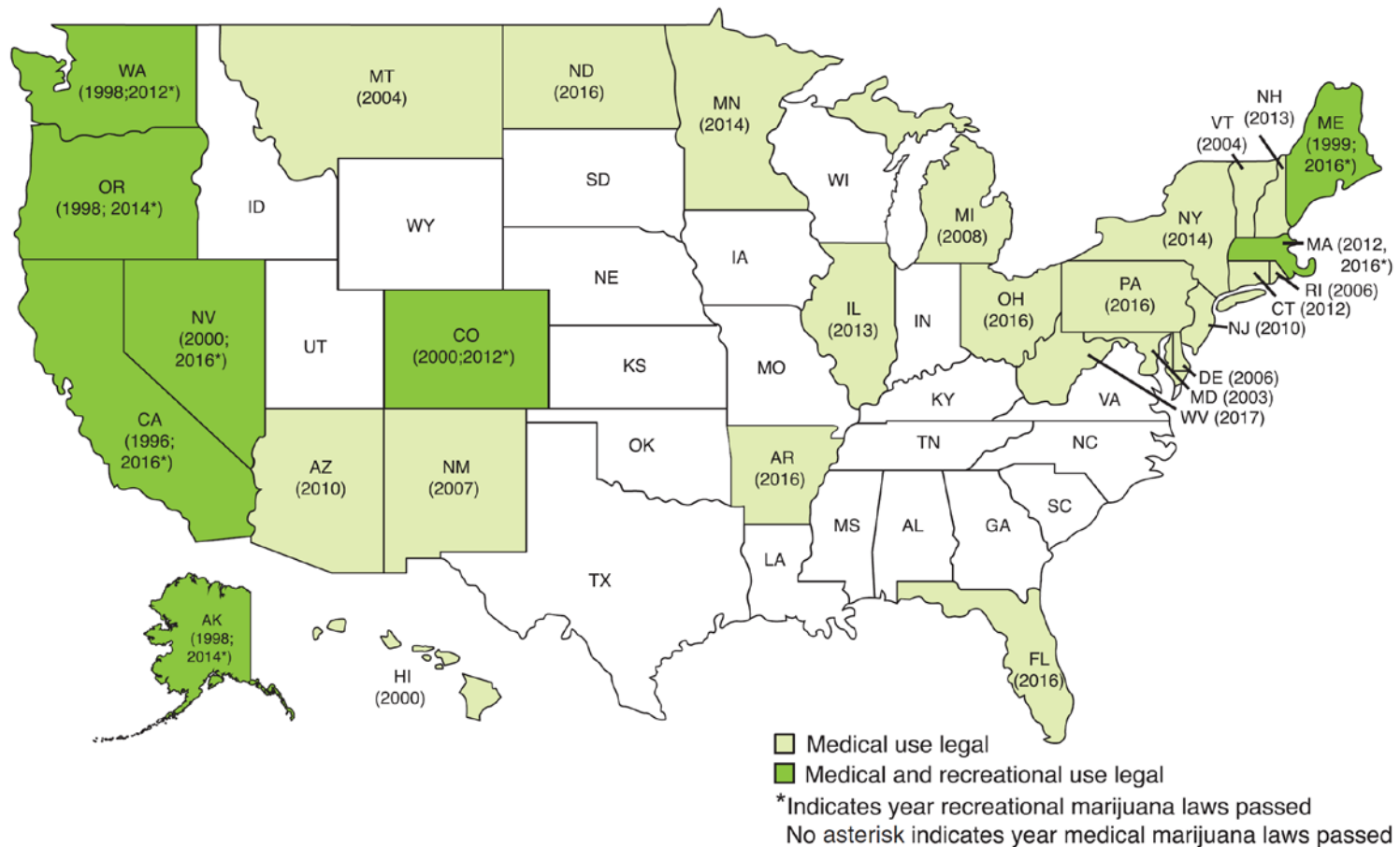
Indica



*“There are biochemically distinct strains of Cannabis, but the sativa/indica distinction as commonly applied in the lay literature is **total nonsense** and an **exercise in futility.**”*



# Legal Status in the United States



**Federal status: Schedule I controlled substance  
(high abuse potential, no therapeutic applications)**



# Legal Status in Canada

**Geneva International  
Convention on  
Narcotics Control**

**1925**

**Marihuana for Medical  
Purposes Regulations  
(MMPR)**

**2001**

**Medical Marihuana  
Access Regulations  
(MMAR)**

**2014**

**Access to Cannabis for  
Medical Purposes  
Regulations (ACMPR)**

**2017**

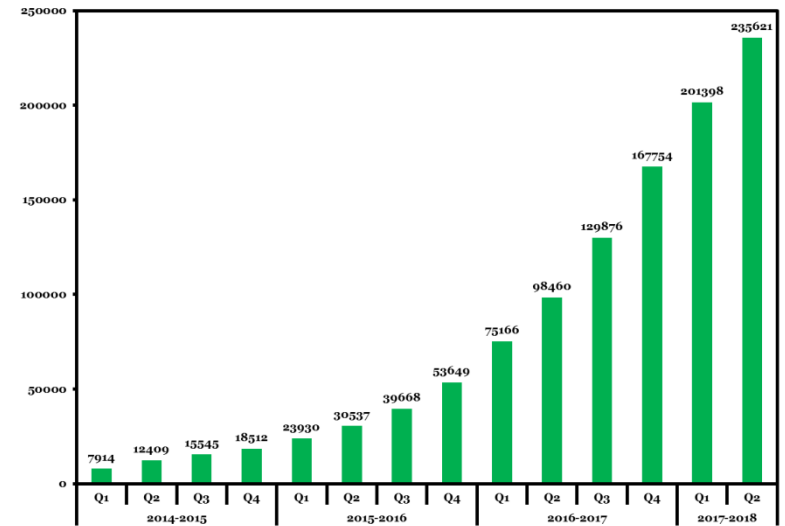
**2018**

**Federal  
Legalization:  
October 17**



# Legal Status in Canada

Registered Medical Cannabis Users, 2014-2017 (Health Canada)



**Geneva International  
Convention on  
Narcotics Control**

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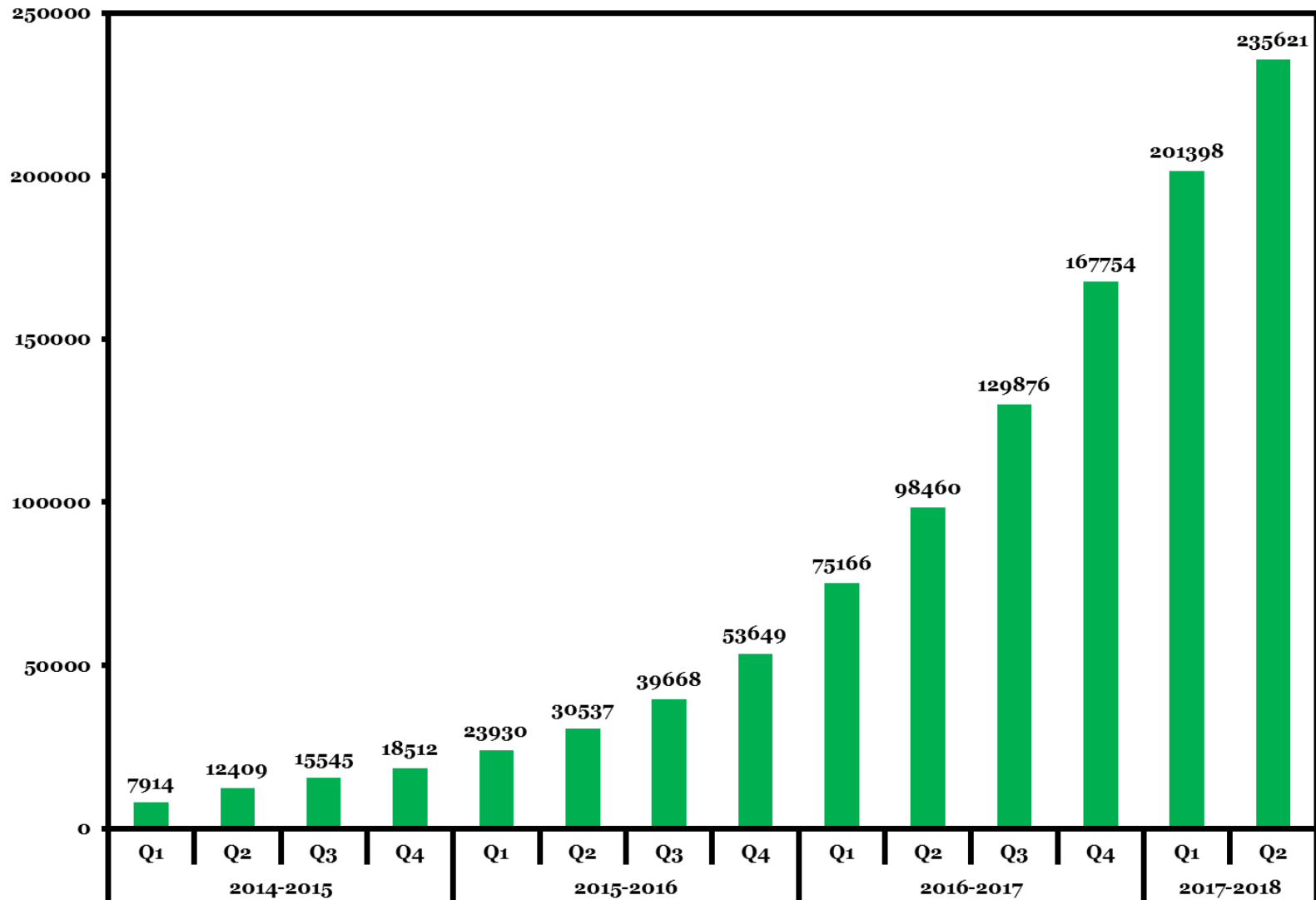
**Medical Marihuana  
Access Regulations  
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**2014 2017 2018**

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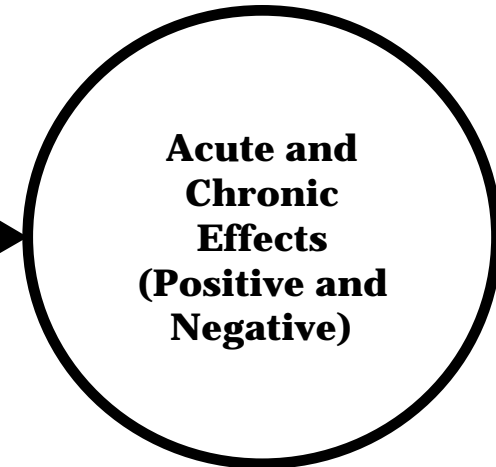
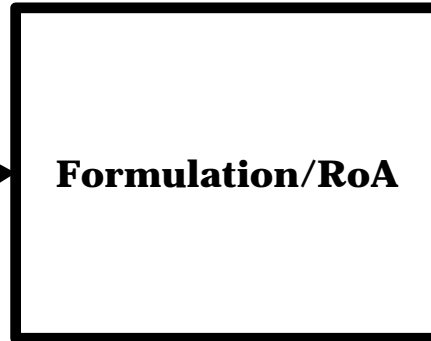
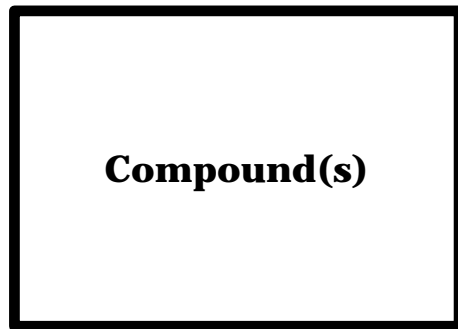
## Registered Medical Cannabis Users, 2014-2017 (Health Canada)



