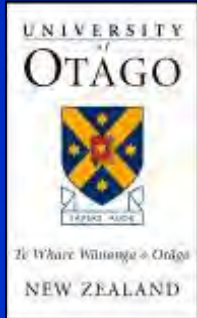


Health consequences of cannabis use

Professor Richie Poulton
**Director, Dunedin Multidisciplinary Health
and Development Research Unit;**
**Co-Director, National Centre for Lifecourse
Research**



Department of Preventive & Social Medicine
Dunedin School of Medicine
University of Otago
Dunedin, New Zealand



Today's talk is about cannabis use and...

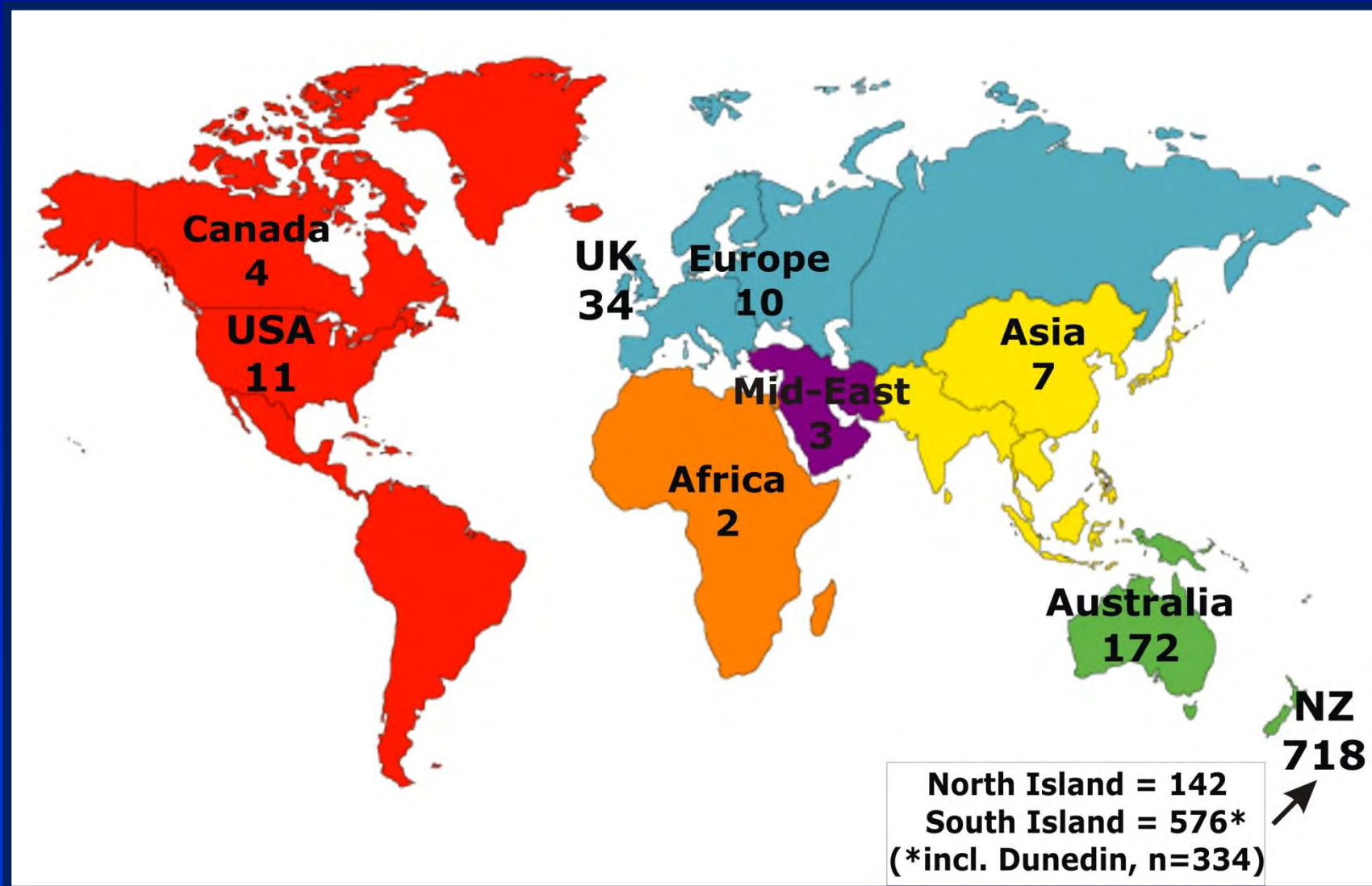
- **Psychosis**
- **Respiratory function**
- **Periodontal disease**
- **Cognition**

Retention in the Dunedin Study

Age	Year	Number	Percent*
Birth	1972-73		
3	1975-76	1037	100%
5	1977-78	991	96%
7	1979-80	954	92%
9	1981-82	955	92%
11	1983-84	925	90%
13	1985-86	850	82%
15	1987-88	976	95%
18	1990-91	993	97%
21	1993-94	992	97%
26	1998-99	980	96%
32	2004-05	972	96%
38	2010-12	961	95%

* Percentage seen of those who were eligible (i.e. alive) at each age

Location of Study Members seen at age 38



Current research activities include studies of:

- **SES inequalities - selection v causation**
- **Pathways to employment**
- **Personality continuities across the life-course**
- **Antisocial behaviour and criminality**
- **Long-term consequences of childhood adversity**
- **Maori health/cultural identity**
- **Cognition and neuropsychology**
- **Family health history study**
- **Mental health (including substance abuse)**
- **Intimate relationships and domestic violence**
- **Oral health**
- **Sexual & reproductive health**
- **Cardiovascular risk factors**
- **Retinal imaging and endothelial function**
- **Respiratory health**
- **Next generation studies (age 3 and age 15 years)**

Current research activities (contd)

- **Blood based studies**

- **Chlamydia trachomatis**
- **Herpes immunity**
- **Cardiovascular disease risk factors**
- **Inflammatory biomarkers**

- **Genetic studies**

- **Mental health phenotypes**
- **Asthma/allergy**
- **Cardiovascular risk factors**
- **Periodontal disease**

