Institute of Psychiatry at the Maudsley

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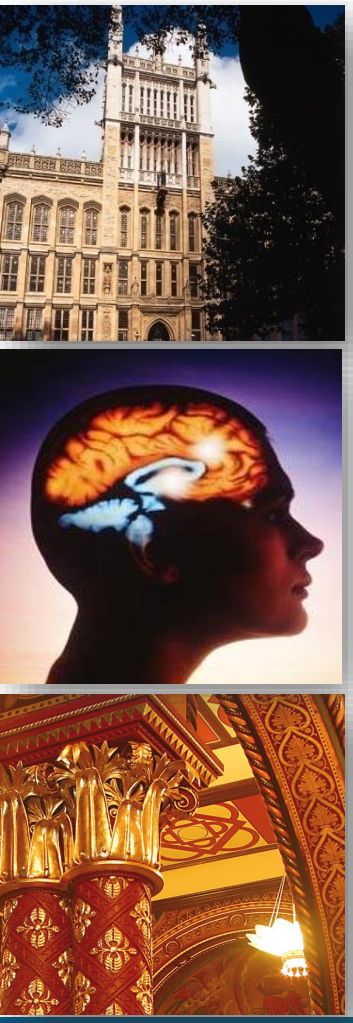

Cannabis, Psychosis, and Violence

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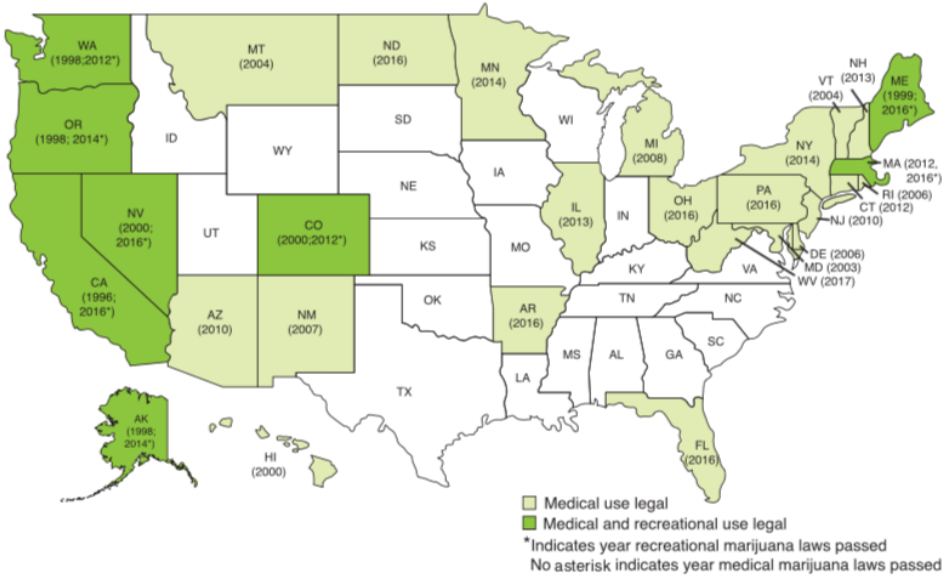
KING'S College LONDON

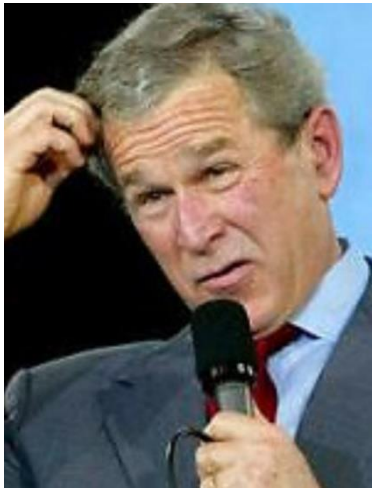
Robin Murray has received honoraria for lectures from Janssen, Lilly, Sunovian, Otsuka and Lundbeck

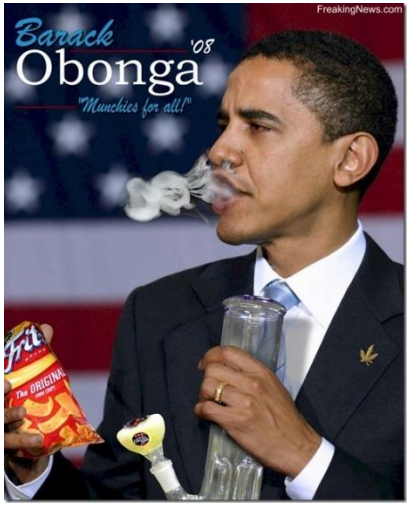


Legalisation has been associated with an increase in adult use and in potency

Haslin et al 2015, 2018

Cannabis and US Presidents





Medicinal Cannabis

Indications:

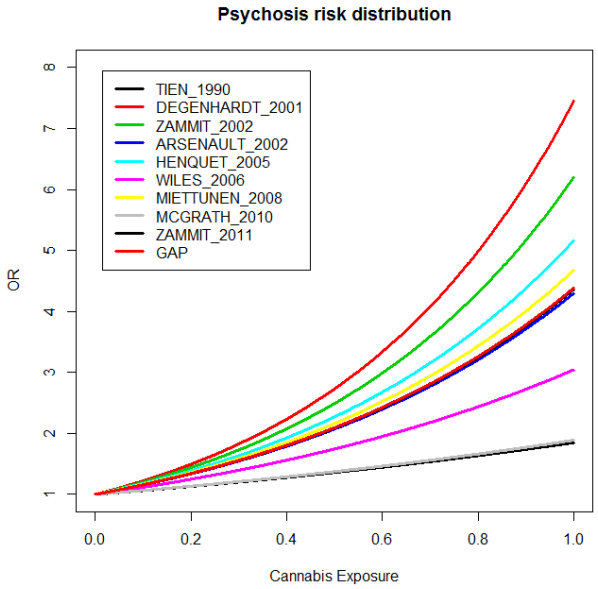
Pain (Dronabinol- synthetic THC)

Intractable Nausea (Nabilone - synthetic THC)

Spasticity (Sativex THC-CBD)

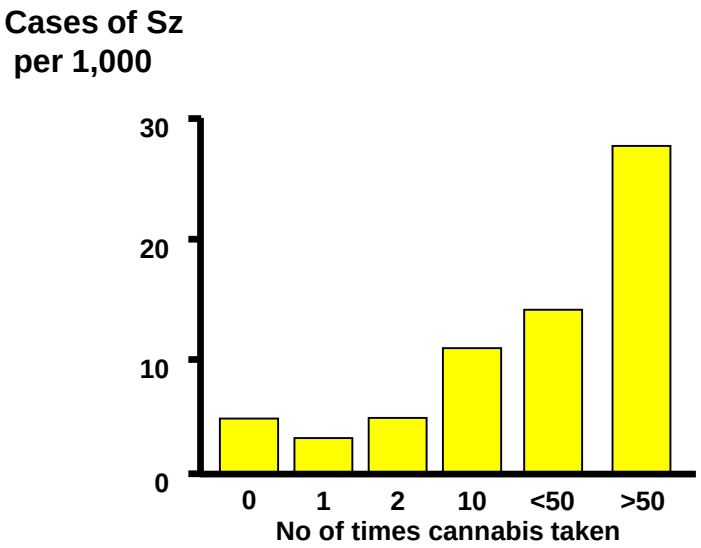
Childhood Epilepsy (CBD)