# Complexities of Cannabis

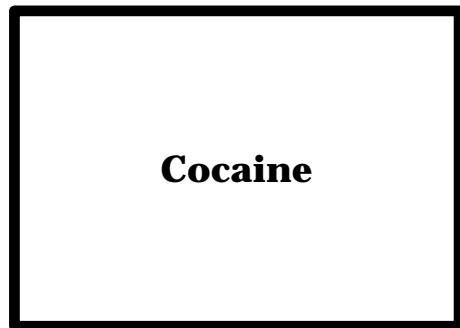
***PHARMACODYNAMICS***

***PHARMACOKINETICS***

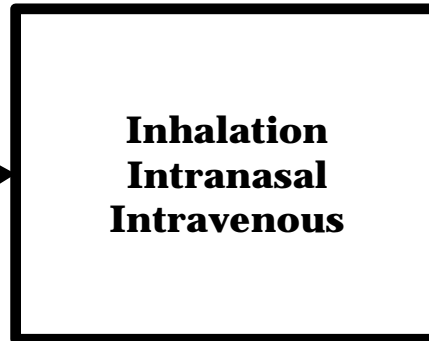


# Complexities of Cannabis

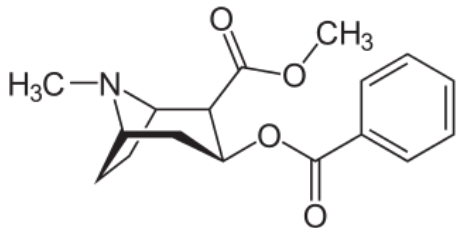
## *PHARMACODYNAMICS*



## *PHARMACOKINETICS*



**Acute and  
Chronic  
Effects  
(Positive and  
Negative)**



# Complexities of Cannabis

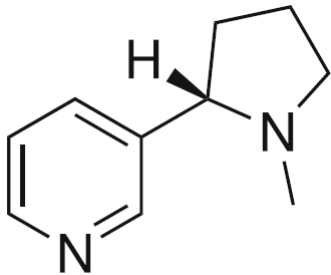
## *PHARMACODYNAMICS*



## *PHARMACOKINETICS*

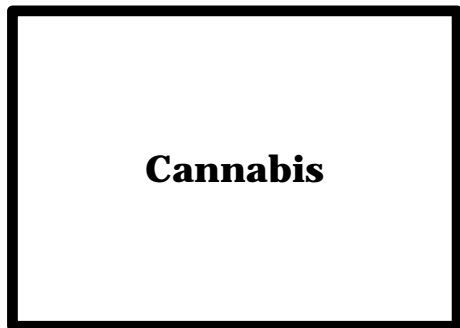
Inhalation  
Oral  
Intranasal  
Transdermal

Acute and  
Chronic  
Effects  
(Positive and  
Negative)

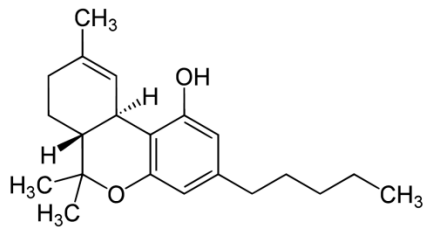


# Complexities of Cannabis

## PHARMACODYNAMICS

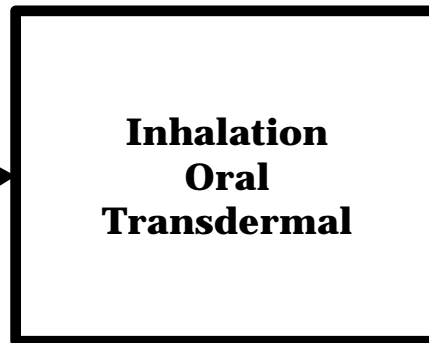


>100 cannabinoids (!)



**THC**

## PHARMACOKINETICS



Cigarette  
Pipe  
Waterpipe  
Vaporizer  
Edible  
Oil  
Patch  
Salve

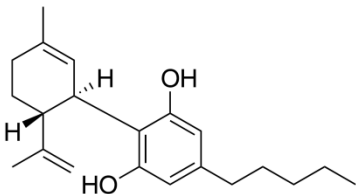
**Acute and  
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Effects  
(Positive and  
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# Complexities of Cannabis

## PHARMACODYNAMICS



>100 cannabinoids (!)



**CBD**

## PHARMACOKINETICS

**Inhalation  
Oral  
Transdermal**

Cigarette  
Pipe  
Waterpipe  
Vaporizer  
Edible  
Oil  
Patch  
Salve

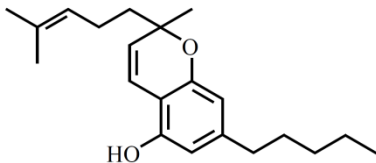
**Acute and  
Chronic  
Effects  
(Positive and  
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# Complexities of Cannabis

## PHARMACODYNAMICS

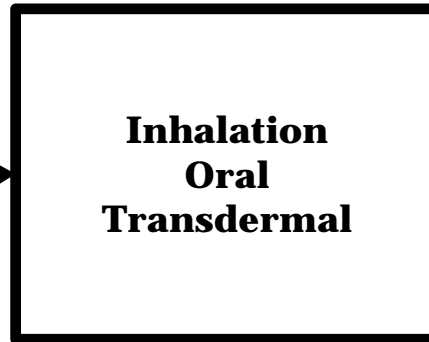


>100 cannabinoids (!)



**CBC**

## PHARMACOKINETICS



Cigarette  
Pipe  
Waterpipe  
Vaporizer  
Edible  
Oil  
Patch  
Salve

**Acute and  
Chronic  
Effects  
(Positive and  
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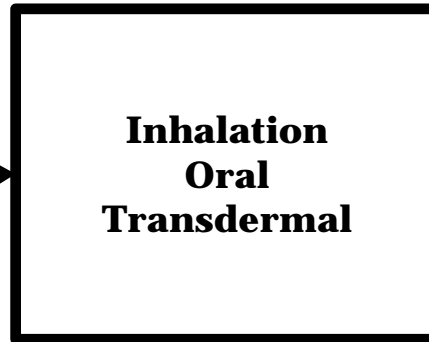
# Complexities of Cannabis

## PHARMACODYNAMICS

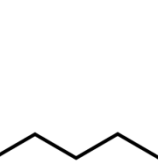
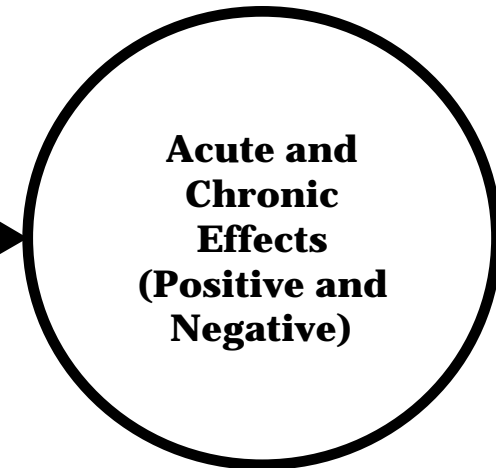


>100 cannabinoids (!)

## PHARMACOKINETICS



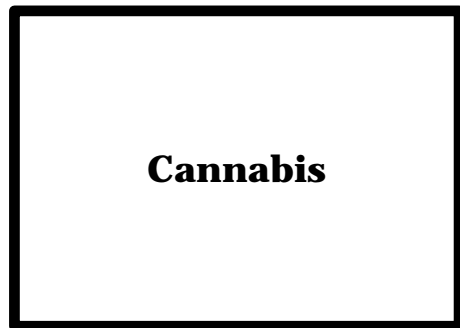
Cigarette  
Pipe  
Waterpipe  
Vaporizer  
Edible  
Oil  
Patch  
Salve



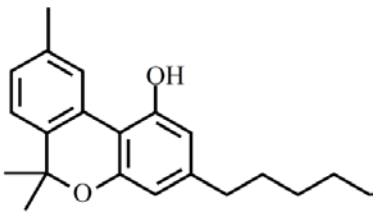
**CBG**

# Complexities of Cannabis

## PHARMACODYNAMICS

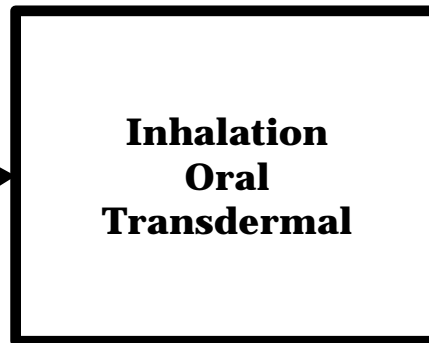


>100 cannabinoids (!)



**CBN**

## PHARMACOKINETICS



Cigarette  
Pipe  
Waterpipe  
Vaporizer  
Edible  
Oil  
Patch  
Salve

**Acute and  
Chronic  
Effects  
(Positive and  
Negative)**

# Complexities of Cannabis

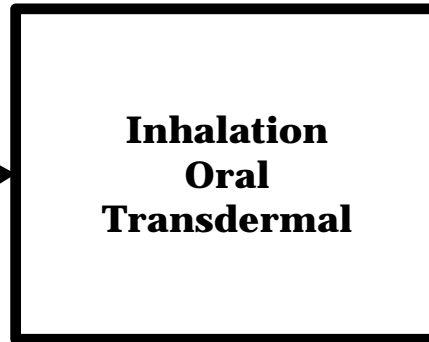
## PHARMACODYNAMICS



>100 cannabinoids (!)

Myrcene	Camphene
Linalool	Terpineol
$\alpha$ Bimalol	$\Delta$ -3-carene
Borneol	Limonene
Caryophyllene	Eucalyptol
$\alpha$ Pinene	Humulene
$\beta$ Pinene	Trans-neroliol

## PHARMACOKINETICS

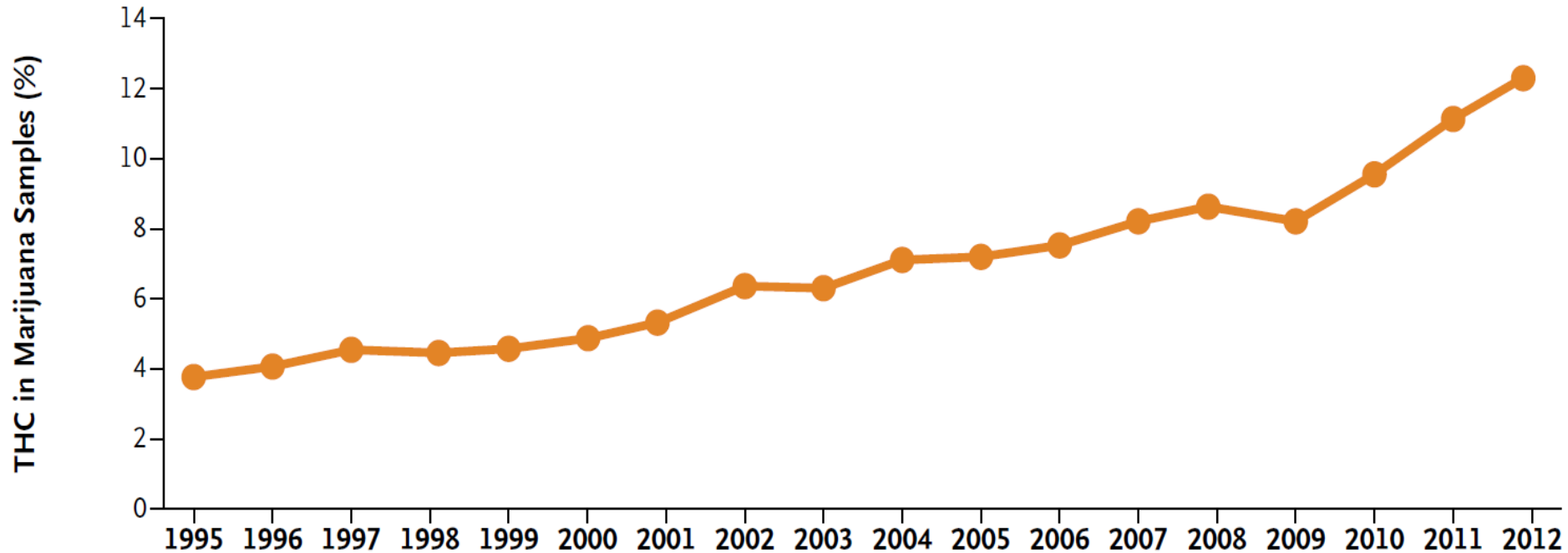


Cigarette  
Pipe  
Waterpipe  
Vaporizer  
Edible  
Oil  
Patch  
Salve

**Acute and  
Chronic  
Effects  
(Positive and  
Negative)**

***“Entourage  
Effect”***

# Escalation in THC Over Time



# New Formulations



**“Wax”**



**“Shatter”**



**“Budder”**

**Butane Hash Oil Extractions (up to 90% THC)  
“Concentrates”**

# Pharmaceutical Cannabinoids

- Dronabinol (Marinol)
- Nabilone (Cesamet)
- Nabiximols (Sativex)
- Cannabidiol (Epidiolex)

## Smoked cannabis for chronic neuropathic pain: a randomized controlled trial

Mark A. Ware MBBS, Tongtong Wang PhD, Stan Shapiro PhD, Ann Robinson RN, Thierry Ducruet MSc, Thao Huynh MD, Ann Gamsa PhD, Gary J. Bennett PhD, Jean-Paul Collet MD PhD

**Table 2:** Pairwise comparisons of the effects of four potencies of smoked cannabis on average daily pain

Potency, % of THC	Potency, % of THC, mean difference (95% CI)							
	0		2.5		6.0		9.4	
0	-	-	-	-	-	-	-	-
2.5	-0.13	(-0.83 to 0.56)	-	-	-	-	-	-
6.0	-0.09	(-0.78-0.60)	0.04	(-0.64 to 0.73)	-	-	-	-
9.4	-0.71	(-1.40 to -0.02)	-0.58	(-1.27 to 0.11)	-0.63	(-1.30 to 0.06)	-	-

Note: CI = confidence interval, THC = tetrahydrocannabinol.

# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

MAY 25, 2017

VOL. 376 NO. 21

## Trial of Cannabidiol for Drug-Resistant Seizures in the Dravet Syndrome

Orrin Devinsky, M.D., J. Helen Cross, Ph.D., F.R.C.P.C.H., Linda Laux, M.D., Eric Marsh, M.D., Ian Miller, M.D., Rima Nabbout, M.D., Ingrid E. Scheffer, M.B., B.S., Ph.D., Elizabeth A. Thiele, M.D., Ph.D., and Stephen Wright, M.D., for the Cannabidiol in Dravet Syndrome Study Group\*

**Table 2. Primary Efficacy End Point of Percentage Change in Convulsive-Seizure Frequency in Each Trial Group.\***

Variable	Cannabidiol	Placebo	Adjusted Median Difference (95% CI) <i>percentage points</i>	P Value†
No. of convulsive seizures per mo — median (range)				
Baseline	12.4 (3.9 to 1717)	14.9 (3.7 to 718)		
Treatment period	5.9 (0.0 to 2159)	14.1 (0.9 to 709)		
Percentage change in seizure frequency — median (range)	-38.9 (-100 to 337)	-13.3 (-91.5 to 230)	<b>-22.8 (-41.1 to -5.4)</b>	<b>0.01</b>



# Low Quality Evidence of Overall Efficacy

Research

Original Investigation

## Cannabinoids for Medical Use A Systematic Review and Meta-analysis

Penny F. Whiting, PhD; Robert F. Wolff, MD; Sohan Deshpande, MSc; Marcello Di Nisio, PhD; Steven Duffy, PgD; Adrian V. Hernandez, MD, PhD; J. Christiaan Keurentjes, MD, PhD; Shona Lang, PhD; Kate Misso, MSc; Steve Ryder, MSc; Simone Schmidtkofer, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD

**IMPORTANCE** Cannabis and cannabinoid drugs are widely used to treat disease or alleviate symptoms, but their efficacy for specific indications is not clear.

**OBJECTIVE** To conduct a systematic review of the benefits and adverse events (AEs) of cannabinoids.

**DATA SOURCES** Twenty-eight databases from inception to April 2015.

**Of 79 trials,  
4 judged to have  
low risk of bias**

**Increased risk of  
short-term AEs**

**Low quality evidence  
in general**

**Moderate quality  
evidence for pain  
and spasticity in MS**

**NAS report also  
identifies anti-nausea  
effects in  
chemotherapy**

# Epidemiology and Harm

## ■ United States

- Last year use = 9.5% in 2012-2013,
  - 4.1% in 2001-2002
- Cannabis use disorder
  - Lifetime prevalence = ~7%
  - 12-month prevalence = 2.9% 2012-2013
    - 1.5% in 2001-2002

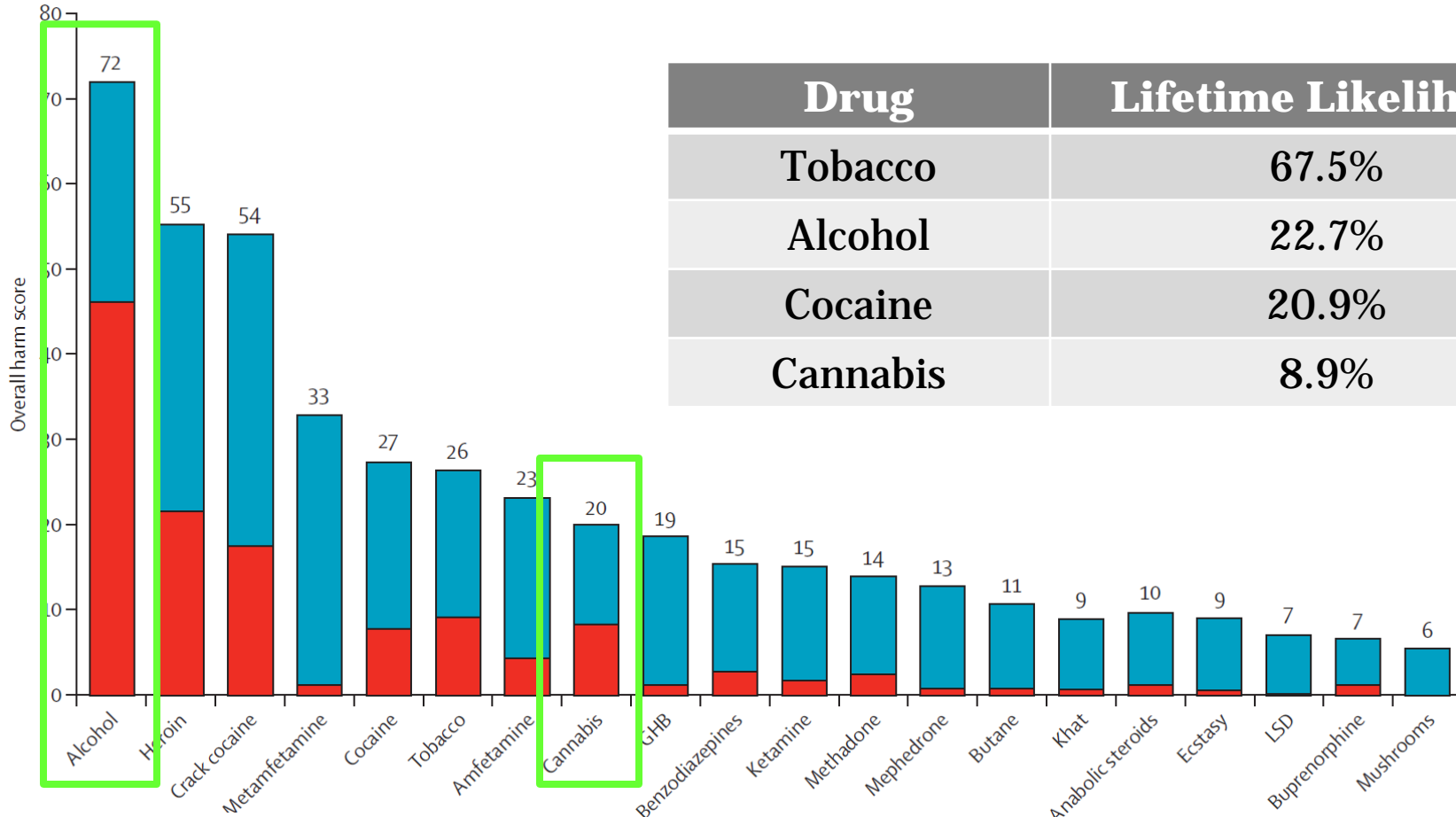
## ■ Canada

- Last year prevalence of use = 12.2% (2012)
- Cannabis Use Disorders:
  - Lifetime prevalence = 6.8%
  - 12-month prevalence = 1.3%

# Epidemiology and Harm

- Increased motor vehicle accident risk
- Chronic bronchitis
- Cannabinoid hyperemesis syndrome
- Cannabinoid-induced delirium/psychosis
- Increased risk of psychotic disorders
- Reduced educational attainment
- Adverse effects on cognition

# Contextualizing Risks and Harm



Drug	Lifetime Likelihood
Tobacco	67.5%
Alcohol	22.7%
Cocaine	20.9%
Cannabis	8.9%

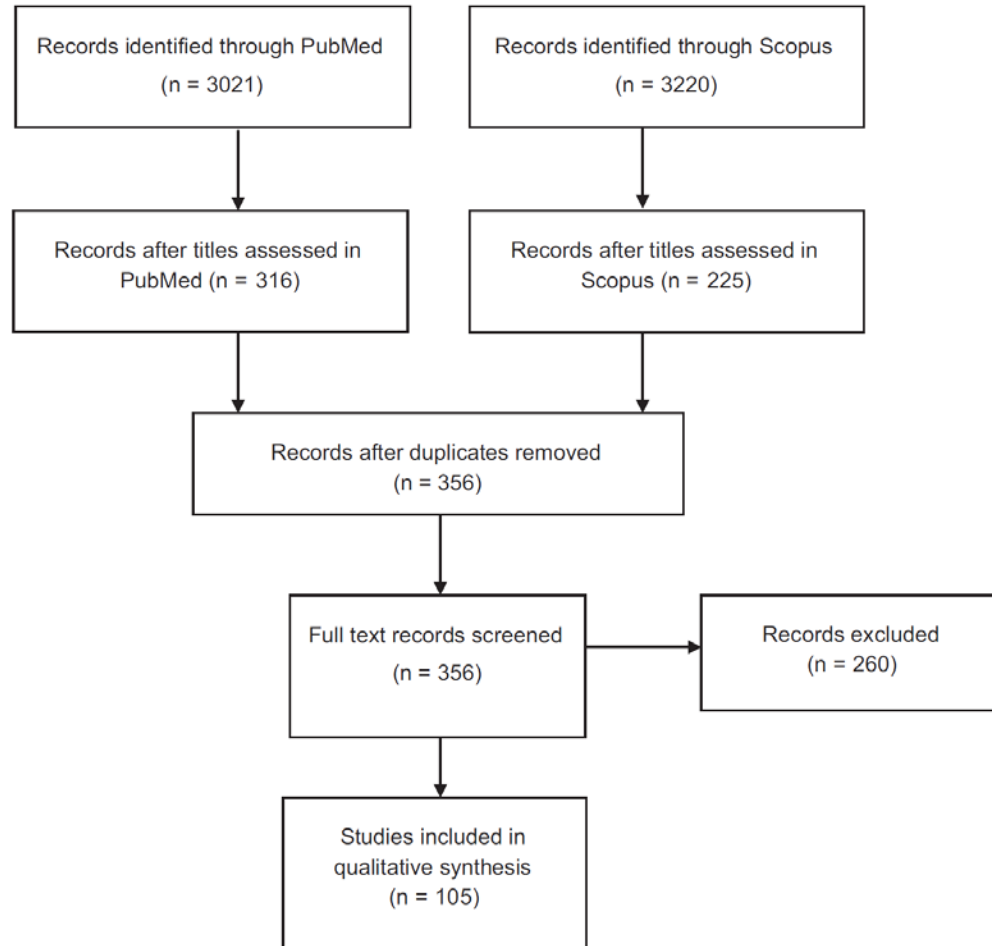
■ Harm to users (CW 46)  
■ Harm to others (CW 54)

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# Cannabis and Cognition

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# Cannabis and Cognition



Cognitive Domain	Acute <sup>b</sup>	Chronic <sup>b</sup>	Persistence With Abstinence <sup>b</sup>	Pertinent Cannabis Use Parameters
<b>Memory</b>				
Verbal learning and memory	+++	+++	+ -	Frequency; lifetime use; duration; age of onset; sex
Working memory	+ -	+ -	+ -	Frequency; lifetime use; recency; sex
Other memory function	+	+ -	-	Age of onset; frequency; recency
<b>Attention</b>				
Attention	+++	+++	+ -	Dose; age of onset; length of abstinence; withdrawal effects
Attentional bias	+	+++	NA	Craving; dependence; frequency; CBD
Psychomotor Function	+++	+	+	
<b>Executive Function</b>				
Planning, reasoning, interference control, and problem solving	+ -	+ -	+ -	Neurodevelopmental stage; age of onset; frequency
Inhibition	++	+ -	NA	Frequency; task complexity
Verbal fluency	-	+ -	+ -	
Time estimation	+ -	-	-	
Decision Making	+ -	+ -	-	Age of onset; lifetime exposure; frequency; cannabis use disorder

Cognitive Domain	Acute <sup>b</sup>	Chronic <sup>b</sup>	Persistence With Abstinence <sup>b</sup>	Pertinent Cannabis Use Parameters
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<b>Psychomotor Function</b>				
	+++	+	+	
<b>Executive Function</b>				
Planning, reasoning, interference control, and problem solving	+ -	+ -	+ -	Neurodevelopmental stage; age of onset; frequency
Inhibition	++	+ -	NA	Frequency; task complexity
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Decision Making	+ -	+ -	-	Age of onset; lifetime exposure; frequency; cannabis use disorder