- **Methodological studies**

- **Comparison of Dunedin sample with national data**
- **Attrition analyses**

Cannabis consequences



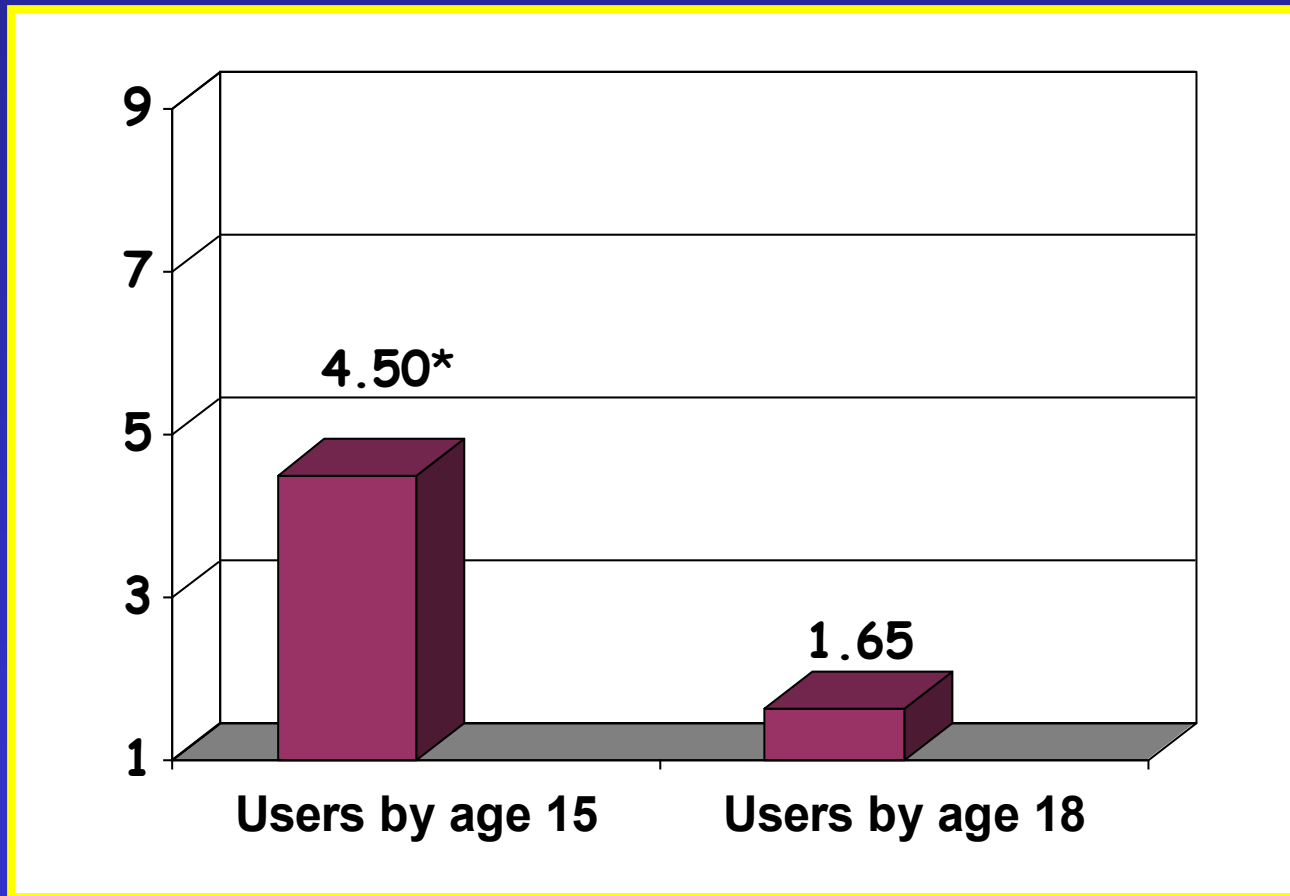


Arseneault, L., Cannon, M., Poulton, R., Murray, R. M., Caspi, A., and Moffitt, T. E. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *BMJ*, 2002, 325(7374): 1212-1213.

Caspi, A., Moffitt, T. E., Cannon, M., McClay, J., Murray, R. M., Harrington, H. L., Taylor, A., Arseneault, L., Williams, B. S., Braithwaite, A., Poulton, R., and Craig, I. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the COMT gene: Longitudinal evidence of a gene x environment interaction. *Biological Psychiatry*, 2005, 57: 1117-1127.

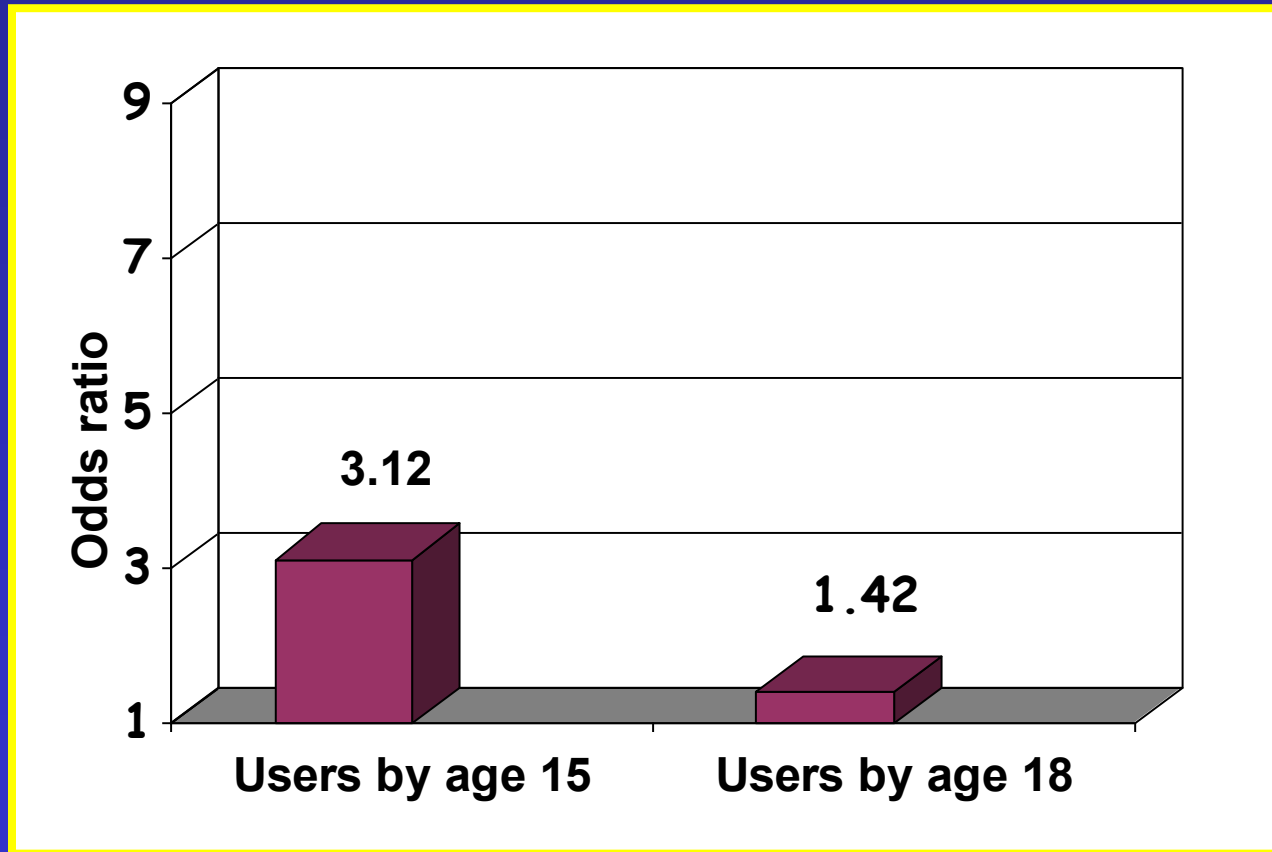
Fergusson, D. M., Poulton, R., Smith, P. F., and Boden, J. M. Cannabis and psychosis: a summary and synthesis of the evidence. *BMJ*, 2006, 332(Jan): 172-175.

Predicting Schizophreniform Disorder at age 26



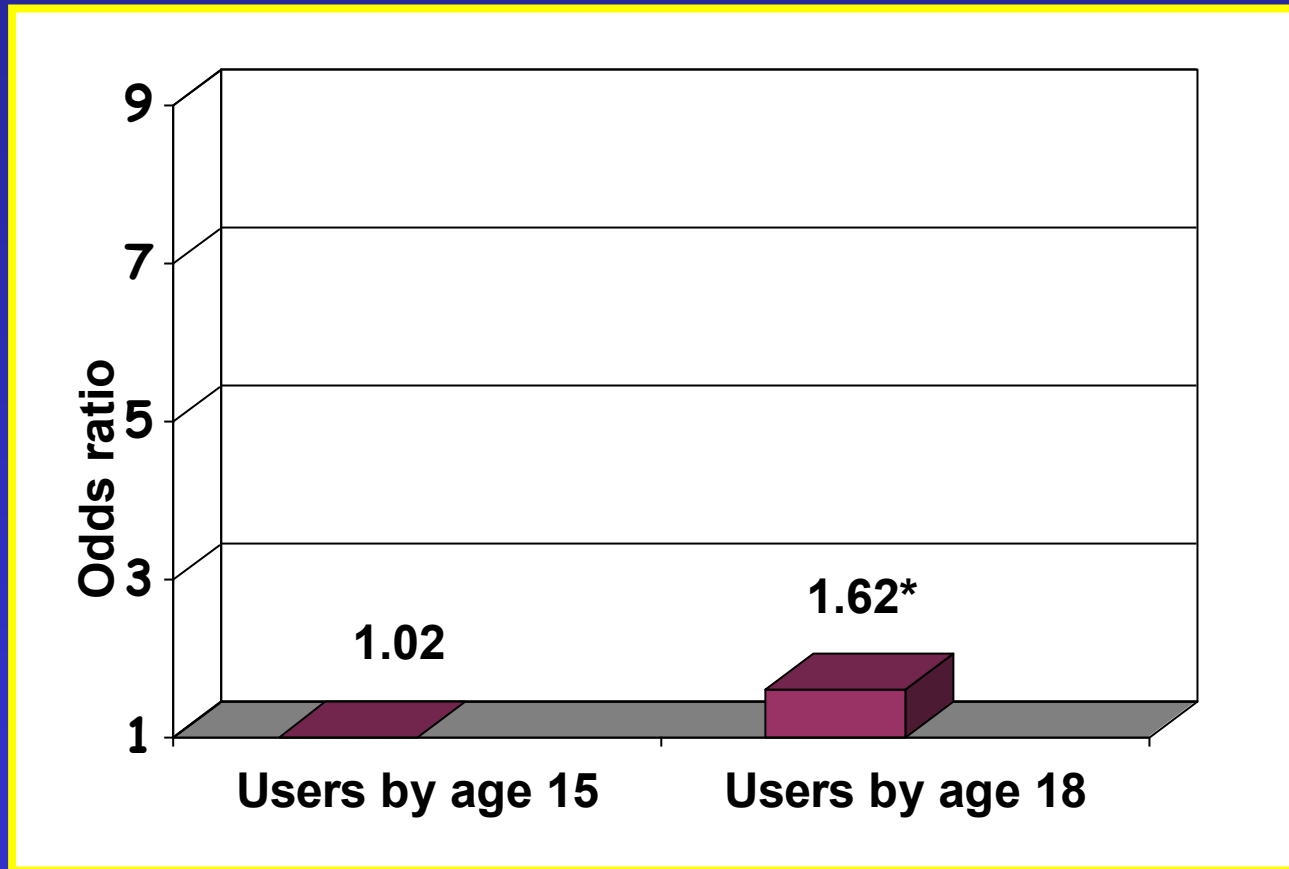
Arseneault et al, BMJ (2002)