Marconi et al 2016



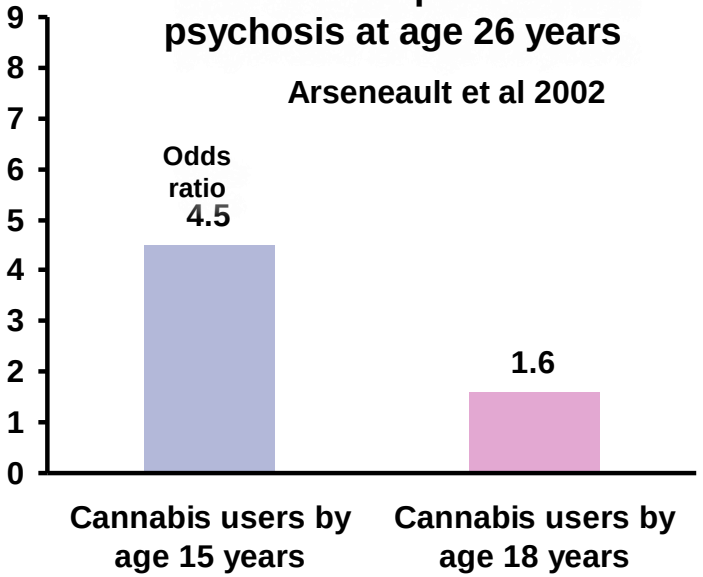
OR=3.9

Swedish Army Study of Andréasson et al 1987



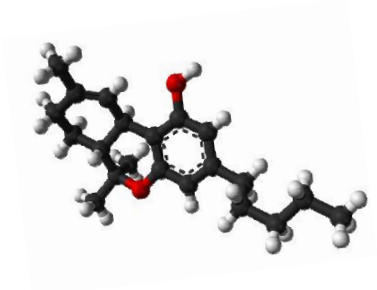
Cohort Studies

Country	n	FU	OR
Sweden	50,053	25 yrs	3.1
NL	4,045	3 yrs	2.8
NL	4,045	3 yrs	12.0
NL	18,000	Retro	3.2
NZ (Chr)	1,265	3 yrs	1.8
NZ (Dun)	1,253	15 yrs	3.1
Germany	2,436	4 yrs	1.7
UK	8,500	18 mths	1.5
Australia	3,800	14 yrs	2.2



The ingredients of cannabis

Tetrahydrocannabinol (THC) – partial agonist at CB1

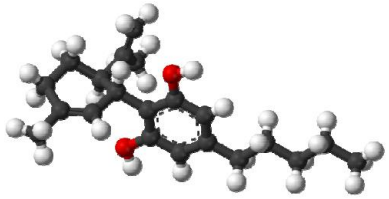


Euphoria

Impairment of attention,memory and learning

Hallucinations and paranoid ideas

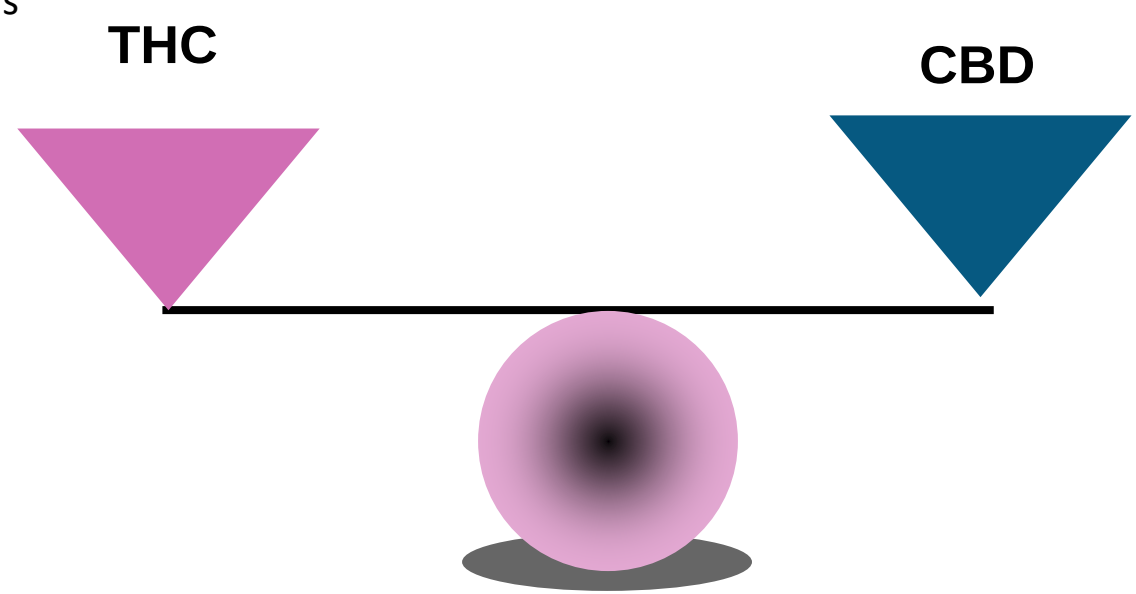
Cannabidiol (CBD)