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	+++	+	+	
<b>Executive Function</b>				
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<b>Attention</b>				
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Attentional bias	+	+++	NA	Craving; dependence; frequency; CBD
<b>Psychomotor Function</b>				
	+++	+	+	
<b>Executive Function</b>				
Planning, reasoning, interference control, and problem solving	+ -	+ -	+ -	Neurodevelopmental stage; age of onset; frequency
Inhibition	++	+ -	NA	Frequency; task complexity
Verbal fluency	-	+ -	+ -	
Time estimation	+ -	-	-	
<b>Decision Making</b>				
	+ -	+ -	-	Age of onset; lifetime exposure; frequency; cannabis use disorder

# Cannabis and Cognition

## ■ Limitations and considerations

❑ Inconsistent empirical findings

❑ Small study (publication) bias

❑ Measurement error

❑ Confounding variables

# Cannabis and Cognition

Neuropsychological Test	Cognitive Function
Penn Word Memory Test	Verbal Episodic Memory
Flanker Task	Inhibitory Control
Dimensional Change Card Sort	Set Shifting
Short Penn CPT	Sustained Attention
Penn Progressive Matrices	Fluid Intelligence
Delay Discounting Tasks	Impulsive Choice Preference
Picture Sequence Task	Non-verbal Episodic Memory
Pattern Completion Task	Processing Speed
List Sorting Task	Working Memory
9-hole Pegboard Task	Psychomotor Dexterity



**Participants (N=1121): 53.4%  
female, M age = 28.83**



Petker et al., under review

# Cannabis and Cognition

Neuropsychological Test	Cognitive Function	$\Delta R^2$	<i>p</i>
Penn Word Memory Test	Verbal episodic memory	--	--
Flanker Task	Inhibitory Control	--	--
Dimensional Change Card Sort	Set Shifting	--	--
Short Penn CPT	Sustained Attention	--	--
Penn Progressive Matrices	Fluid Intelligence	.010	.004
Delay Discounting Tasks	Impulsive Choice Preference	--	--
Picture Sequence Task	Non-verbal Episodic Memory	.011	.004
Pattern Completion Task	Processing Speed	.014	.001
List Sorting Task	Working Memory	--	--
9-hole Pegboard Task	Psychomotor dexterity	--	--



**Participants (N=1121): 53.4%  
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**THC+**

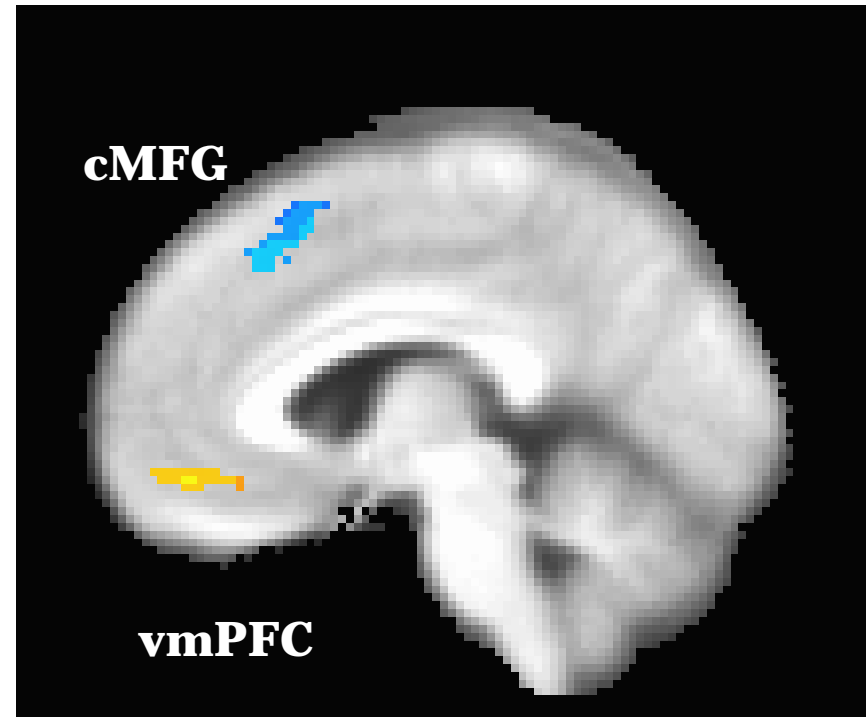
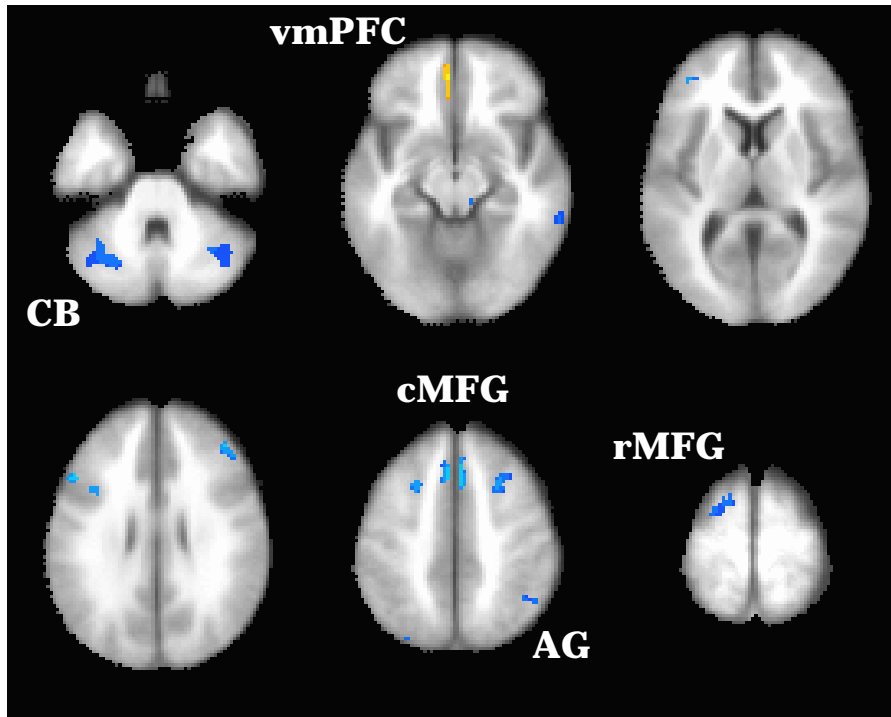
**CUD+**



Petker et al., under review

# Cannabis and Cognition

**THC+ Status and N-Back Performance**  
(covariate-adjusted  $\beta = -.08$ ,  $t = 2.58$ ,  $p = .01$ )



**Participants (N=1042):**  
**54.3% female, M age = 28.8**

*No differences based on lifetime consumption,  
CUD status, or age of first use*

# Cannabis and Cognition

Domain/Day	Former vs CTL	Active vs CTL
Total Recall		
0	<i>ns</i>	<i>p&lt;.01</i>
1	<i>ns</i>	<i>p&lt;.01</i>
7	<i>ns</i>	<i>p&lt;.001</i>
28	<i>ns</i>	<i>ns</i>
Long-term Storage		
0	<i>ns</i>	<i>p&lt;.01</i>
1	<i>ns</i>	
7	<i>ns</i>	<i>p&lt;.01</i>
28	<i>ns</i>	<i>ns</i>
Consistent Long-term Retrieval		
0	<i>ns</i>	<i>p&lt;.001</i>
1	<i>ns</i>	<i>p&lt;.001</i>
7	<i>ns</i>	<i>p&lt;.001</i>
28	<i>ns</i>	<i>ns</i>

## Post 28 Days Abstinence

Test	CTL	Former	Active
WMS total	REF	<i>ns</i>	<i>ns</i>
COWAT	REF	<i>ns</i>	<i>ns</i>
WCST	REF	<i>ns</i>	<i>ns</i>
WAIS-BD	REF	<i>ns</i>	<i>ns</i>
Stroop	REF	<i>ns</i>	<i>ns</i>
RPM	REF	<i>ns</i>	<i>ns</i>

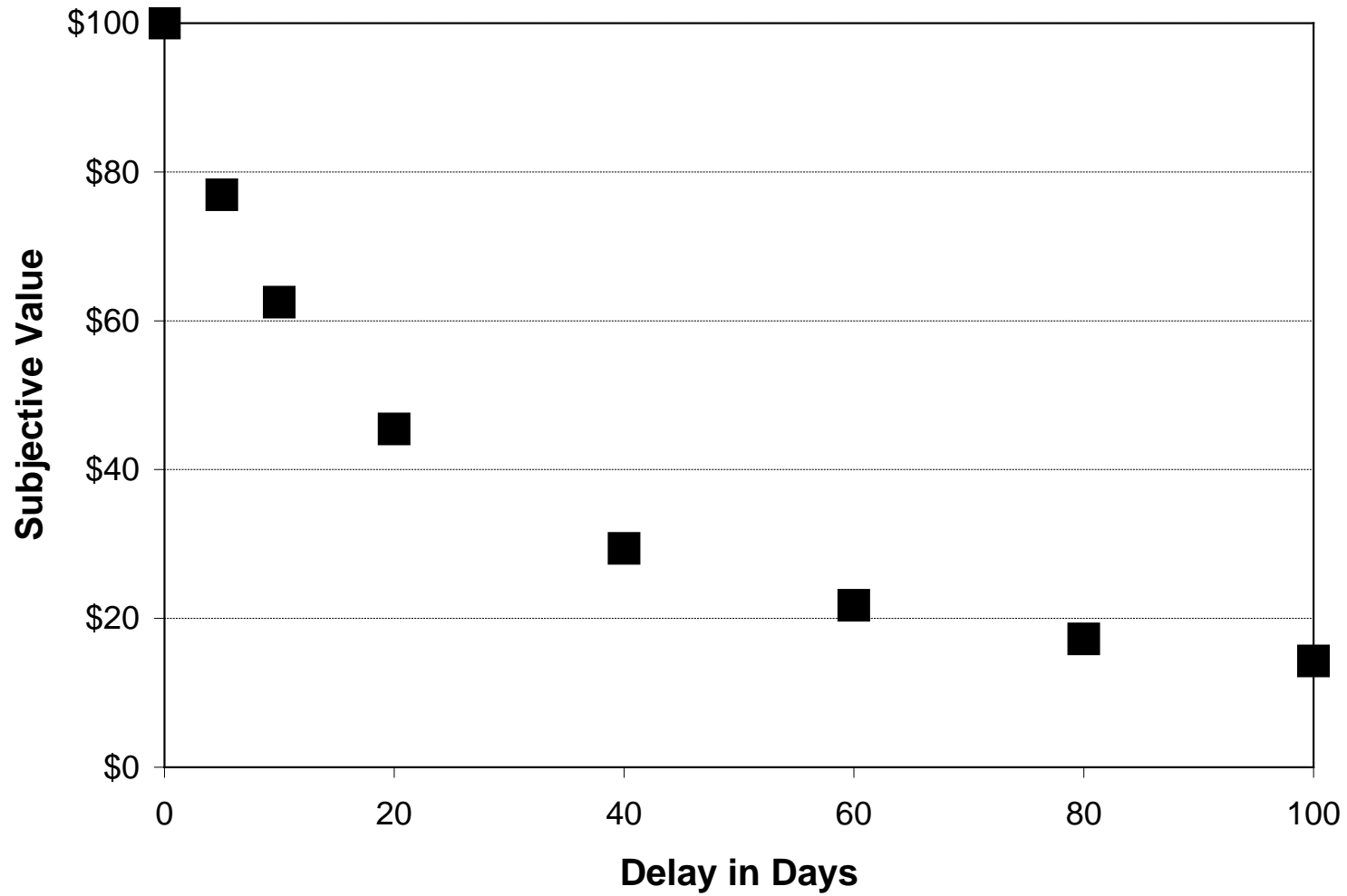
# Impulsivity as Measured by Delay Discounting

- Behavioral economic index of self-control (impulsivity)
  - ❑ Delay discounting refers to the amount that a reward is discounted based on its delay in time
  - ❑ Smaller-Sooner vs. Larger-Later Preference
- Delay Discounting Task
  - ❑ Would you rather have \$**A** today or \$**B** in **C** days?
  - ❑ Points of indifference gathered across time periods
  - ❑ Temporal Discounting Function(s):