Predicting Schizophreniform Disorder at age 26, controlling for psychotic symptoms at age 11

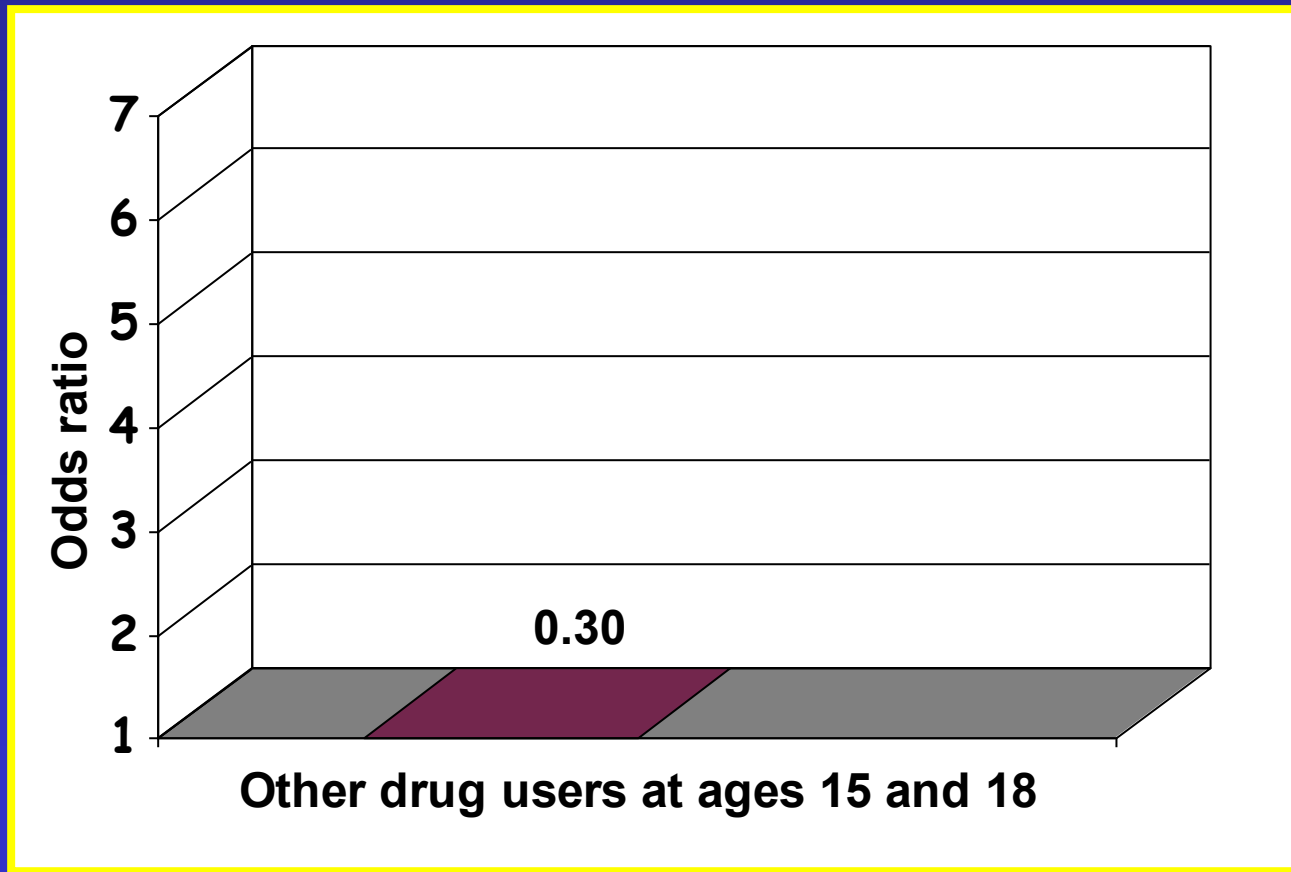


Arseneault et al, BMJ (2002)

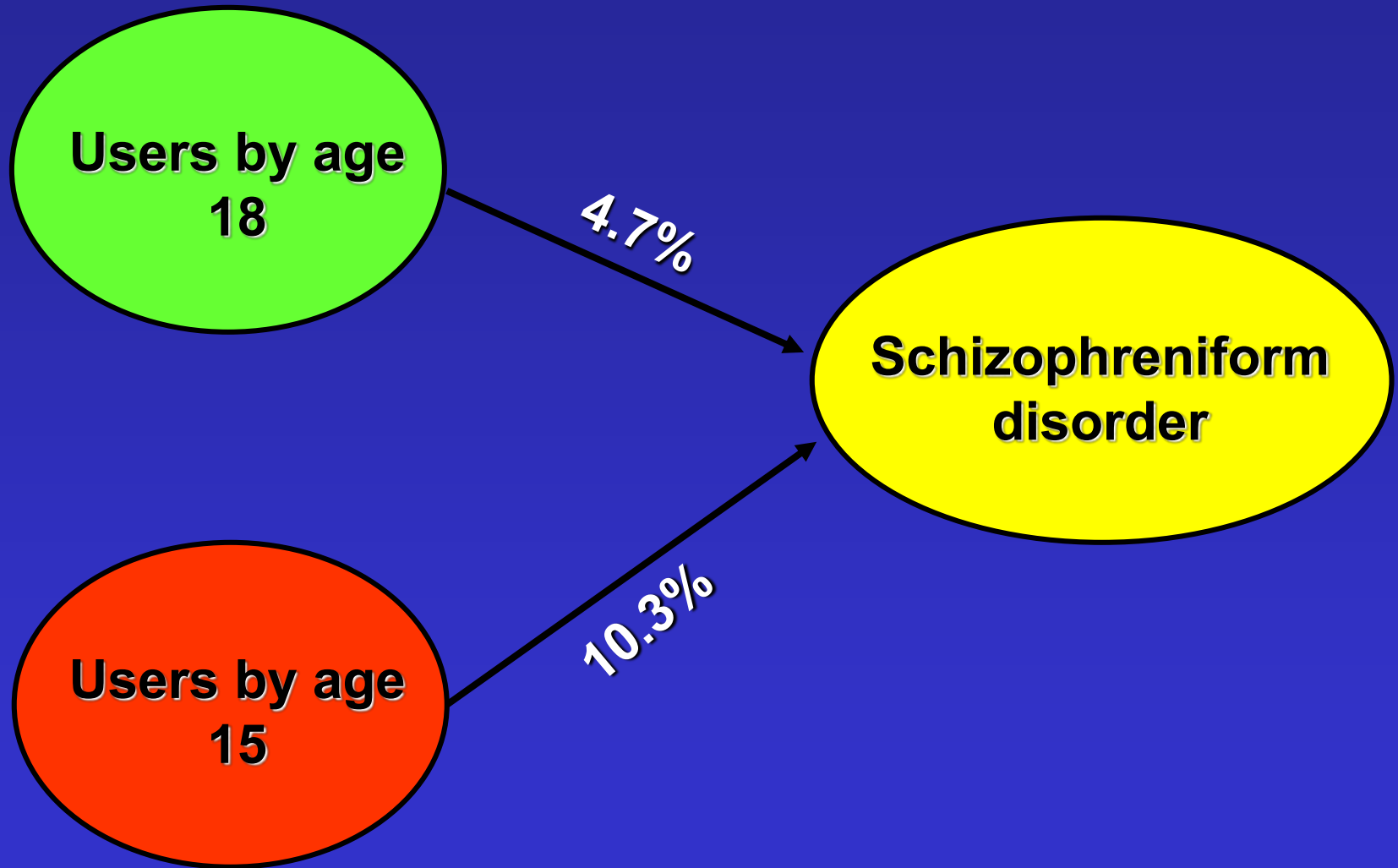
Predicting Depressive Disorder at age 26