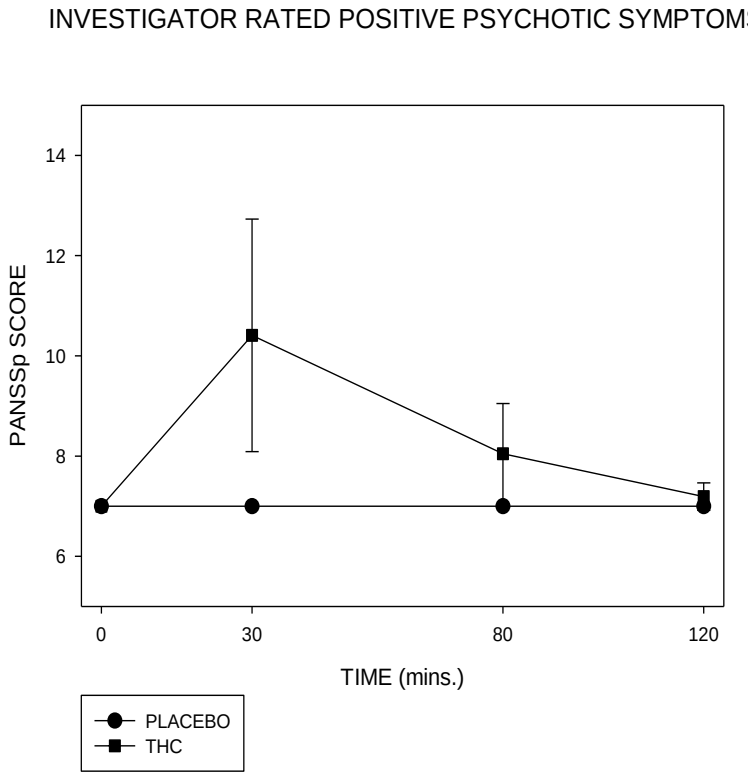
Is not hallucinogenic

Has anxiety relieving properties

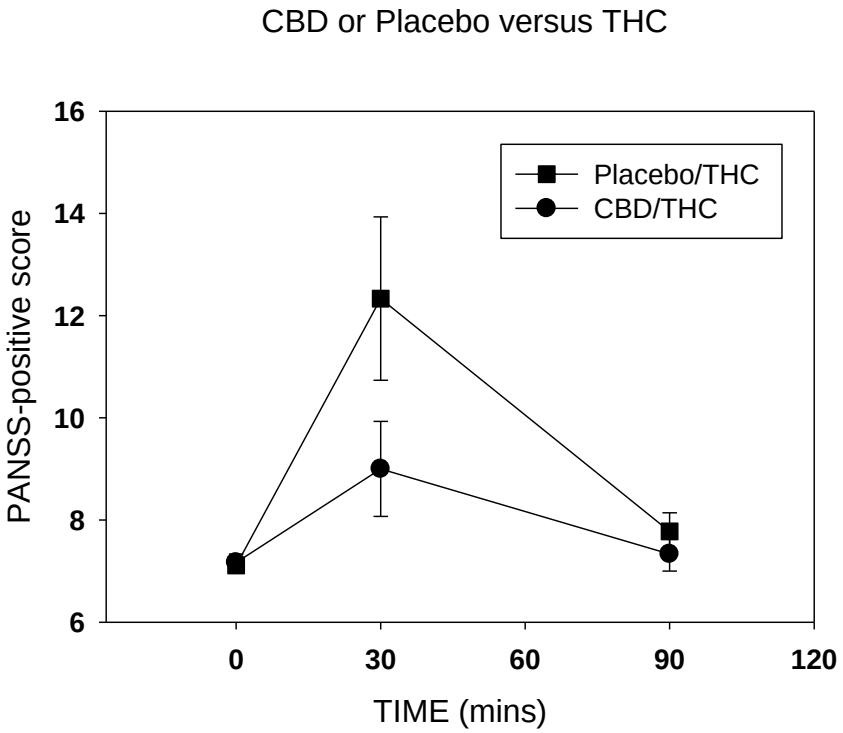
Antagonise effects of THC?



Psychotogenic effect of acute administration of 2.5 mg of IV Tetrahydrocannabinol (THC) .



THC induces transient psychotic symptoms



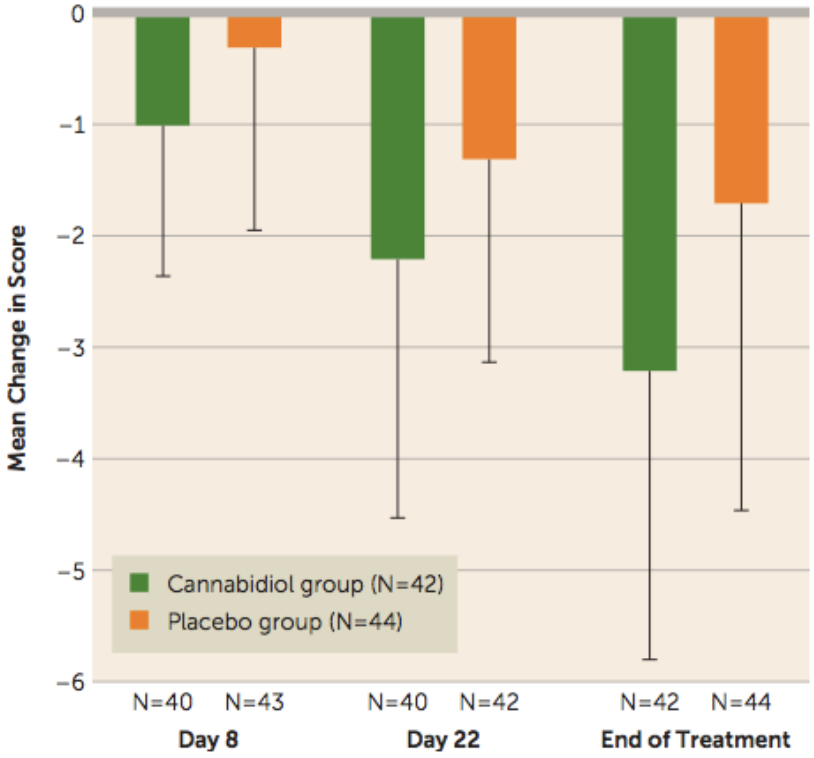
Cannabidiol (CBD) blocks the effects of THC

Morrison et al, 2009 Bhattacharyya et al 2010, Englund et al, 2012

Cannabidiol (CBD) as an Adjunctive Therapy in Schizophrenia: A Multicenter Randomized Controlled Trial

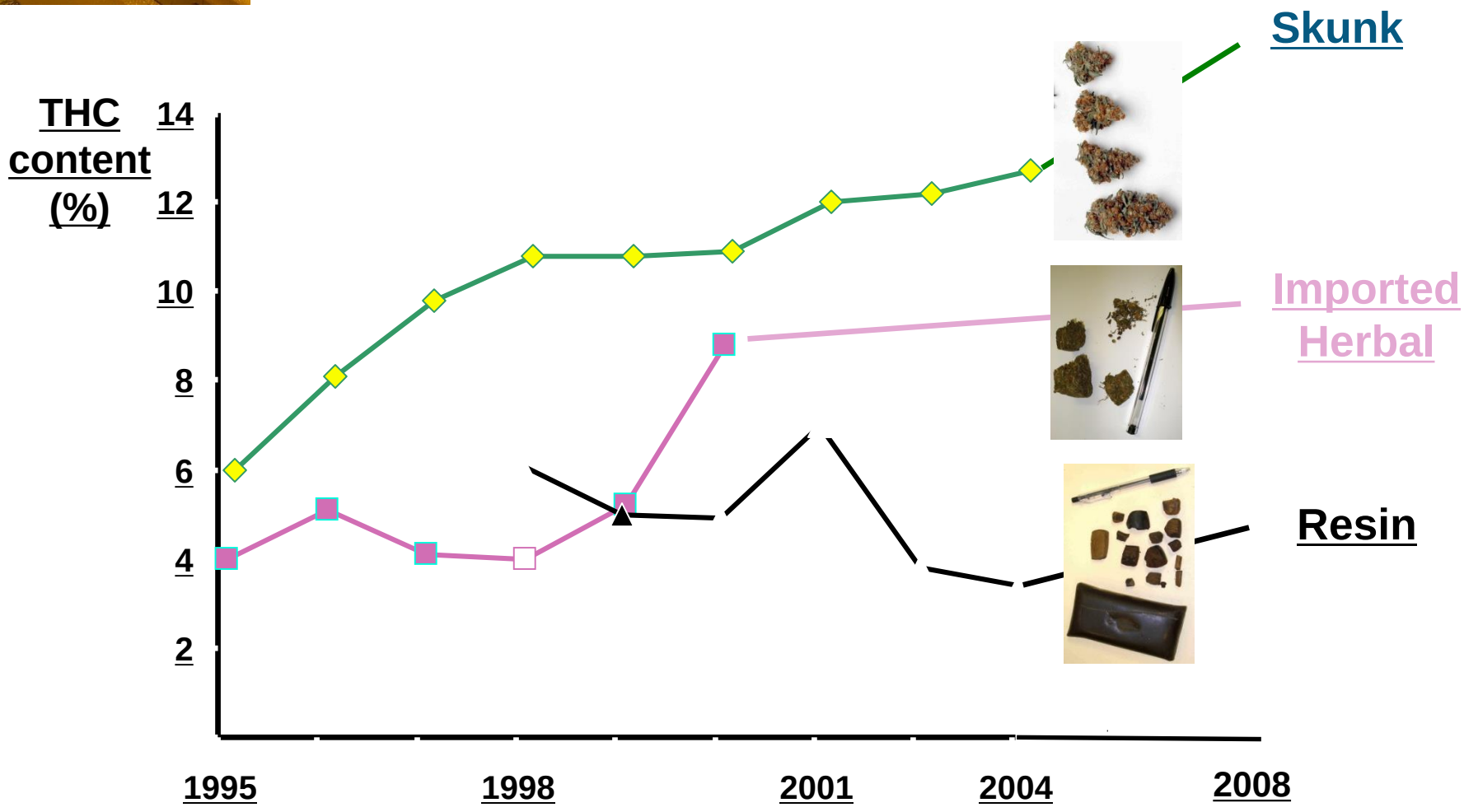
Philip McGuire, F.R.C.Psych., F.Med.Sci., Philip Robson, M.R.C.P., F.R.C.Psych., Wieslaw Jerzy Cubala, M.D., Ph.D., Daniel Vasile, M.D., Ph.D., Paul Dugald Morrison, Ph.D., M.R.C.Psych., Rachel Barron, B.Vet.Med., M.R.C.V.S., Adam Taylor, Ph.D., Stephen Wright, F.R.C.P.(Edin), F.F.P.M.