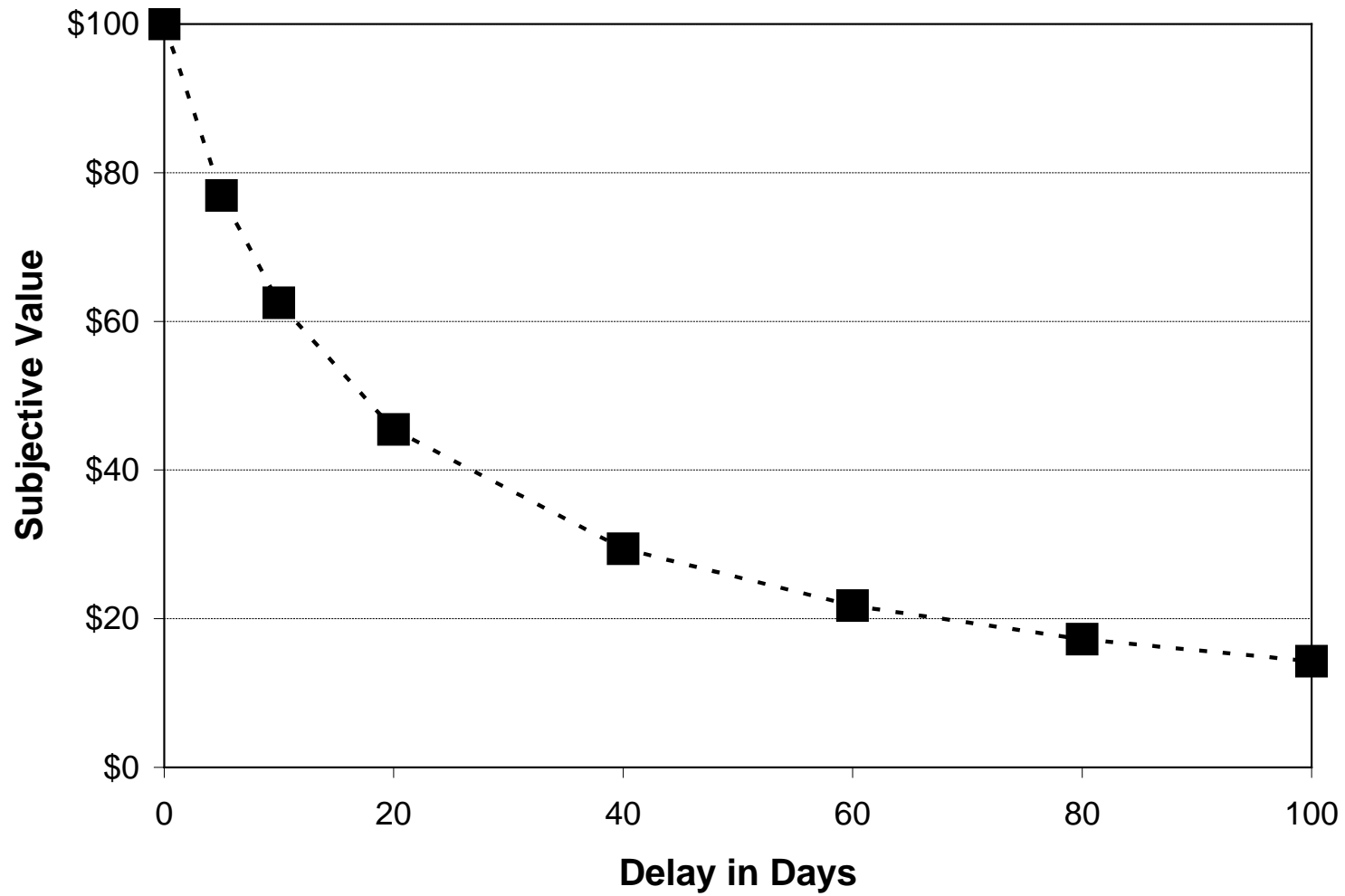
$$V = A/(1 + kD)$$



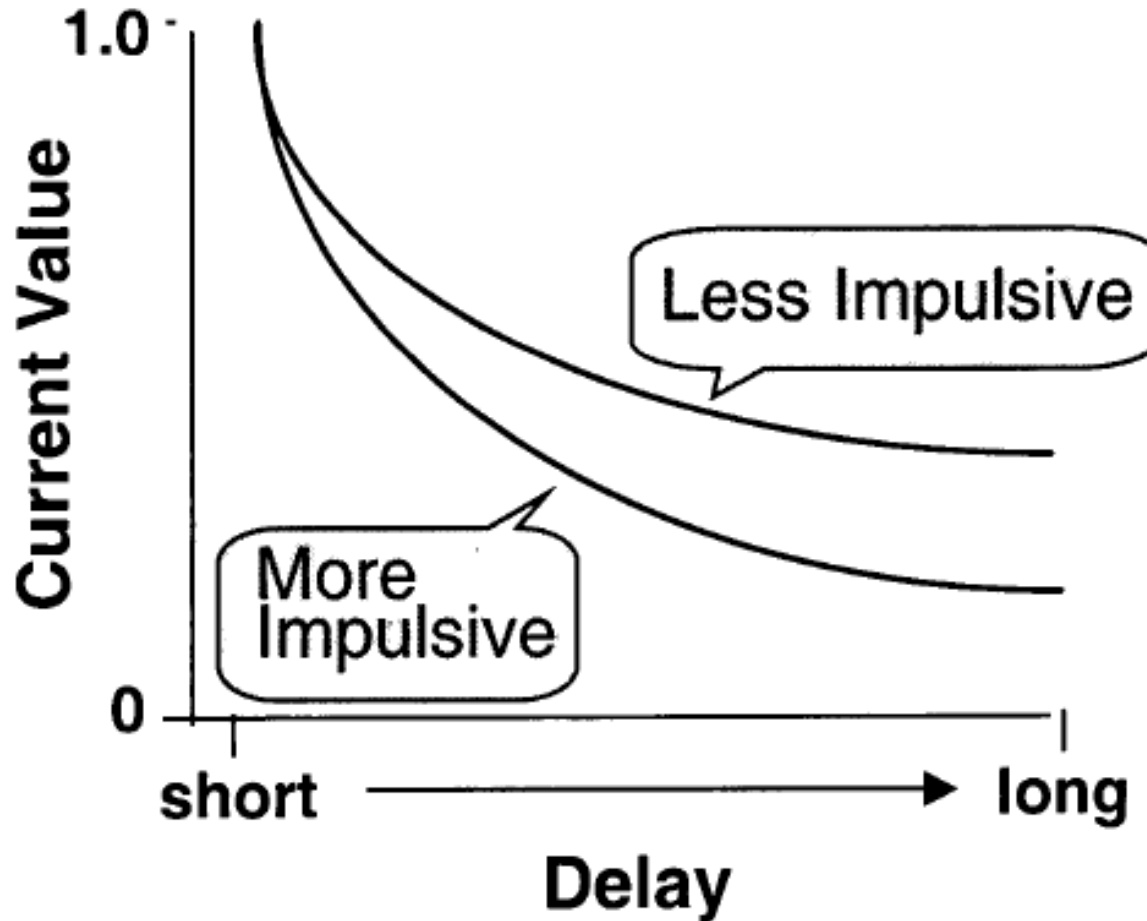
# Temporal Discounting Function



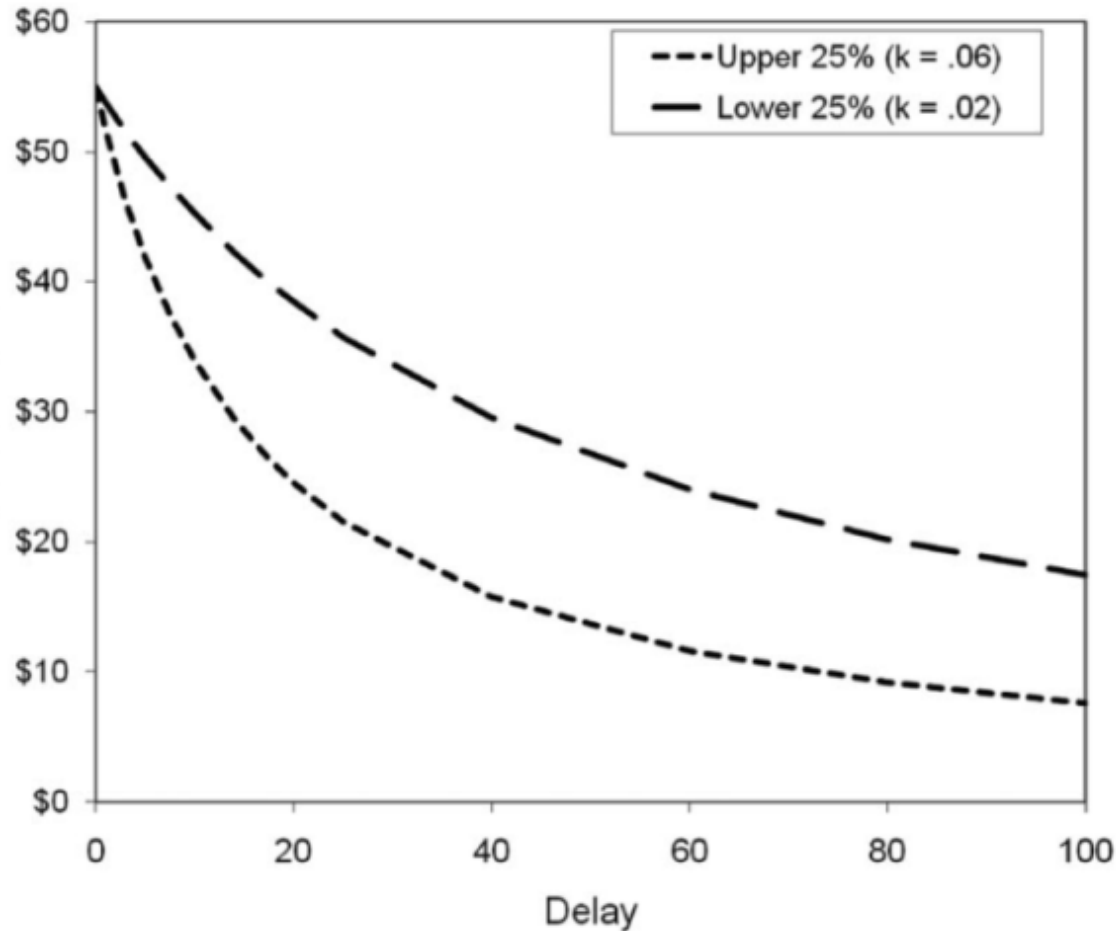
# Temporal Discounting Function



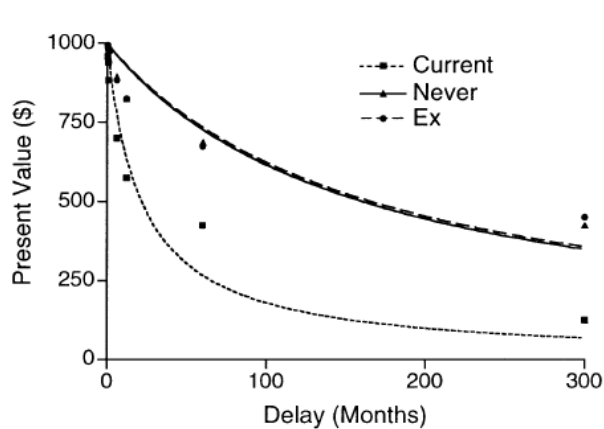
# Relative Levels of Delay Discounting



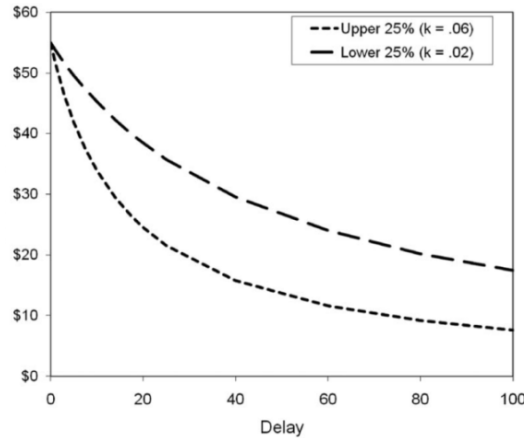
# Delay Discounting and AUD Severity



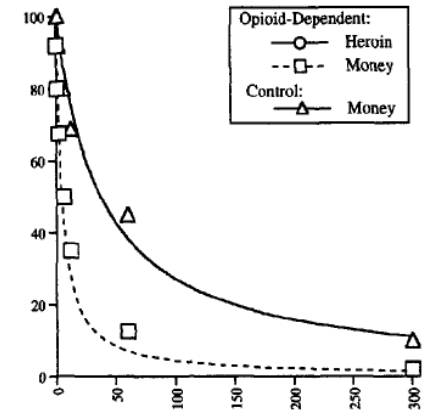
# Findings from Case-Control Designs



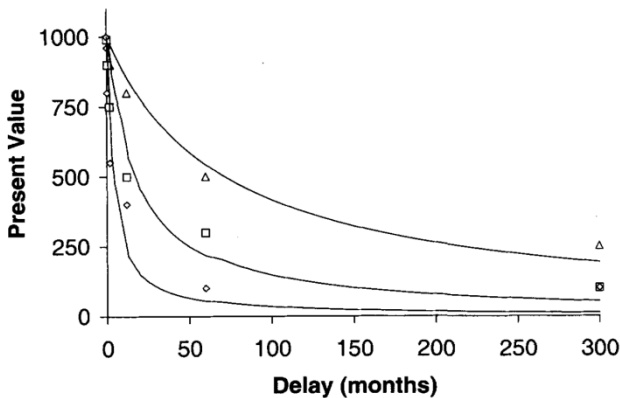
**Tobacco Use Disorder**



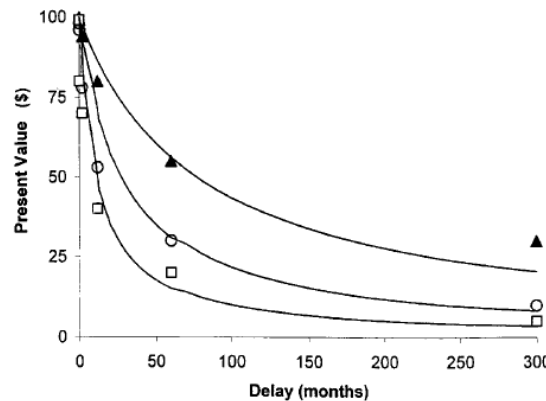
**Alcohol Use Disorder**



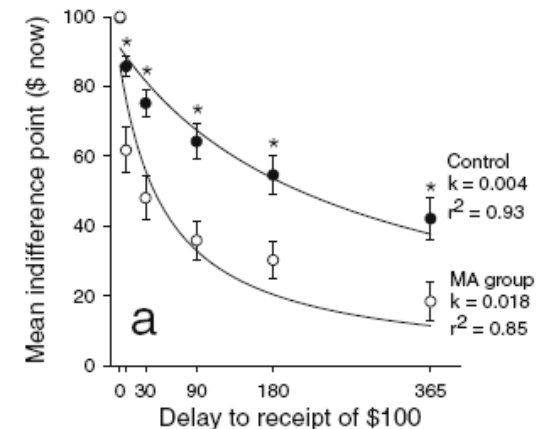
**Opioid Use Disorder**



**Gambling Disorder**

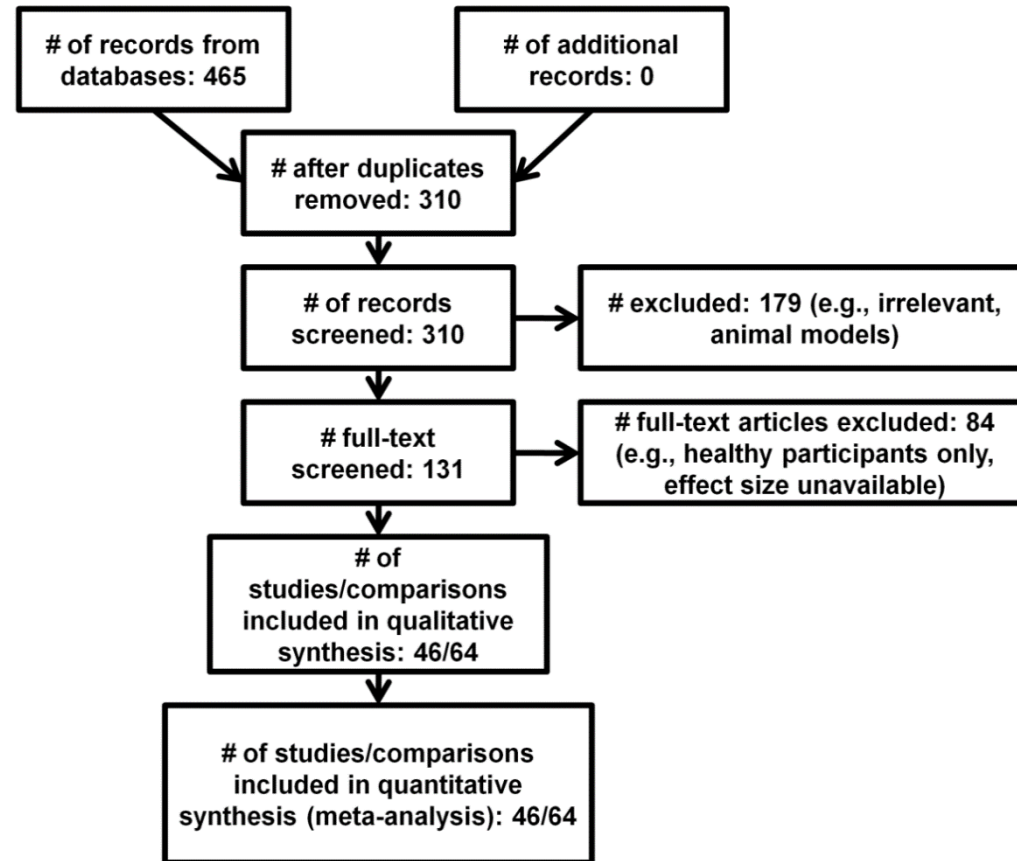


**Alcohol Use Disorder**



**Stimulant Use Disorder**

# Meta-Analysis of Case-Control Studies

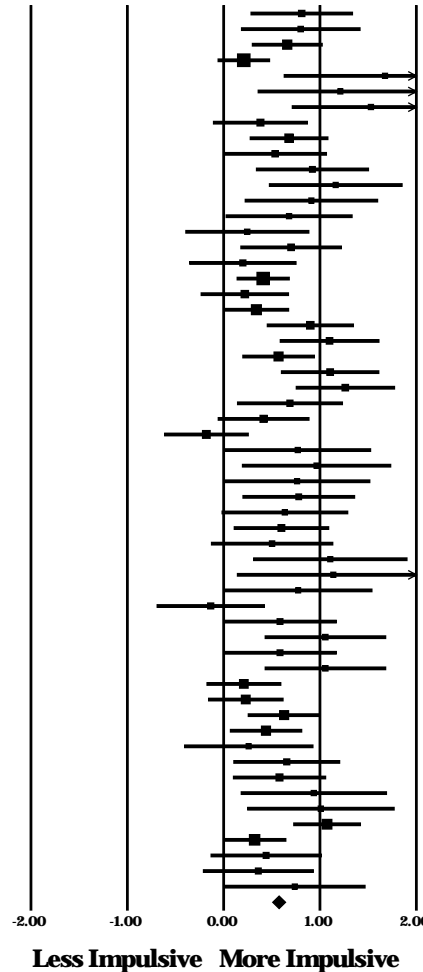


**Total N = 56,013**

# Meta-Analysis of Case-Control Studies

Model	Study name	Statistics for each study						
		Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Baker et al., 2003	0.810	0.269	0.072	0.284	1.336	3.016	0.003
	Bickel et al., 1999	0.800	0.314	0.098	0.185	1.415	2.551	0.011
	Bjork et al., 2004	0.660	0.185	0.034	0.298	1.022	3.571	0.000
	Bobova et al., 2009	0.209	0.136	0.019	-0.058	0.476	1.536	0.125
	Boettiger et al., 2007	1.675	0.534	0.285	0.629	2.721	3.138	0.002
	Coffey et al., 2003	1.212	0.435	0.190	0.358	2.065	2.783	0.005
	Dixon et al., 2003	1.529	0.417	0.174	0.713	2.346	3.670	0.000
	Field et al., 2007	0.382	0.249	0.062	-0.105	0.869	1.536	0.124
	Fields et al., 2009	0.679	0.206	0.042	0.275	1.082	3.299	0.001
	Heil et al., 2006	0.534	0.271	0.074	0.002	1.066	1.969	0.049
	Heyman & Gibb, 2006	0.922	0.297	0.088	0.340	1.503	3.106	0.002
	Hoffman et al., 2006	1.163	0.351	0.123	0.475	1.852	3.313	0.001
	Hoffman et al., 2008	0.911	0.351	0.123	0.224	1.598	2.597	0.009
	Holt et al., 2003a	0.679	0.334	0.111	0.025	1.333	2.036	0.042
	Holt et al., 2003b	0.245	0.326	0.106	-0.393	0.884	0.753	0.451
	Johnson et al., 2007	0.700	0.266	0.071	0.179	1.221	2.632	0.008
	Johnson et al., 2010	0.200	0.281	0.079	-0.351	0.751	0.711	0.477
	Jones et al., 2009	0.411	0.138	0.019	0.140	0.681	2.971	0.003
	Kirby & Petry, 2004a	0.220	0.231	0.053	-0.233	0.673	0.953	0.341
	Kirby & Petry, 2004b	0.340	0.171	0.029	0.005	0.675	1.992	0.046
	Kirby & Petry, 2004c	0.900	0.228	0.052	0.454	1.346	3.951	0.000