Other drug use and Schizophreniform Disorder at age 26



Proportion of Cannabis Users



GxE analysis

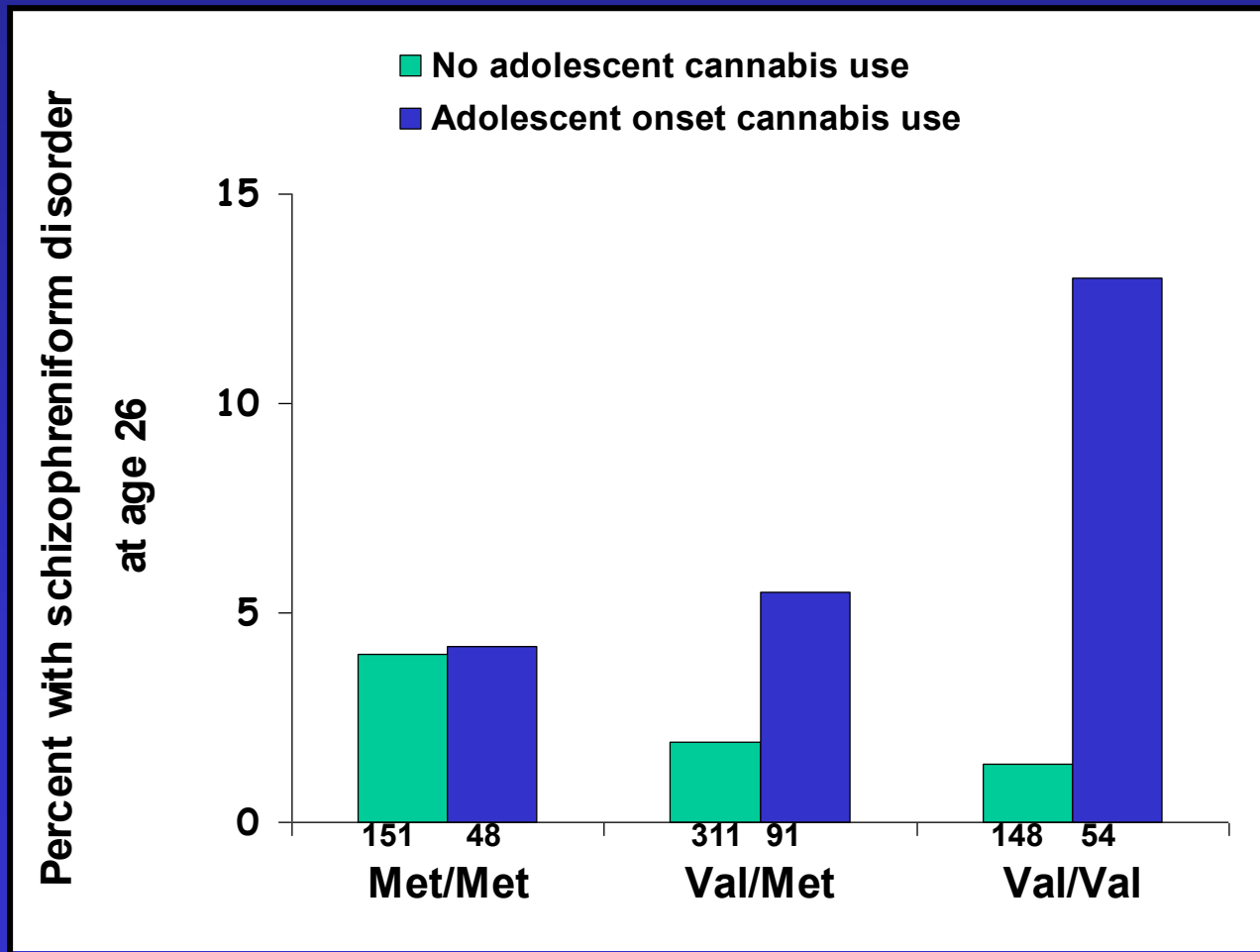
‘E’

Adolescent-onset cannabis use:
Any use of cannabis before 15 or
frequent use before age 18 (26%)

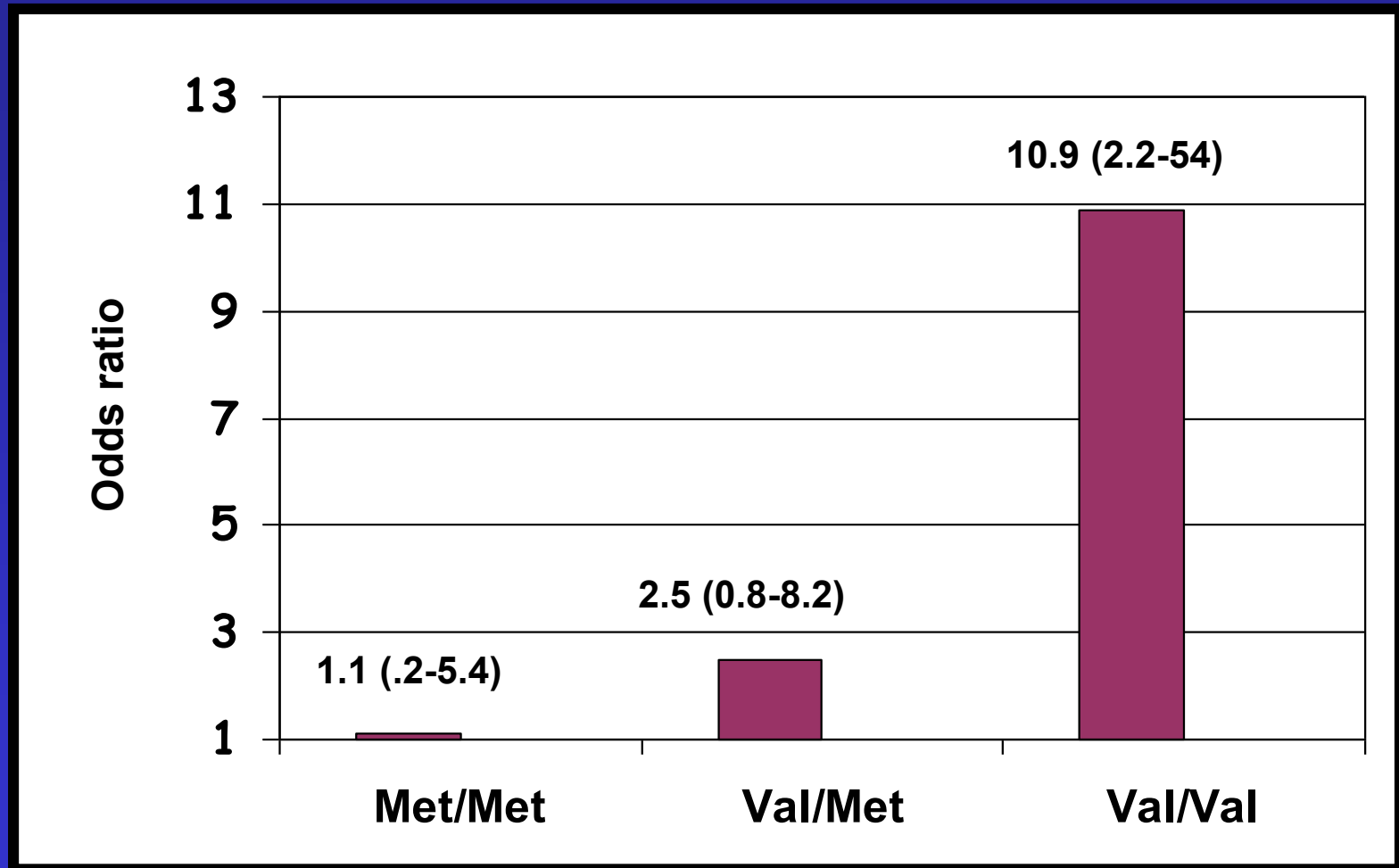
‘G’