FIGURE 1. Change in PANSS Positive Scores From Baseline to End of Treatment in a Study of Adjunctive Cannabidiol in Schizophrenia (Intention-to-Treat Analysis Set)[a]



[a] PANSS=Positive and Negative Syndrome Scale.

Cannabis potency in England



Potter et al 2008, DoH, 2008

2017 Survey:

Skunk not more portent but now accounts for 94% of market

The ingredients of cannabis

THC causes

Impairment of attention, memory and learning

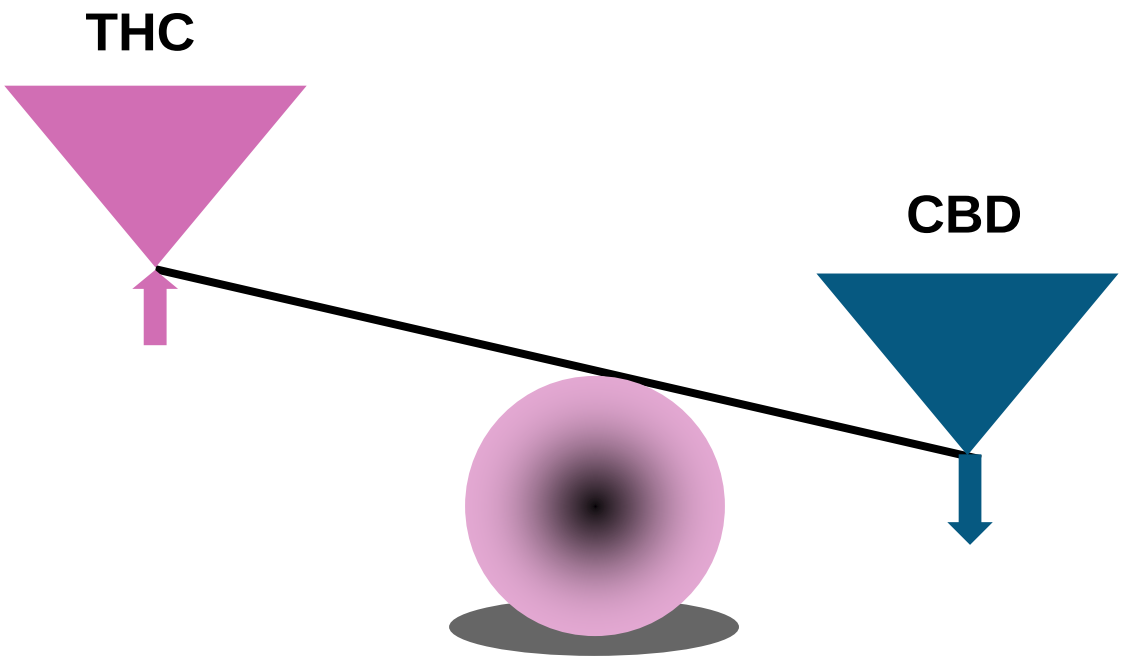
Hallucinations and paranoid ideas

Cannabidiol (CBD)

Is not hallucinogenic

Has anxiety relieving properties

No adverse effect on cognition



Case-control study of cannabis and psychosis

- **410 patients in their 1st episode of psychosis.**
- **370 population-based healthy controls**

(screened for psychosis)

All interviewed using the cannabis experience questionnaire

Di Forti et al, BJPsych 2009; Schiz Bull 2013; Lancet Psychiatry, 2015

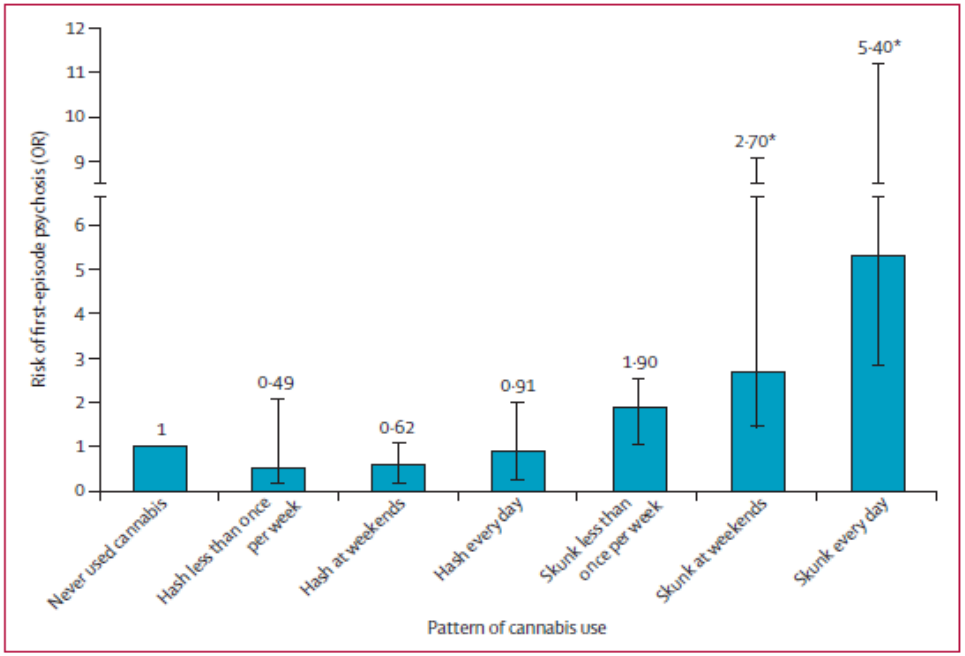
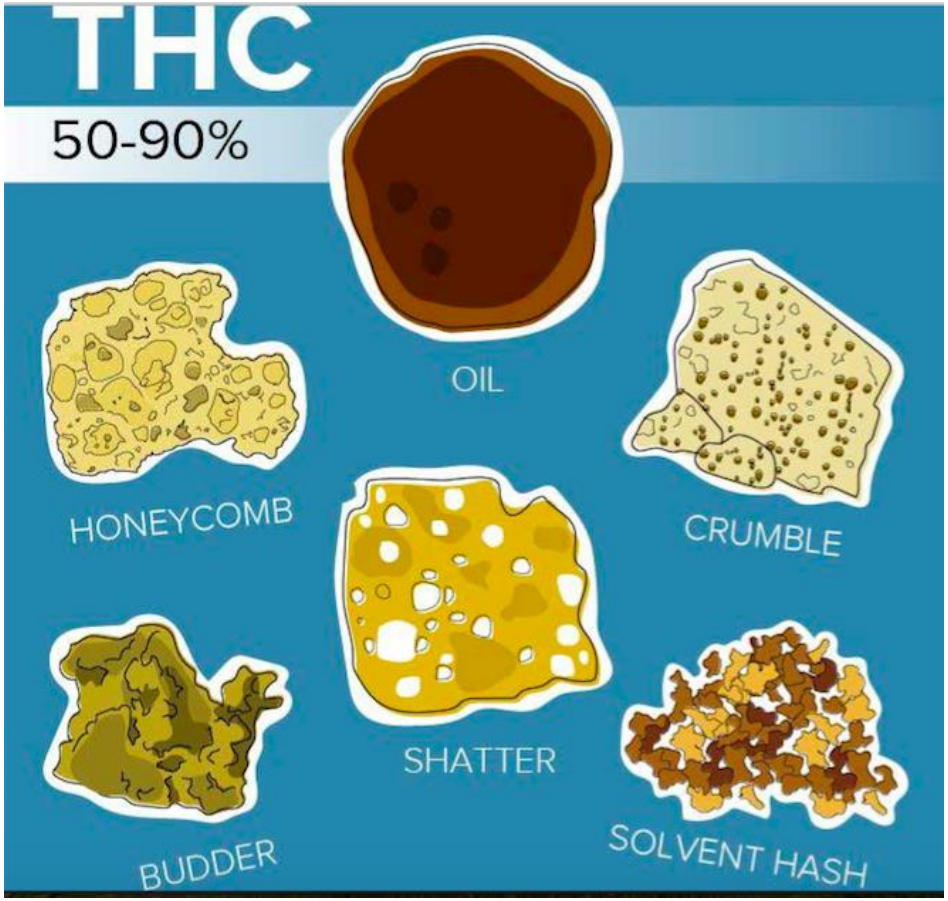