	Kirby & Petry, 2004d	1.100	0.261	0.068	0.588	1.612	4.209	0.000
	Kirby et al., 1999	0.570	0.190	0.036	0.199	0.941	3.007	0.003
	Ledgerwood et al., 2009a	1.105	0.258	0.066	0.600	1.610	4.292	0.000
	Ledgerwood et al., 2009b	1.263	0.260	0.068	0.753	1.773	4.854	0.000
	MacKillop et al., 2006a	0.688	0.278	0.077	0.144	1.232	2.480	0.013
	MacKillop et al., 2006b	0.415	0.240	0.058	-0.056	0.885	1.728	0.084
	MacKillop et al., 2007	-0.179	0.221	0.049	-0.613	0.255	-0.808	0.419
	MacKillop et al., 2010a	0.770	0.385	0.148	0.015	1.525	2.000	0.045
	MacKillop et al., 2010b	0.965	0.393	0.154	0.195	1.734	2.457	0.014
	MacKillop et al., 2010c	0.763	0.385	0.148	0.009	1.517	1.982	0.047
	Madden et al., 1997	0.780	0.295	0.087	0.201	1.359	2.640	0.008
	Madden et al., 2009	0.635	0.333	0.111	-0.016	1.287	1.911	0.056
	Melanko et al., 2009	0.600	0.250	0.062	0.110	1.089	2.401	0.016
	Mitchell et al., 1999	0.503	0.321	0.103	-0.127	1.132	1.566	0.117
	Mitchell et al., 2005	1.107	0.406	0.165	0.311	1.902	2.727	0.006
	Mitchell et al., 2007	1.139	0.508	0.258	0.143	2.135	2.241	0.025
	Montrosso et al., 2007	0.774	0.390	0.152	0.008	1.539	1.981	0.048
	Ohnura et al., 2005	-0.134	0.284	0.081	-0.691	0.423	-0.471	0.638
	Petry & Cassarella, 1999a	0.585	0.297	0.088	0.003	1.168	1.971	0.049
	Petry & Cassarella, 1999b	1.056	0.319	0.102	0.431	1.682	3.309	0.001
	Petry & Cassarella, 1999c	0.585	0.297	0.088	0.003	1.168	1.971	0.049
	Petry & Cassarella, 1999d	1.056	0.319	0.102	0.431	1.682	3.309	0.001
	Petry, 2002a	0.210	0.195	0.038	-0.173	0.593	1.075	0.283
	Petry, 2002b	0.230	0.197	0.039	-0.156	0.616	1.168	0.243
	Petry, 2003a	0.628	0.191	0.036	0.255	1.001	3.296	0.001
	Petry, 2003b	0.440	0.189	0.036	0.070	0.809	2.331	0.020
	Reynolds et al., 2003	0.260	0.340	0.115	-0.405	0.926	0.766	0.444
	Reynolds et al., 2004	0.655	0.280	0.078	0.106	1.204	2.339	0.019
	Reynolds et al., 2007	0.580	0.244	0.060	0.101	1.058	2.375	0.018
	Reynolds et al., 2009	0.936	0.385	0.148	0.182	1.690	2.434	0.015
	Reynolds, 2006	1.009	0.388	0.150	0.249	1.769	2.603	0.009
	Sweitzer et al., 2008a	1.073	0.177	0.031	0.727	1.419	6.078	0.000
	Sweitzer et al., 2008b	0.322	0.165	0.027	-0.001	0.645	1.956	0.050
	Vuchinich & Simpson, 1998a	0.442	0.292	0.085	-0.131	1.015	1.512	0.130
	Vuchinich & Simpson, 1998b	0.361	0.291	0.085	-0.210	0.931	1.239	0.215
	Vuchinich & Simpson, 1998c	0.739	0.371	0.138	0.011	1.467	1.989	0.047
	Fixed	0.575	0.033	0.001	0.509	0.641	17.174	0.000