COMT genotypes:
Val/Val (25%)
Val/Met (50%)
Met/Met (25%)

RESULT: The influence of early-onset cannabis use on adult psychosis **IS** moderated by COMT genotype



Predicting Schizophreniform Disorder at age 26



RESULTS: main GXE analysis

	B (SE)	z	p
COMT genotype	0.05 (.27)	0.17	0.800
Early-onset cannabis use	1.13 (.38)	2.90	0.030
Genotype X early-onset cannabis use	1.26 (.57)	2.20	0.025

Adult-onset (>18) cannabis use

	B (SE)	z	p
COMT genotype	0.05 (.27)	.17	0.80
Adult-onset cannabis use	0.59 (.81)	.73	0.47
Genotype X adult-onset cannabis use	-0.60 (.74)	.84	0.40

Alternative explanations

- **Adult-onset cannabis use (ages 21 or 26 years) (19%)**
- **Use of amphetamines or hallucinogens at age 21 or 26**
- **Psychotic Symptoms at age 11**
- **IQ ages 7, 9, 11, 13 years**
- **Conduct disorder (ages 11, 13, 15, or 18)**

Controlling for confounders

	B (SE)	t/z	p
Baseline	1.26 (0.7)	2.24	0.025
Adult cannabis use	1.32 (0.6)	2.28	0.022
Adult drug use	1.29 (0.6)	2.22	0.026
Childhood psychotic sx	1.42 (0.7)	2.14	0.032
Childhood IQ	1.36 (0.6)	2.30	0.020
Conduct disorder	1.30 (0.6)	2.30	0.020

Some Implications

- This study does not identify a MAJOR risk for psychosis
- *ADOLESCENCE* is a sensitive period of neurobiological vulnerability to psychosis for some young people
- Policy/law makers need to concentrate on delaying onset of cannabis use at least until late adolescence

Public Health Implications

Office of National Drug
Control Policy – Executive
Office of the President, **USA**,
2005.

Advisory Council on the
Misuse of Drugs, London,
United Kingdom.
September 2005.

MARIJUANA AND YOUR TEEN'S MENTAL HEALTH

Depression. Suicidal Thoughts. Schizophrenia.

If you have outdated perceptions about marijuana, you might be putting your teen at risk. New research is giving us better insight into the serious consequences of teen marijuana use, especially how it impacts mental health.

Did you know that young people who use marijuana weekly have double the risk of depression later in life?¹ And that teens aged 12 to 17 who smoke marijuana weekly are three times more likely than non-users to have suicidal thoughts?²

And if that's not bad enough, marijuana use in some teens has been linked to increased risk for schizophrenia in later years.³

Today's teens are smoking a more potent drug⁴ and starting use at increasingly younger ages during crucial brain development years.⁵ Still think marijuana's no big deal?

Remember, you are the most important influence in your teen's life when it comes to drugs,⁶ so tell your teen the facts about marijuana. Teens who learn about the risks from their parents are less likely to smoke marijuana or use other drugs than teens who don't.

Let your teens know you don't want them using marijuana. Their mental health may depend on it.

Signed,

- American Psychiatric Association
- American Academy of Child and Adolescent Psychiatry
- American Society of Addiction Medicine
- Asian Community Mental Health Services
- Association for Medical Education and Research in Substance Abuse
- Institute for Behavior and Health, Inc.
- National Asian American Pacific Islander Mental Health Association
- National Association of Addiction Treatment Providers
- National Council for Community Behavioral Healthcare
- National Latino Behavioral Health Association
- National Medical Association
- Office of National Drug Control Policy
- Partnership for a Drug-Free America

PARENTS.
THE ANTI-DRUG.
1-800-788-2800
www.theantidrug.com

¹Patton, GC et al. Cannabis use and mental health in young people: cohort study. *British Medical Journal*, 325: 1195-1198, 2002. ²Greenblatt, J. Adolescent self-reported behaviors and their association with marijuana use. *Substance Abuse and Mental Health Services Administration (SAMHSA)*, 1999. ³Arseneault, L et al. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *British Medical Journal*, 325: 1212-1213, 2002. ⁴Yoon, N et al. Cannabis use and age at onset of schizophrenia. *The American Journal of Psychiatry*, 161: 501-506, 2004. ⁵*Marijuana Potency Monitoring Project, Report No. 83*, University of Mississippi, 2003. ⁶SAMHSA. *Trends in Initiation of Substance Use*, 2003. ⁶SAMHSA. *Parental Disapproval of Youths' Substance Abuse*, 2002.



Taylor, D. R., Poulton, R., Moffitt, T. E., Ramankutty, P., and Sears, M. R. The respiratory effects of cannabis dependence in young adults. *Addiction*, 2000, 95(11): 1669-1677.

Taylor, D. R., Fergusson, D. M., Milne, B. J., Horwood, L. J., Moffitt, T. E., Sears, M. R., and Poulton, R. A longitudinal study of the effects of tobacco and cannabis exposure on lung function in young adults. *Addiction*, 2002, 97(8): 1055-1061.

Hancox, R. J., Poulton, R., Ely, M., Welch, D., Taylor, D. R., McLachlan, C. R., Greene, J. M., Moffitt, T. E., Caspi, A., and Sears, M. R. Effects of cannabis on lung function: a population-based cohort study. *European Respiratory Journal*, 2010, 35(1): 42-47.

Bad lungs...what about gums?

- Tobacco smoking exerts its periodontal effects via a systemic route:
 - Lungs → Blood → Gums
 - Destruction > Repair
 - Smokers have much worse gums
- Is cannabis smoking having periodontal effects?





Periodontal Disease

Periodontal disease (unhealthy gums and teeth) often reflects serious health risks. Mild inflammation of the gums (gingivitis) can be prevented by regularly brushing and flossing teeth to remove plaque (buildup of a film on the teeth). This stops the development of tartar (hardened accumulation of plaque at the gum line), which can only be removed by dental cleaning. More serious infection, called periodontitis, can cause not only disease of the gums, but loss of teeth and the bone structures that support the teeth. Periodontitis may be associated with heart disease, stroke, and systemic (whole body) infections. There is also evidence that premature births happen more often to women who have gum disease before or during their pregnancies. The February 6, 2008, issue of JAMA includes an article about an association between periodontal disease and smoking marijuana.

CAUSES

- Poor dental hygiene—not brushing your teeth or using dental floss regularly—allows the buildup of plaque and tartar, making the gum tissue unhealthy.
- Smoking causes decreased oxygen delivery to the gum tissue and makes it easier for bacteria to invade the gums.
- Some medications may cause gingival hyperplasia (overgrowth of gum tissue) or receding gums.
- Viral or fungal infection
- Poor nutrition, especially vitamin and mineral deficiencies, may cause gum disease or loss of teeth.
- Chronic medical conditions, including diabetes, may lead to greater risk of infections or poor healing in the gums as well as in other body tissues.

SIGNS AND SYMPTOMS

- Receding or puffy, swollen gums
- Painful gums
- Bleeding when you brush your teeth
- Tooth loss or loose teeth in adults
- Pus draining from the gums
- Bad breath that is not related to food and does not go away

PREVENTION AND TREATMENT

- Brush your teeth at least twice a day.
- Use dental floss daily.
- Periodontitis does not cause symptoms initially, so it is important to have regular dental checkups.
- Maintain good nutrition by eating fruits, vegetables, and whole grains and making sure your diet contains plenty of calcium.
- Do not smoke.
- Control chronic medical problems, especially diabetes (maintaining normal blood sugar levels decreases your risk of infection).
- In severe cases of periodontitis, advanced dental treatments may be offered, including gum surgery, bone grafts, or placement of antibiotics into the gum tissue itself.

Symptoms of Periodontal Disease



FOR MORE INFORMATION

- American Dental Association www.ada.org
- National Institute of Dental and Craniofacial Research www.nidcr.nih.gov
- American Heart Association www.americanheart.org

INFORM YOURSELF

To find this and previous JAMA Patient Pages, go to the Patient Page link on JAMA's Web site at www.jama.com. Many are available in English and Spanish.

Sources: National Institute of Dental and Craniofacial Research, American Dental Association, American Heart Association

Janet M. Torpy, MD, Writer
 Alison E. Burke, MA, Illustrator
 Richard M. Glass, MD, Editor

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What's in the smoke?