Figure 2: **Probability of individuals having a psychotic disorder by pattern of cannabis use**
OR adjusted for age, gender, ethnic origin, education, employment status, and tobacco use. OR=odds ratio.
*p<0·05.

GAP study; Lancet Psychiatry 2015

The race to more potent forms of cannabinoids



The arrival of synthetic cannabinoids puts the psychotogenic effect beyond doubt

Psychopharmacology
DOI 10.1007/s00213-013-3188-4

REVIEW

Spicing things up: synthetic cannabinoids

Max Spaderna · Peter H. Addy · Deepak Cyril D'Souza

While THC is a partial agonist at the CB1 Receptor, synthetic Cannabinoids are full agonists. Therefore they have much more powerful effects

Users are 30 times more likely to seek emergency treatment than users of regular cannabis
Winstock A ,Global Drug Survey 2014

Hum. Psychopharmacol Clin Exp 2013; **28**: 379–389.
Published online in Wiley Online Library
(wileyonlinelibrary.com) **DOI**: 10.1002/hup.2312

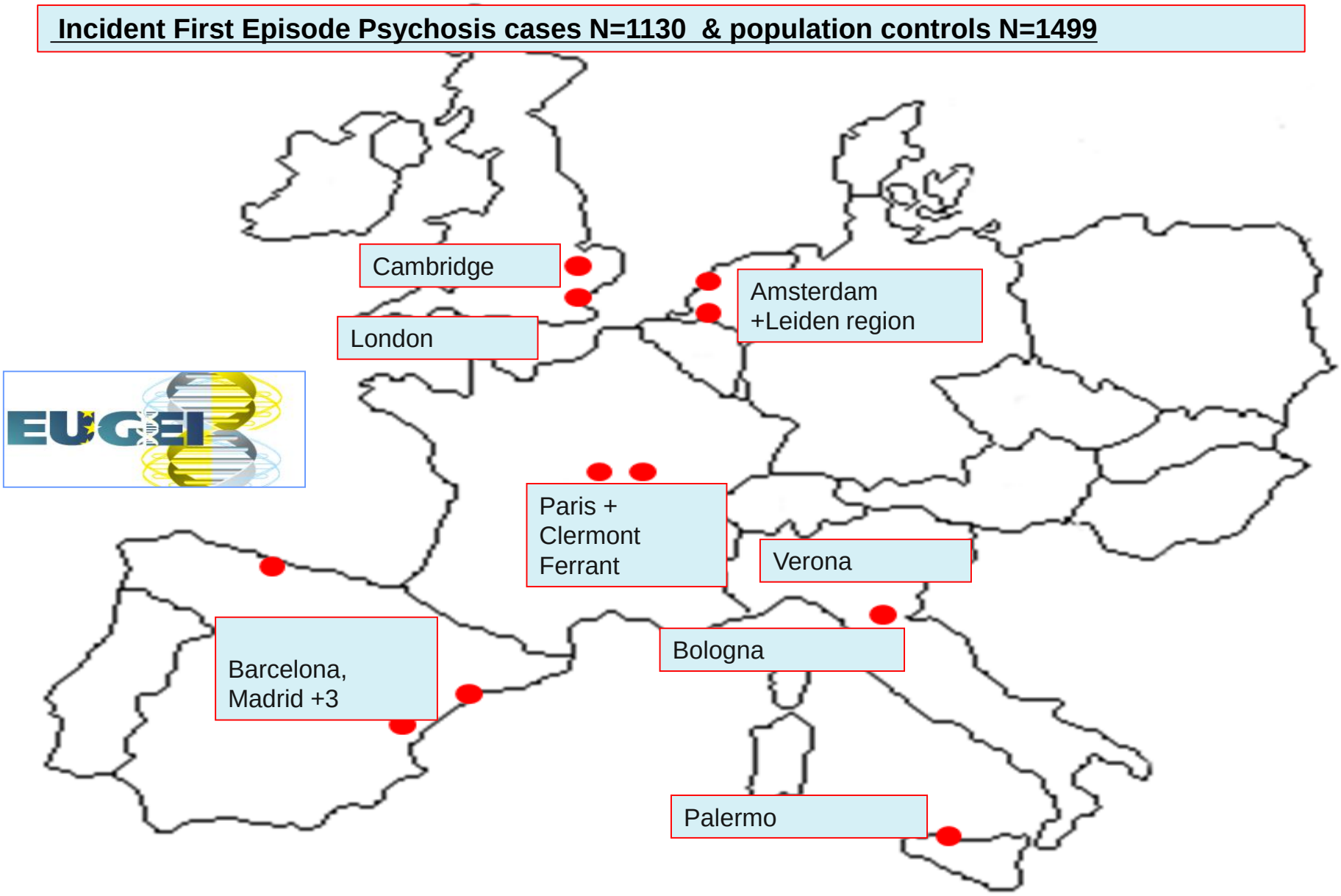
SPECIAL ISSUE ON NOVEL PSYCHOACTIVE SUBSTANCES

"Spiceophrenia": a systematic overview of "Spice"-related psychopathological issues and a case report

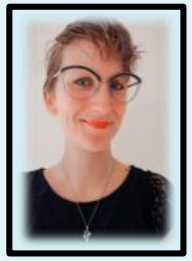
Duccio Papanti[1,2]*, Fabrizio Schifano[3], Giulia Botteon[1,2], Francesca Bertossi[4], Jason Mannix[5], Daniela Vidoni[6], Matteo Impagnatiello[2], Elisabetta Pascolo-Fabrici[1,7] and Tommaso Bonavigo[1,4]