Std diff in means and 95% CI



**Overall  $d = .49, p < 10^{-8}$**

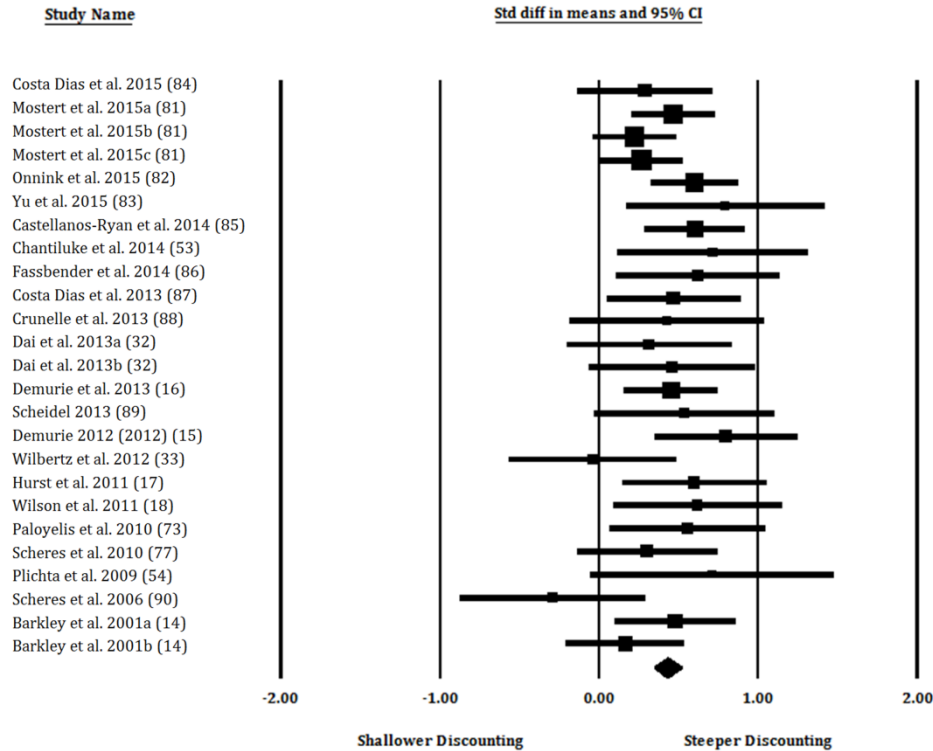
**Clinical  $d = .67, p < 10^{-5}$**

**Subclinical  $d = .46, p < 10^{-10}$**

**All individual addictive behaviors significant except cannabis**

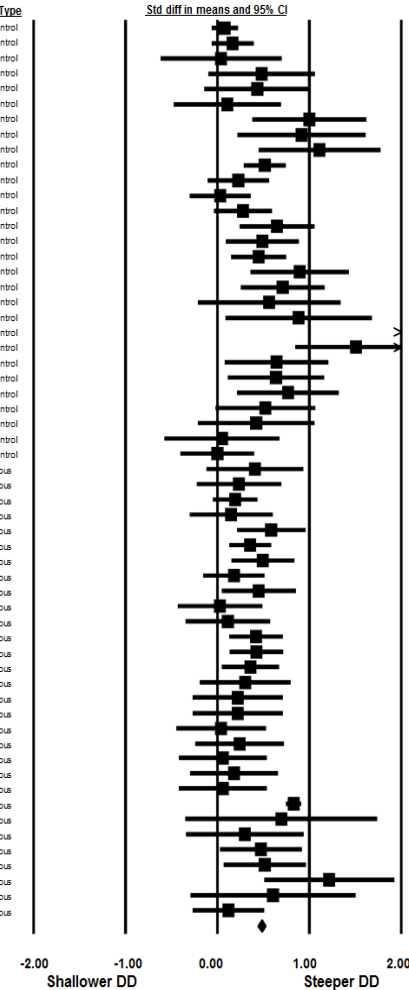
**Minimal evidence of publication bias**

# Delay Discounting, ADHD, and Obesity



**$d = .43$**   
 **$p < 10^{-15}$**   
 **$N = 3913$**

Study Name	Study Type
Bickel et al. 2014	Case-Control
Bongers et al. 2015	Case-Control
Buono et al. 2015	Case-Control
Daniel et al. 2013a	Case-Control
Daniel et al. 2013b	Case-Control
Eisenstein et al. 2015	Case-Control
Feda et al. 2015	Case-Control
Fields et al. 2011	Case-Control
Fields et al. 2013	Case-Control
Garza et al. 2015	Case-Control
Hendrickson & Rasmussen 2013a	Case-Control
Hendrickson & Rasmussen 2013b	Case-Control
Hsu & Vlaev 2014	Case-Control
Jamulowicz et al. 2014	Case-Control
Kulendran et al. 2014	Case-Control
Lavryer et al. 2015	Case-Control
Manwaring et al. 2011	Case-Control
Mole et al. 2014	Case-Control
Rasmussen et al. 2010a	Case-Control
Rasmussen et al. 2010b	Case-Control
Schiff et al. 2015a	Case-Control
Schiff et al. 2015b	Case-Control
Simmark et al. 2015	Case-Control
Verdejo-Garcia et al. 2010	Case-Control
Weller et al. 2008a	Case-Control
Weller et al. 2008b	Case-Control
Weller et al. 2008c	Case-Control
Weller et al. 2008d	Case-Control
Yeomans et al. 2008	Case-Control
Appelhans et al. 2011	Continuous
Appelhans et al. 2012	Continuous
Borghans & Golsteyn 2008a	Continuous
Brace & Yeomans 2015	Continuous
Chabris et al. 2008a	Continuous
Chabris et al. 2008b	Continuous
Dassen et al. 2015a	Continuous
Dassen et al. 2015b	Continuous
Duwoerth et al. 2010	Continuous
Epstein et al. 2009a	Continuous
Epstein et al. 2009b	Continuous
Epstein et al. 2014a	Continuous
Epstein et al. 2014b	Continuous
Garza et al. 2013	Continuous
Hendrickson et al. 2015a	Continuous
Hendrickson et al. 2015b	Continuous
Hendrickson et al. 2015c	Continuous
Hendrickson et al. 2015d	Continuous
Hendrickson et al. 2015e	Continuous
Hendrickson et al. 2015f	Continuous
Hendrickson et al. 2015g	Continuous
Hendrickson et al. 2015h	Continuous
Ieda et al. 2010	Continuous
Kishinevsky et al. 2012	Continuous
Lim & Bruce 2015	Continuous
Lu et al. 2014a	Continuous
Lu et al. 2014b	Continuous
Schiff et al. 2015c	Continuous
Slovic et al. 2013	Continuous
Slovic et al. 2014	Continuous
OVERALL EFFECT	



**$d = .43$**   
 **$p < 10^{-14}$**   
 **$N = 10,278$**

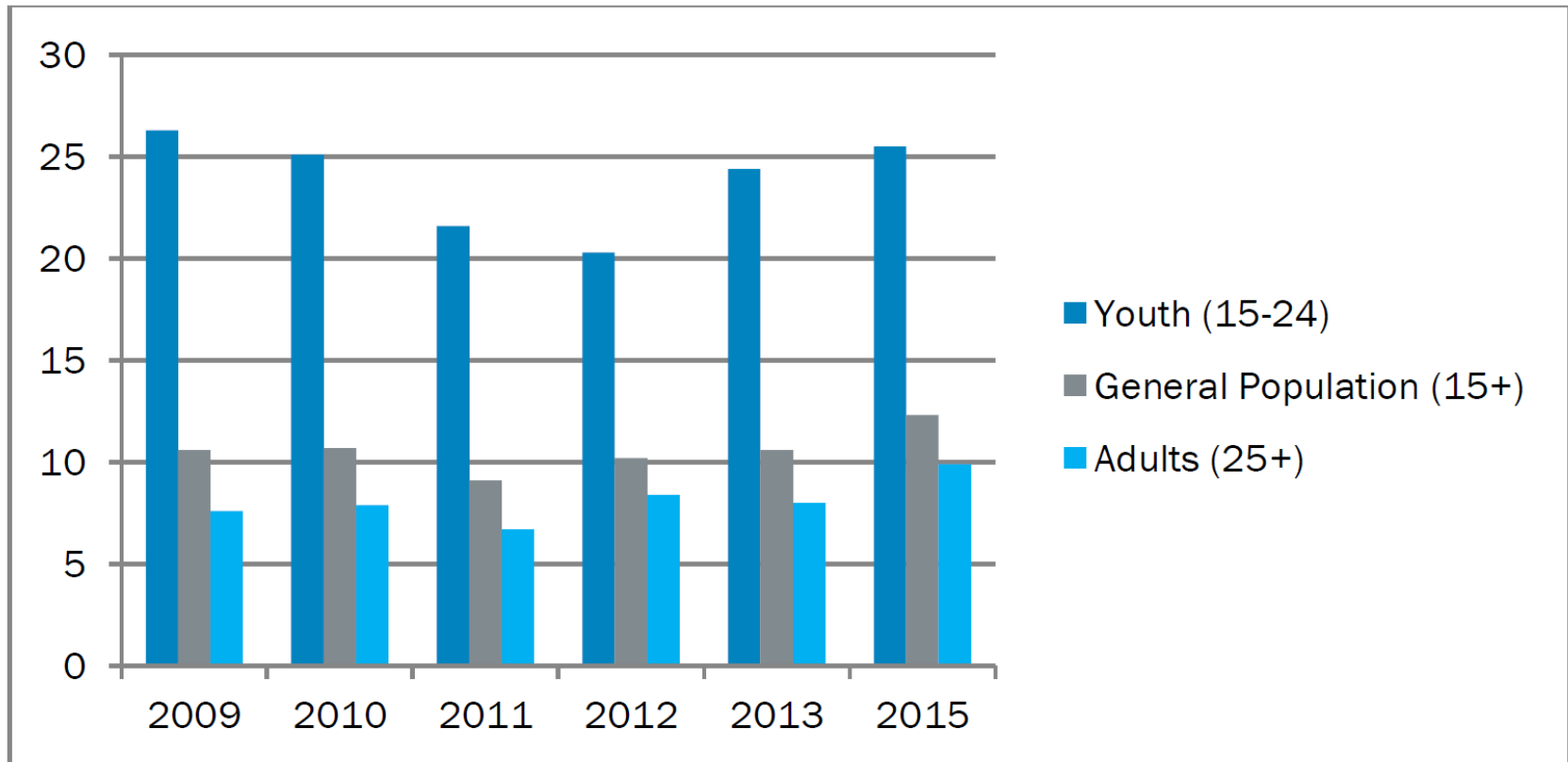


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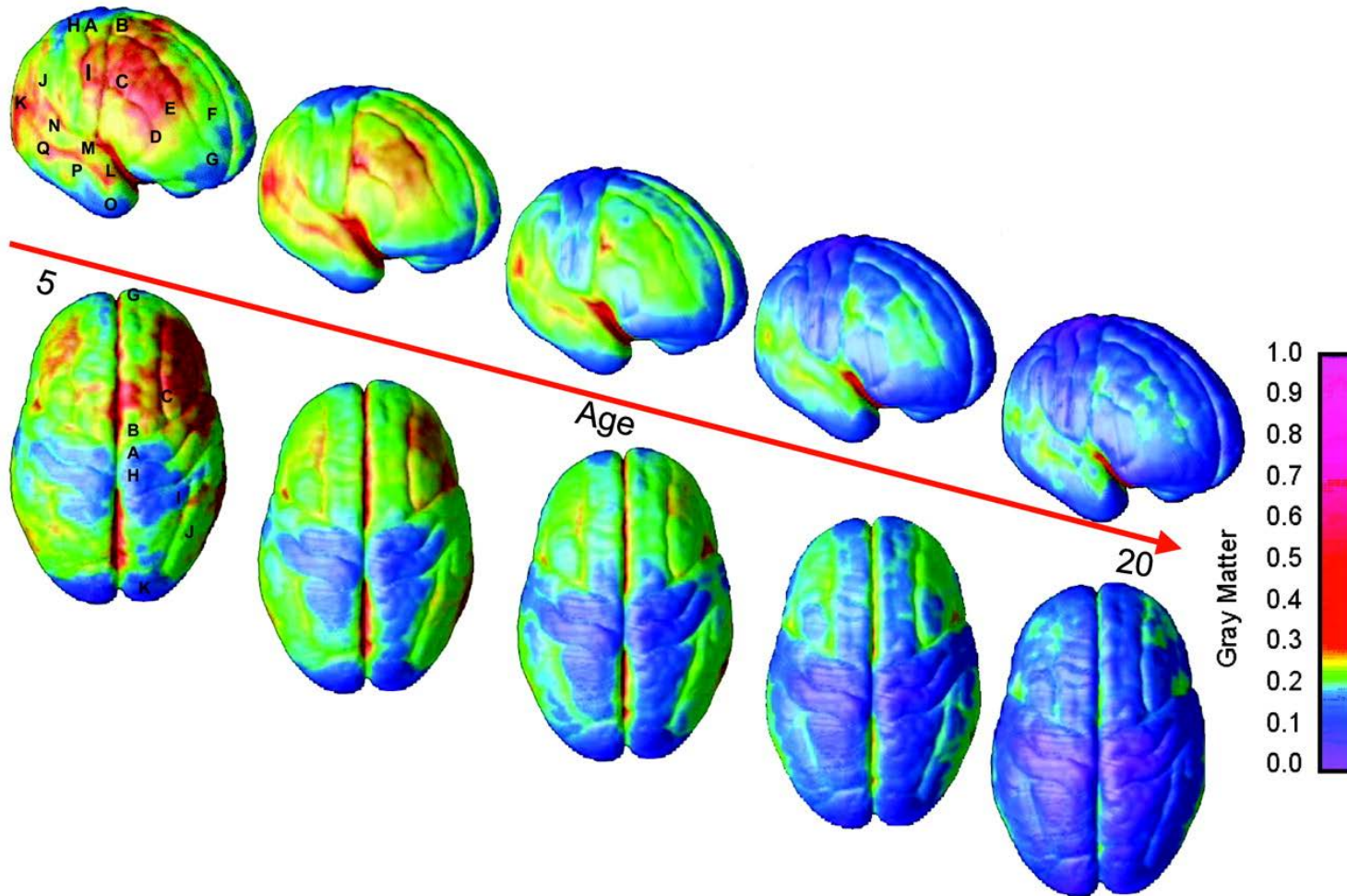
# Developmental Considerations