Tobacco smoke

400+ combustion products
Carbon monoxide

Nicotine



Cannabis smoke

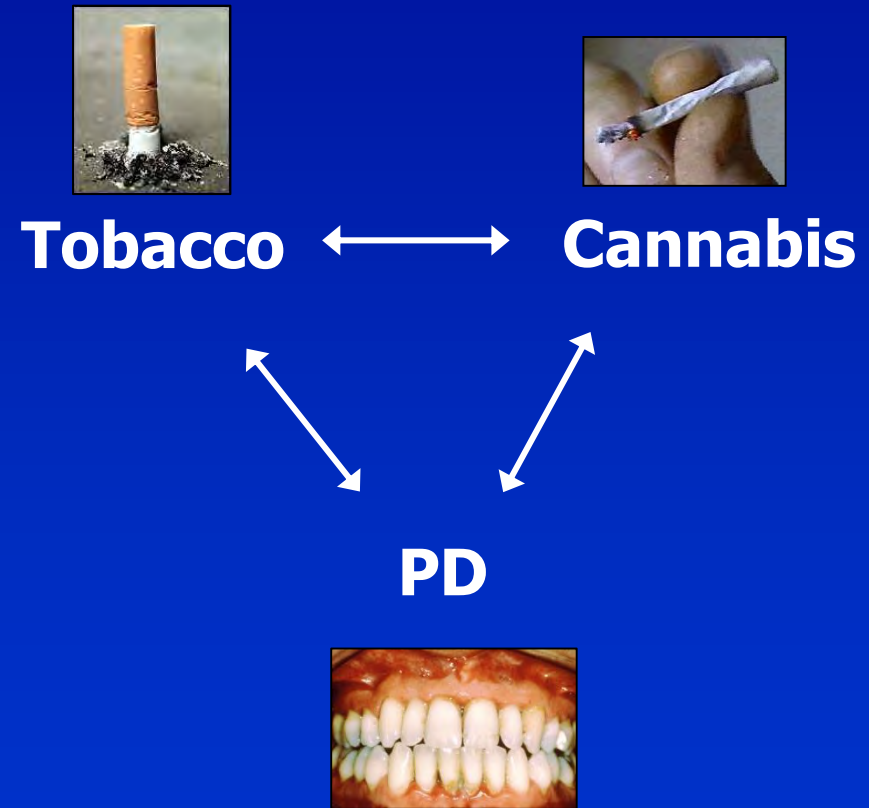
400+ combustion products
Carbon monoxide

Tetrahydrocannabinol



The challenge

- Tobacco smoking likely to be a confounder
 - Associated with both:
 - Cannabis use
 - Periodontal disease
- Need to control for it if we want to see whether cannabis smoking is a risk factor






Methods – exposure variables

- **Cigarette smoking**
 - Smoking status over previous year recorded at ages 15, 18, 21, 26 and 32
 - Computed total pack-years exposure to age 32
- **Cannabis smoking**
 - Ages 18, 21, 26 and 32 – number of times in previous year
 - Used the mean of the usage over those 4 ages (Cronbach's alpha = 0.79) in allocating to 3 cannabis exposure groups

Numbers

- Complete data available for 903 individuals

- Cannabis exposure

- None 32.3% ( 0 occasions/year)
- Some 47.4% ( 1-40)
- High 20.2% ( 41+)



- Cigarette smoking at age 32

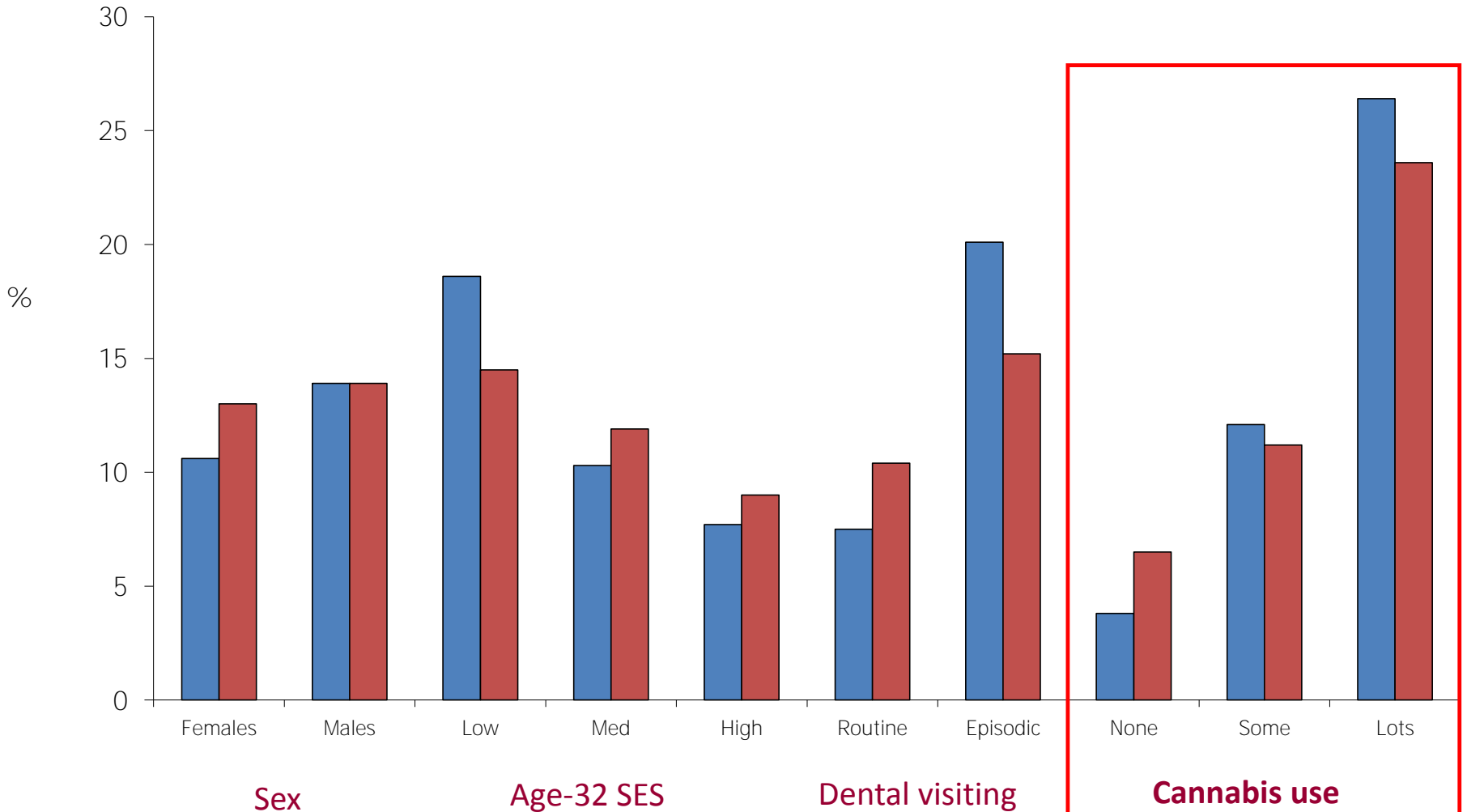
- 51.5% never smokers
- 31.2% current smokers
- 17.3% former smokers



Gum disease to age 32

■ Prevalence 5+mm CAL @ 32

■ New case 26-32



Multivariate model for 5+mm CAL



	Relative risk	95% CI
Highest 20% cannabis exp.	3.1	1.3, 6.4
Some cannabis exp.	2.5	1.3, 4.7
Pack-years of tobacco use	1.1	1.0, 1.1
Female	1.0	0.7, 1.4
Low SES	1.3	0.7, 2.8
Medium SES	1.0	0.6, 1.8
Episodic visitor @ 26 & 32	1.5	1.0, 2.3
Plaque score at 32	1.0	0.7, 1.4