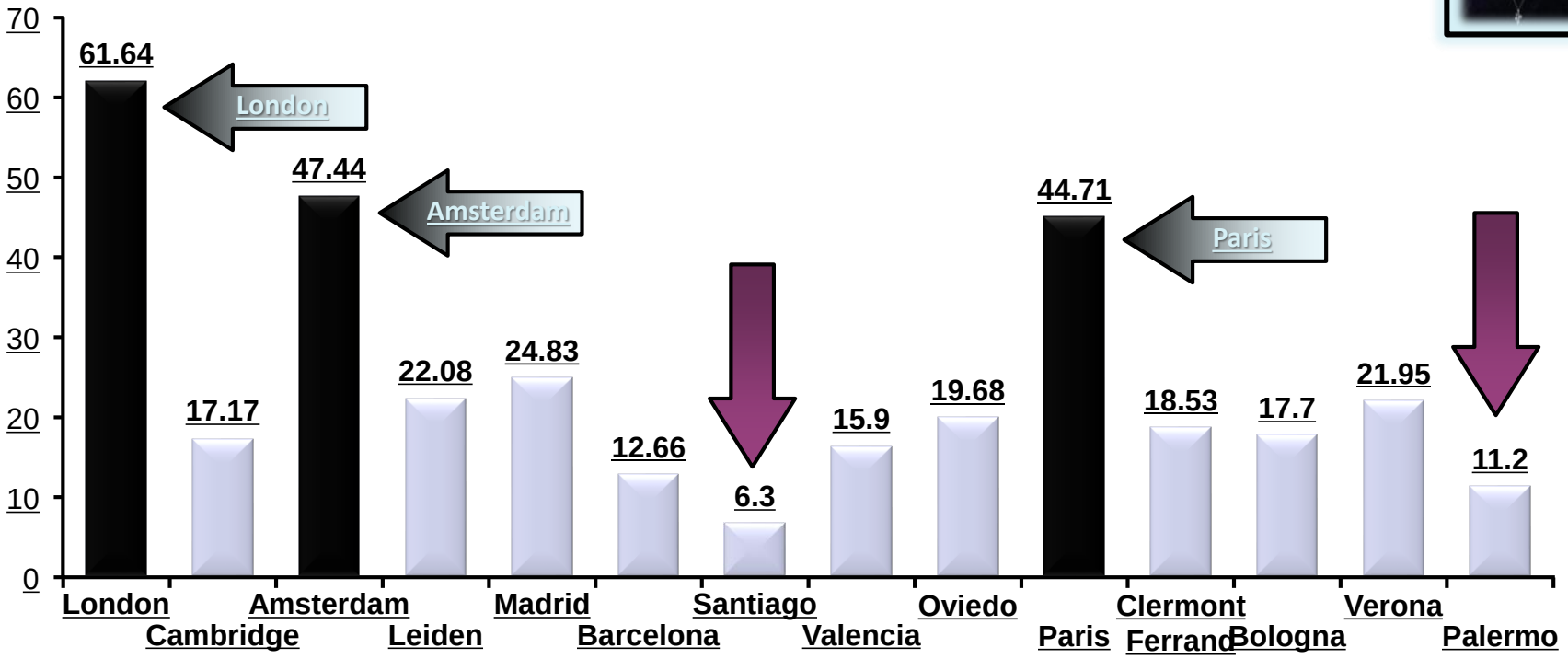
Is there a relationship between prevalence of cannabis use in the population and the Incidence rates of Psychosis?

Incident First Episode Psychosis cases N=1130 & population controls N=1499



Incidence of first episode psychosis across Europe





Jongsma *et al. JAMA Psychiatry* 2018

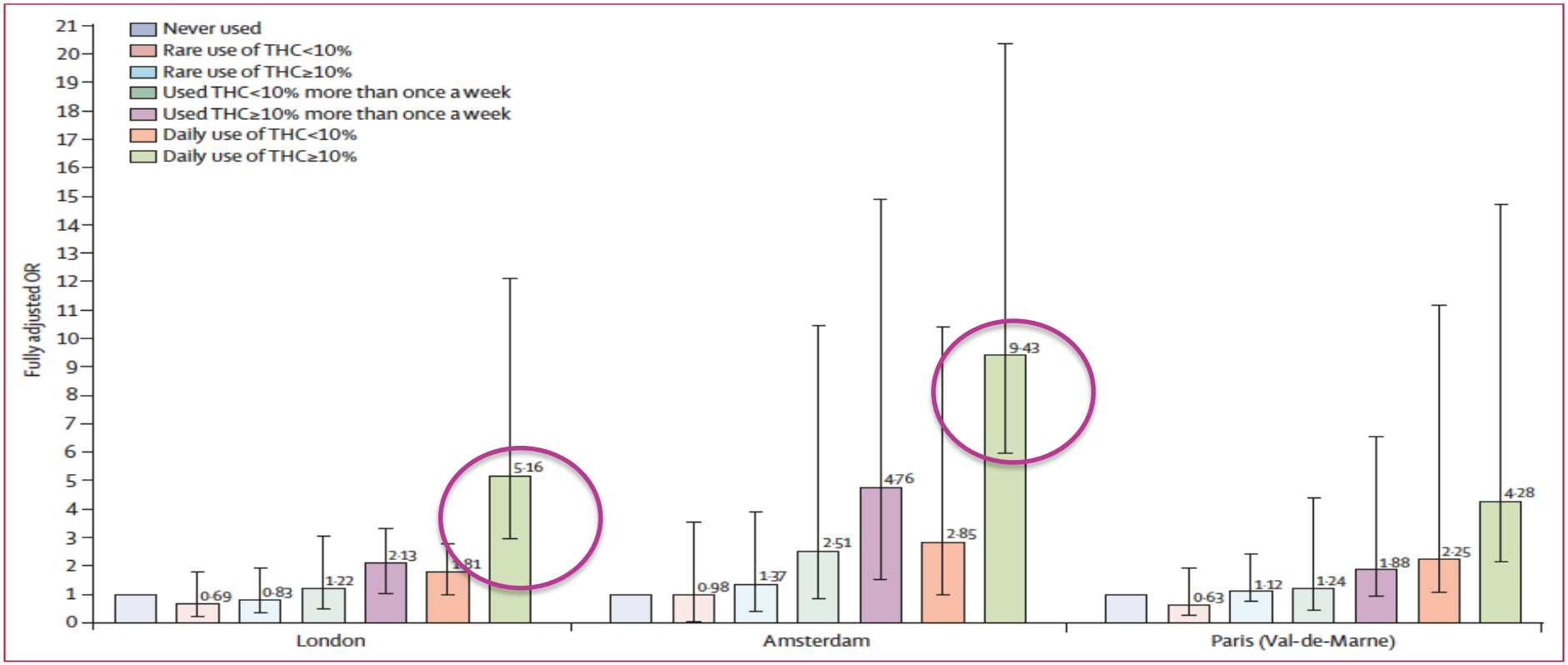
What is the explanation for the low rates in Italy/Spain?

Migration

Families v **social isolation**?