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# Developmental Considerations



# Developmental Considerations



# Developmental Considerations



## Persistent cannabis users show neuropsychological decline from childhood to midlife

Madeline H. Meier<sup>a,b,1</sup>, Avshalom Caspi<sup>a,b,c,d,e</sup>, Antony Ambler<sup>e,f</sup>, HonaLee Harrington<sup>b,c,d</sup>, Renate Houts<sup>b,c,d</sup>, Richard S. E. Keefe<sup>d</sup>, Kay McDonald<sup>f</sup>, Aimee Ward<sup>f</sup>, Richie Poulton<sup>f</sup>, and Terrie E. Moffitt<sup>a,b,c,d,e</sup>

<sup>a</sup>Duke Transdisciplinary Prevention Research Center, Center for Child and Family Policy, <sup>b</sup>Department of Psychology and Neuroscience, and <sup>1</sup>Institute for Genome Sciences and Policy, Duke University, Durham, NC 27708; <sup>c</sup>Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC 27710; <sup>d</sup>Social, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, King's College London, London SE5 8AF, United Kingdom; and <sup>e</sup>Dunedin Multidisciplinary Health and Development Research Unit, Department of Preventive and Social Medicine, School of Medicine, University of Otago, Dunedin 9054, New Zealand

Edited by Michael I. Posner, University of Oregon, Eugene, OR, and approved July 30, 2012 (received for review April 23, 2012)

IQ test/subtest	Never used, never diagnosed, <i>n</i> = 242	Used, never diagnosed, <i>n</i> = 479	1 diagnosis, <i>n</i> = 80	2 diagnoses, <i>n</i> = 35	3+ diagnoses, <i>n</i> = 38	Linear trend <i>t</i> test*	<i>P</i>
Full-scale IQ	0.05	-0.07	-0.11	-0.17	-0.38	-4.45	<0.0001
Verbal IQ	0.02	-0.05	-0.13	-0.19	-0.31	-4.15	<0.0001
Information subtest	0.05	-0.08	0.02	-0.25	-0.15	-2.40	0.0168
Similarities subtest	0.03	-0.05	-0.03	-0.19	-0.44	-2.78	0.0056
Vocabulary subtest	0.07	-0.05	-0.16	-0.16	-0.45	-3.67	0.0003
Arithmetic subtest	-0.05	-0.07	-0.05	0.00	0.06	-0.73	0.47
Performance IQ	0.08	-0.08	-0.09	-0.08	-0.42	-2.84	0.0046
Digit symbol coding subtest	0.15	-0.09	-0.17	-0.23	-0.62	-5.60	<0.0001
Block design subtest	-0.03	-0.07	-0.01	-0.11	0.02	-0.55	0.58
Picture completion subtest	-0.01	-0.08	0.08	0.05	0.15	1.18	0.24

# Developmental Considerations



## Persistent cannabis users show neuropsychological decline from childhood to midlife

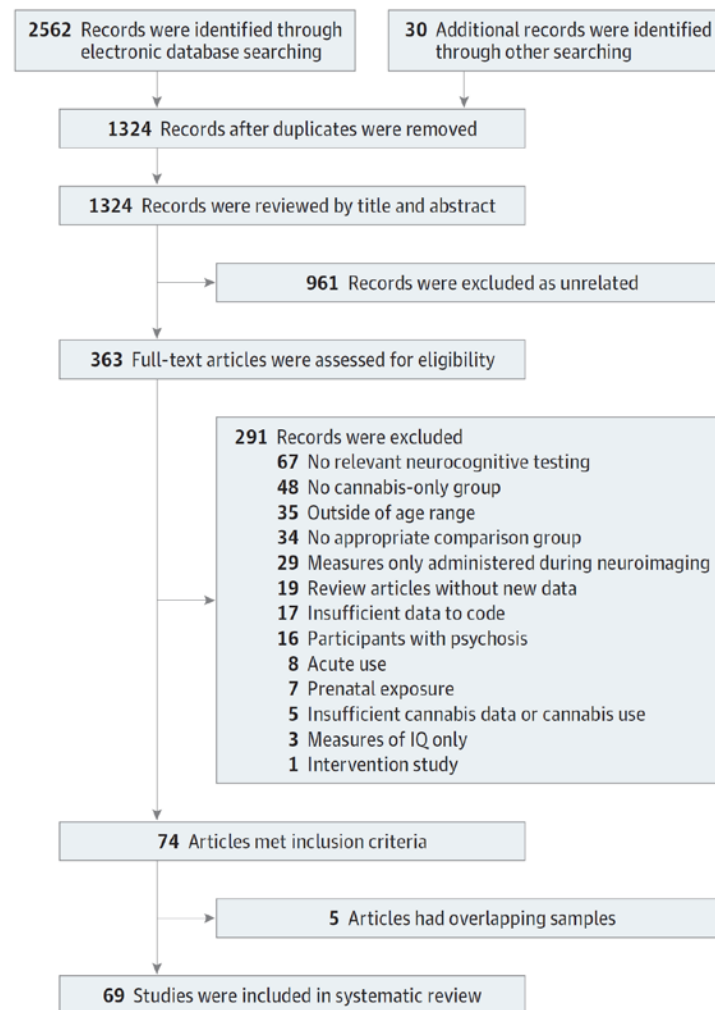
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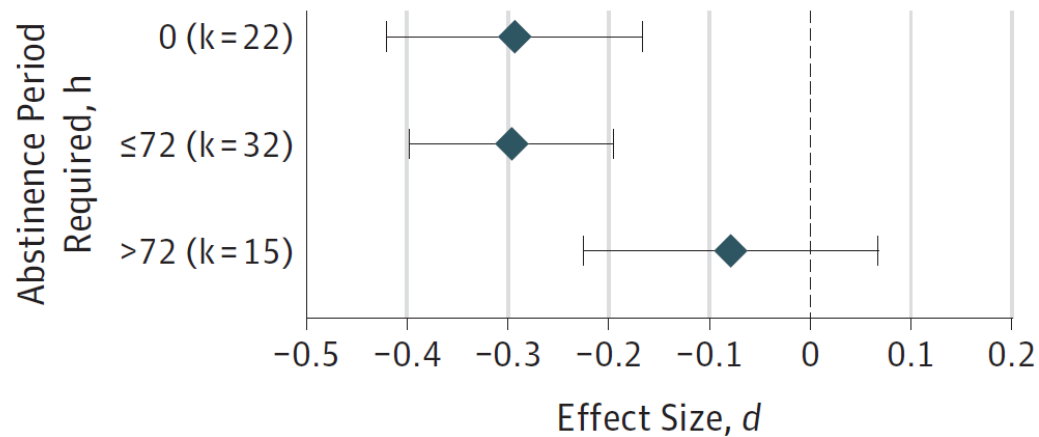
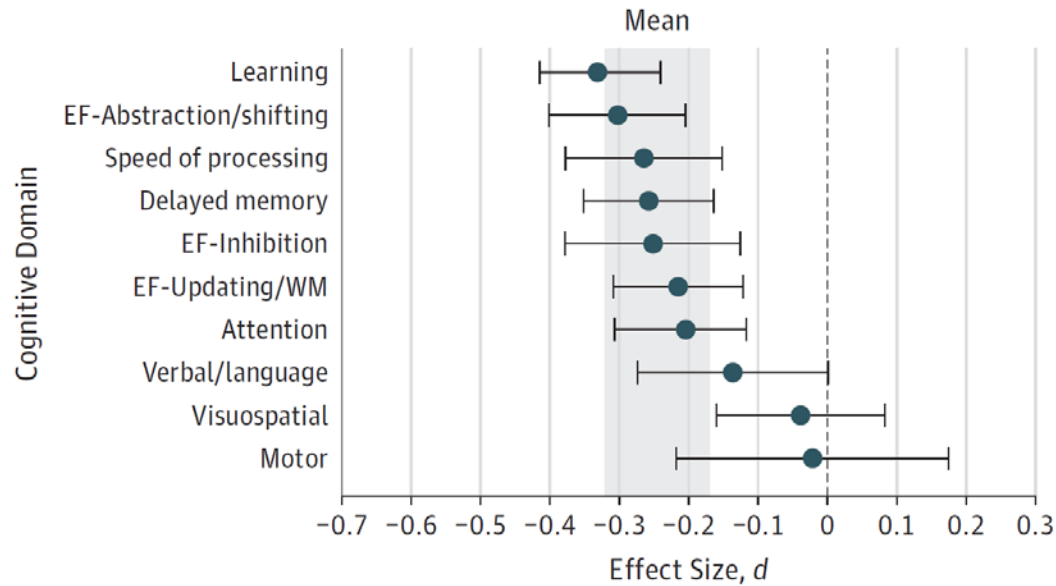
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Performance IQ	0.08	-0.08	-0.09	-0.08	-0.42	-2.84	0.0046
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Block design subtest	-0.03	-0.07	-0.01	-0.11	0.02	-0.55	0.58
Picture completion subtest	-0.01	-0.08	0.08	0.05	0.15	1.18	0.24

# Developmental Considerations



# Developmental Considerations



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# Practical Recommendations & Conclusions

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# Assessment Resources

- Cannabis Use Questionnaire
- Cannabis Use Disorder Identification Test - Revised (CUDIT-R)
- Marijuana Motives Questionnaire
- Reasons for Using Medical Marijuana
- Urine Drug Screens

# Conclusions

- Cannabis is a complex, widely-used drug with acute and chronic effects on cognition that are highly relevant to neuropsychologists
- Acute effects
  - Psychomotor impairment
  - Diminished behavioral inhibition
  - Reduced attention
  - Impaired verbal learning and memory

# Conclusions

- Cannabis is a complex, widely-used drug with acute and chronic effects on cognition that are highly relevant to neuropsychologists
- Chronic/residual effects
  - Reduced attention
  - Impaired verbal learning and memory
  - Psychomotor impairment
- \*Closely linked to recent use\*

# Conclusions

- Cannabis is a complex, widely-used drug with acute and chronic effects on cognition that are highly relevant to neuropsychologists
- Long-term effects post-abstinence
  - Evidence of decrements in very heavy users
  - Lower overall IQ
  - Ambiguities
    - Less consistent findings
    - Dose-decrement relationship unclear
    - Small effect sizes

# Conclusions

- Cannabis is a complex, widely-used drug with acute and chronic effects on cognition that are highly relevant to neuropsychologists
- Developmental considerations
  - Differential impact is a highly credible hypothesis
  - Inconsistent findings, but reasonable to err on the side of caution



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CANNABIS RESEARCH

<https://cannabisresearch.mcmaster.ca>

# Evidence-based Information



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**Synopses of high impact research publications from clinical and research experts studying cannabis.**



## Evidence Briefs

**Consolidated overviews of the state of medicinal cannabis across various clinical and research areas.**



## Evidence Syntheses

**'Deep dive' explorations of topics related to medicinal cannabis via the McMaster Health Forum**

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<https://www.drugabuse.gov>



Canadian Centre  
**on Substance Abuse**

Centre canadien de lutte  
**contre les toxicomanies**

<http://www.ccdus.ca>



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# Thank You

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