Summary of models

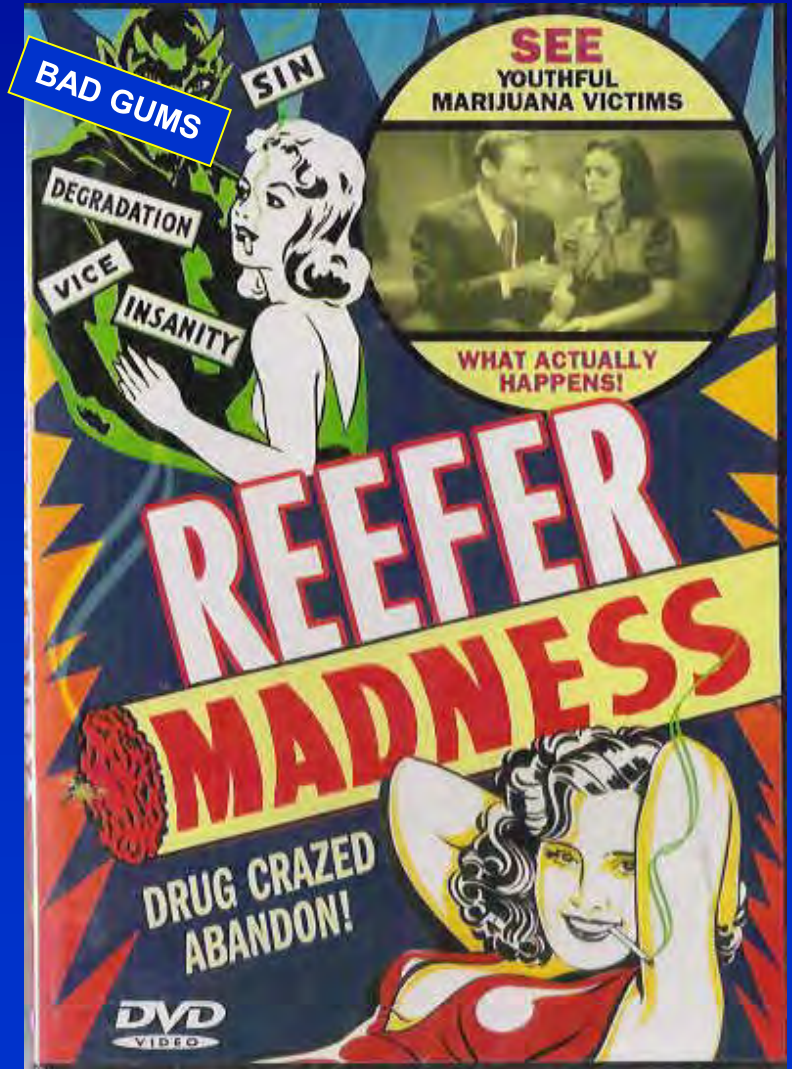
	Highest 20% cannabis exposure	Highest 10% cannabis exposure
Prevalence (age 32)		
1+ sites with 4+mm CAL	1.61 (1.16, 2.24)	1.82 (1.29, 2.56)
1+ sites with 5+mm CAL	3.13 (1.53, 6.38)	3.02 (1.44, 6.31)
RR for those who had never smoked tobacco = 4.6		
Incidence (age 26 to 32)		
1+ sites with 3+mm increase in CAL	2.15 (1.20, 3.85)	2.31 (1.21, 4.41)



Conclusion

- Cannabis smoking is associated with detrimental periodontal effects over and above those of cigarette smoking
- Smoking **anything** is bad for your gums

Thomson WM et al, JAMA 2008; 299: 525-531



Persistent cannabis users show neuropsychological decline from childhood to midlife

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

^aDuke Transdisciplinary Prevention Research Center, Center for Child and Family Policy, ^bDepartment of Psychology and Neuroscience, and ^cInstitute for Genome Sciences and Policy, Duke University, Durham, NC 27708; ^dDepartment of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC 27710; ^eSocial, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, King's College London, London SE5 8AF, United Kingdom; and ^fDunedin Multidisciplinary Health and Development Research Unit, Department of Preventive and Social Medicine, School of Medicine, University of Otago, Dunedin 9054, New Zealand



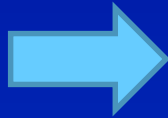
Rationale

- Previous research has suggested that adolescents may be particularly vulnerable to the effects of cannabis on mental ability.
- These studies could not address whether deficits in mental ability predate cannabis use.
- We asked whether persistent cannabis use was associated with IQ decline and whether IQ decline was concentrated among adolescent-onset cannabis users.
- This is an important topic for research as fewer of today's teens believe marijuana poses a serious health risk.

IQ Testing



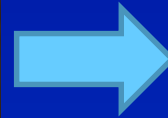
Age 7-13



Cannabis Assessments



Age 18-38



IQ Testing



Age 38

Table 1. IQ before and after cannabis use

	<i>N</i>	% male	Age 7–13 full-scale IQ	Age 38 full-scale IQ	Δ IQ effect size*
Persistence of cannabis dependence					
Never used, never diagnosed	242	38.84	99.84 (14.39)	100.64 (15.25)	0.05
Used, never diagnosed	479	49.48	102.32 (13.34)	101.25 (14.70)	−0.07
1 diagnosis	80	70.00	96.40 (14.31)	94.78 (14.54)	−0.11
2 diagnoses	35	62.86	102.14 (17.08)	99.67 (16.11)	−0.17
3+ diagnoses	38	81.58	99.68 (13.53)	93.93 (13.32)	−0.38
Persistence of regular cannabis use					
Never used	242	38.84	99.84 (14.39)	100.64 (15.25)	0.05
Used, never regularly	508	50.59	102.27 (13.59)	101.24 (14.81)	−0.07
Used regularly at 1 wave	47	72.34	101.42 (14.41)	98.45 (14.89)	−0.20
Used regularly at 2 waves	36	63.89	95.28 (10.74)	93.26 (11.44)	−0.13
Used regularly at 3+ waves	41	78.05	96.00 (16.06)	90.77 (13.88)	−0.35

Means (SDs) are presented for child and adult full-scale IQ as a function of the number of study waves between ages 18 y and 38 y for which study members met criteria for cannabis dependence or reported using cannabis on a regular basis (at least 4 d/wk). The last column shows that study members with more persistent cannabis use showed greater IQ decline from childhood to adulthood.

*This coefficient indicates change in IQ from childhood to adulthood, with negative values indicating decreases in IQ. These change scores are in SD units, with values of 0.20, 0.50, and 0.80 reflecting small, medium, and large changes, respectively.