High Potency Cannabis

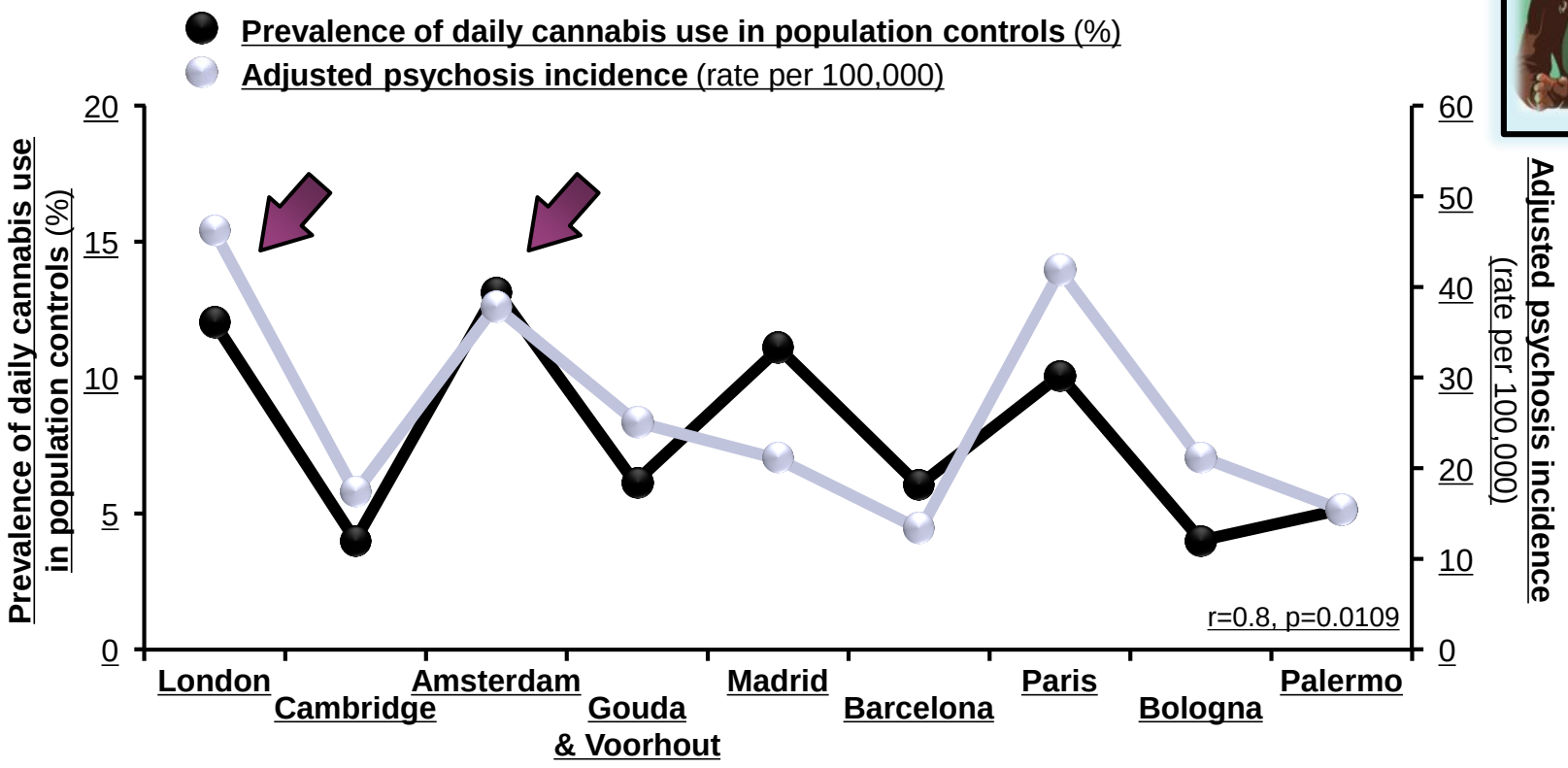
The effect of daily use of high-potency cannabis on the odds for psychotic was particularly visible in **London and Amsterdam**



*Adjusted for age, gender, ethnicity, level of Ed, employment status and other drugs (tobacco, alcohol, stimulants, Ketamine, Legal highs, Hallucinogenics).

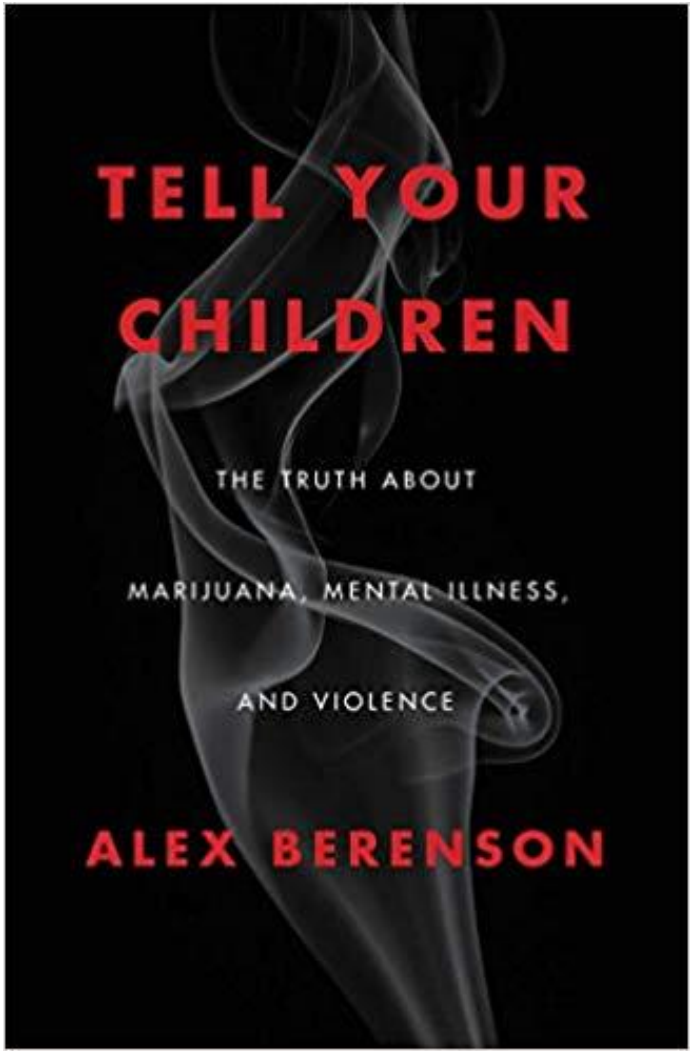
Di Forti et al, Lancet Psych, On Line March 23 2019

Relationship between the frequency of cannabis use and the rate of psychosis



Population Attributable Fraction

If nobody smoked high potency cannabis, 12% of all cases of first episode psychosis across Europe would be prevented, rising to 32% in London and 50% in Amsterdam


TELL YOUR CHILDREN
THE TRUTH ABOUT
MARIJUANA, MENTAL ILLNESS,
AND VIOLENCE
ALEX BERENSON

National Homicide Enquiry, 2018

Table 15: Patient homicide in England: primary diagnosis and history of alcohol and/or drug misuse

Primary diagnosis	History of alcohol misuse	History of drug misuse	History of alcohol and/or drug misuse	No history of alcohol or drug misuse
Schizophrenia (& other delusional disorders)	141 (71%)	164 (83%)	174 (87%)	25 (13%)
Affective disorder	41 (61%)	32 (48%)	45 (67%)	22 (33%)
Personality disorder	61 (85%)	62 (87%)	67 (92%)	6 (8%)
All patients	**417 (71%)**	**457 (77%)**	**515 (86%)**	**81 (14%)**

Almost half of all patients with schizophrenia misused cannabis (90, 49% excluding unknowns), or misused alcohol (93, 48%), whilst 61 (33%) misused stimulants.