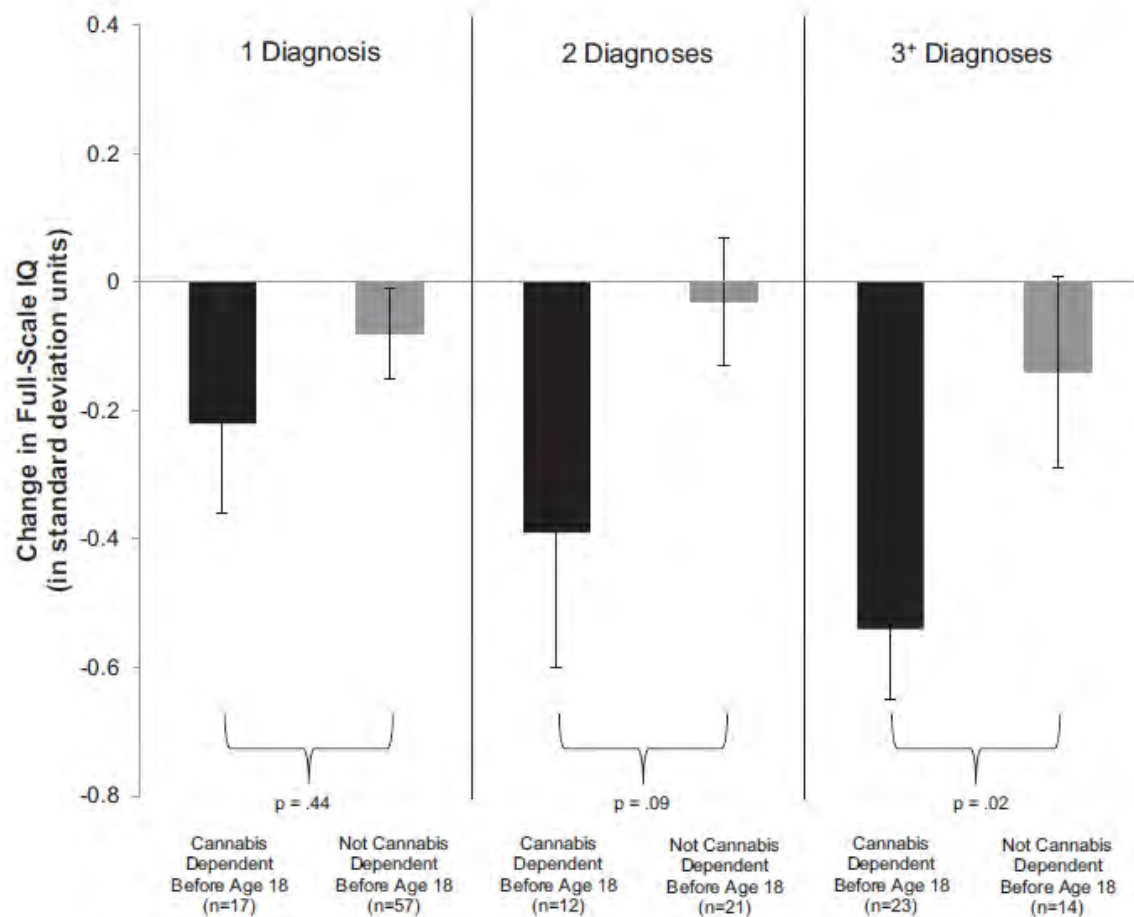
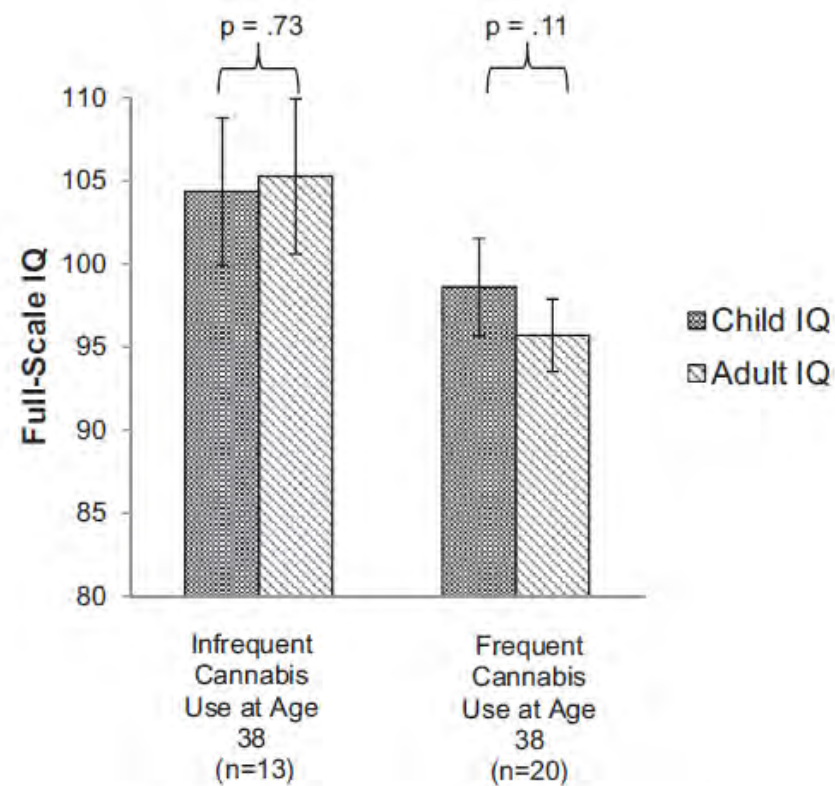
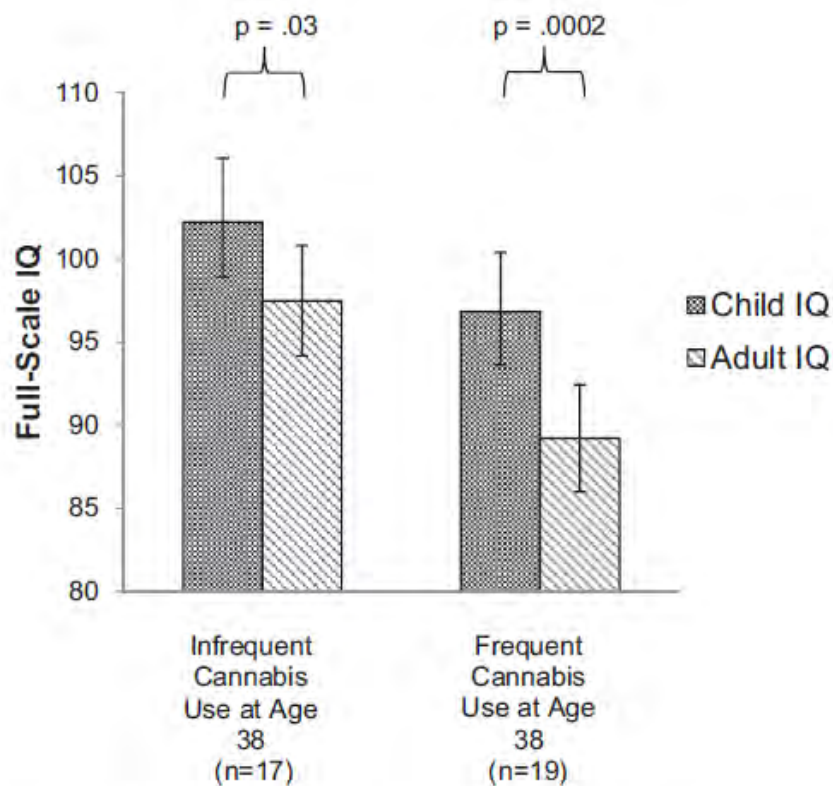


Fig. 2. Adolescent vulnerability. Shown is change in full-scale IQ (in SD units) from childhood to adulthood among study members with 1, 2, or 3+ diagnoses of cannabis dependence as a function of age of onset of cannabis dependence. Individuals with adolescent-onset cannabis dependence (black bars) experienced greater IQ decline than individuals with adult-onset cannabis dependence (gray bars). IQ decline of approximately -0.55 SD units among individuals with adolescent-onset cannabis dependence in the 3+ group represents a decline of 8 IQ points. Error bars = SEs.



Adolescent-Onset (Used Cannabis Weekly Before Age 18)

Adult-Onset (Did Not Use Cannabis Weekly Before Age 18)

Fig. 3. Postcessation IQ among former persistent cannabis users. This figure is restricted to persistent cannabis users, defined as study members with two or more diagnoses of cannabis dependence. Shown is full-scale IQ in childhood and adulthood. IQ is plotted as a function of (i) age of onset of at least weekly cannabis use and (ii) the frequency of cannabis use at age 38 y. Infrequent use was defined as weekly or less frequent use in the year preceding testing at age 38 y. Median use among infrequent and frequent adolescent-onset cannabis users was 14 (range: 0–52) and 365 (range: 100–365) d, respectively. Median use among infrequent and frequent adult-onset cannabis users was 6 (range: 0–52) and 365 (range: 100–365) d, respectively. IQ decline was apparent even after cessation of cannabis use for adolescent-onset former persistent cannabis users. Error bars = SEs.

Conclusion

- **Adolescent-onset cannabis users, but not adult-onset cannabis users, showed marked IQ decline from childhood to adulthood. For example, individuals who started using cannabis in adolescence and used it for years thereafter showed an average 8-point IQ decline.**
- **Quitting or reducing cannabis use did not appear to fully restore intellectual functioning among adolescent-onset former persistent cannabis users.**
- **IQ decline could not be explained by alcohol or other drug use or by reduced years of education among persistent cannabis users.**

Reply to Rogeberg and Daly: No evidence that socioeconomic status or personality differences confound the association between cannabis use and IQ decline



Moffitt, Meier, Caspi & Poulton, PNAS 2013, 110(11), E981

Take home messages

- **Dose-response relations have policy implications.**
 - Irregular use of small amounts = negligible health effects.
 - Regular use of large amounts = non-trivial, negative health effects.
- **Effects are across multiple physiological systems**
- **Burden of disease associated with regular, heavy use is probably under-estimated.**
- **Cannabis should be viewed as a health issue, not a legal issue.**

Acknowledgements

- This on-going research would not have been possible without the co-operation and commitment of the Study members, their families and friends over a long period of time.
- Core funding for the Dunedin Multidisciplinary Health and Development Research Unit comes from the Health Research Council of New Zealand.

For copies of research articles referred to in this presentation or other information on the Study, contact Michelle McCann:



03 479-8507



email: *dmhdru@otago.ac.nz*

[http://www.otago.ac.nz/dunedin study](http://www.otago.ac.nz/dunedin_study)