How Cannabis Causes Paranoia: Using the Intravenous Administration of Δ^9-Tetrahydrocannabinol (THC) to Identify Key Cognitive Mechanisms Leading to Paranoia

Daniel Freeman[*,1], Graham Dunn[2], Robin M. Murray[3], Nicole Evans[1], Rachel Lister[1], Angus Antley[1], Mel Slater[4,5], Beata Godlewska[1], Robert Cornish[6], Jonathan Williams[7], Martina Di Simplicio[8], Artemis Igoumenou[9], Rudolf Brenneisen[10], Elizabeth M. Tunbridge[1], Paul J. Harrison[1], Catherine J. Harmer[1], Philip Cowen[1], and Paul D. Morrison[3]

THC significantly increased paranoia, negative affect (anxiety, worry, depression, negative thoughts about the self), and a range of anomalous experiences, and reduced working memory capacity. In this largest study of intravenous THC, it was definitively demonstrated that the drug triggers paranoid thoughts in vulnerable individuals.

Cannabis use and violence in patients with severe mental illnesses: A meta-analytical investigation

Laura Dellazizzo[a,b,c], Stéphane Potvin[a,b], Mélissa Beaudoin[a,b,c], Mimosa Luigi[a,b,c], Bo Yi Dou[a], Charles-Édouard Giguère[a], Alexandre Dumais[a,b,c,*]

[a] *Centre de recherche de l'Institut Universitaire en Santé Mentale de Montréal, Montreal, Canada*
[b] *Department of Psychiatry and Addictology, Faculty of Medicine, Université de Montréal, Montreal, Canada*
[c] *Institut national de psychiatrie légale Philippe-Pinel, Montreal, Canada*

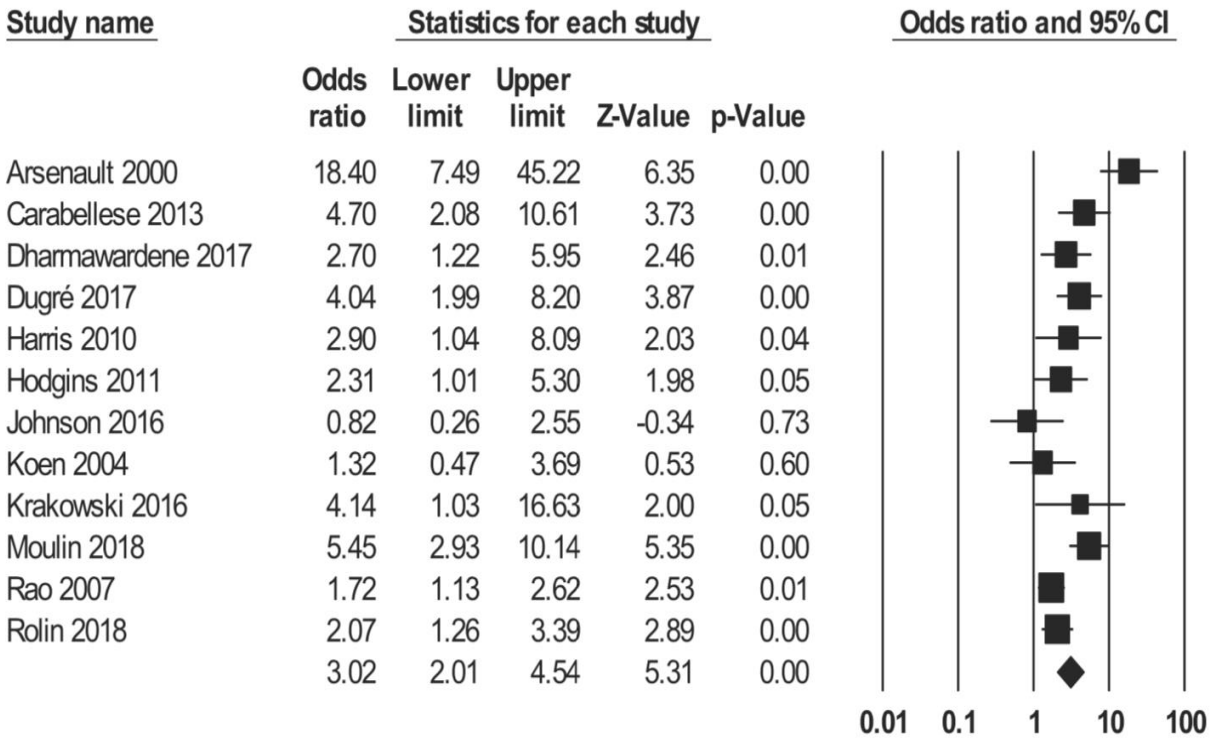


Fig. 3. Forest plot of the association between cannabis use and violence in patients with severe mental illnesses.

121 schizotypal individuals were randomised to receive THC or placebo

Mean (S.D.) Paranoia Score

after Placebo 6.8 (9.8)

after THC 15.6 (17.3)

Dan Freeman et al, Schiz Bull, 2014

Cannabis use and violence in patients with severe mental illnesses: A meta-analytical investigation

Laura Dellazizzo[a,b,c], Stéphane Potvin[a,b], Mélissa Beaudoin[a,b,c], Mimosa Luigi[a,b,c], Bo Yi Dou[a], Charles-Édouard Giguère[a], Alexandre Dumais[a,b,c,*]

[a] *Centre de recherche de l'Institut Universitaire en Santé Mentale de Montréal, Montreal, Canada*
[b] *Department of Psychiatry and Addictology, Faculty of Medicine, Université de Montréal, Montreal, Canada*
[c] *Institut national de psychiatrie légale Philippe-Pinel, Montreal, Canada*

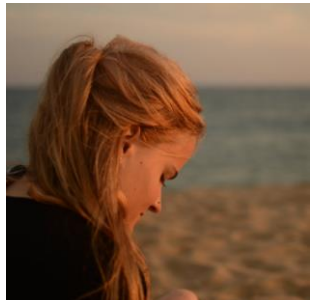
The OR from the pooled 12 studies was 3.02 (CI = 2.01–4.54) The risk of violence was significantly higher for cannabis use disorder (OR = 5.08, CI = 3.27–10.28) in comparison to cannabis use (OR = 2.04, CI = 1.36–3.05).

Outcome and treatment

Continued Versus Discontinued Cannabis Use in Patients with Psychosis

Continued cannabis use after onset of psychosis predicts adverse outcome, including higher relapse rates, longer hospital admissions, and more severe positive symptoms than for individuals who discontinue cannabis use and those who are non-users.


Continued versus discontinued cannabis use in patients with psychosis: a systematic review and meta-analysis



Cannabis and Psychosis Clinic- Psychosocial Treatment

Ceasing or Reducing use are the targets; failing that moving to less potent types

Limited evidence concerning effective psychosocial interventions to reduce cannabis use in people with early psychosis

Motivational interviewing (MI) has some limited support in reducing cannabis use in general

CBT combined with MI

Contingency management - bribery


CAUSES DELUSIONS, HALLUCINATIONS...
Peter Brookes
21 iii 19
HAVE A TOKE!
NO DEAL
NO DEAL
NO DEAL
NO DEAL