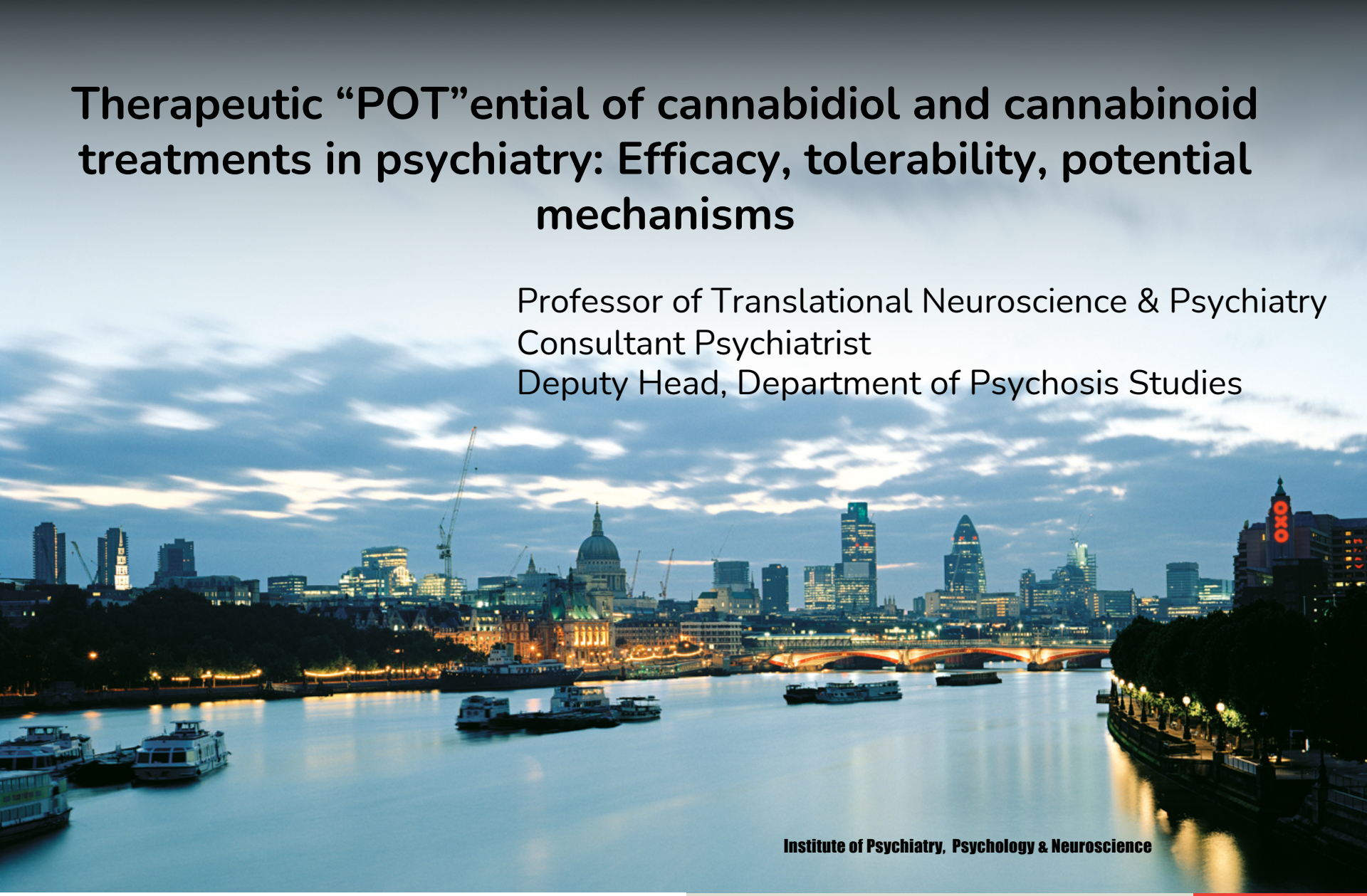
Therapeutic “POT”ential of cannabidiol and cannabinoid treatments in psychiatry: Efficacy, tolerability, potential mechanisms

Professor of Translational Neuroscience & Psychiatry
Consultant Psychiatrist
Deputy Head, Department of Psychosis Studies



Institute of Psychiatry, Psychology & Neuroscience

KING'S HEALTH PARTNERS

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Disclosures

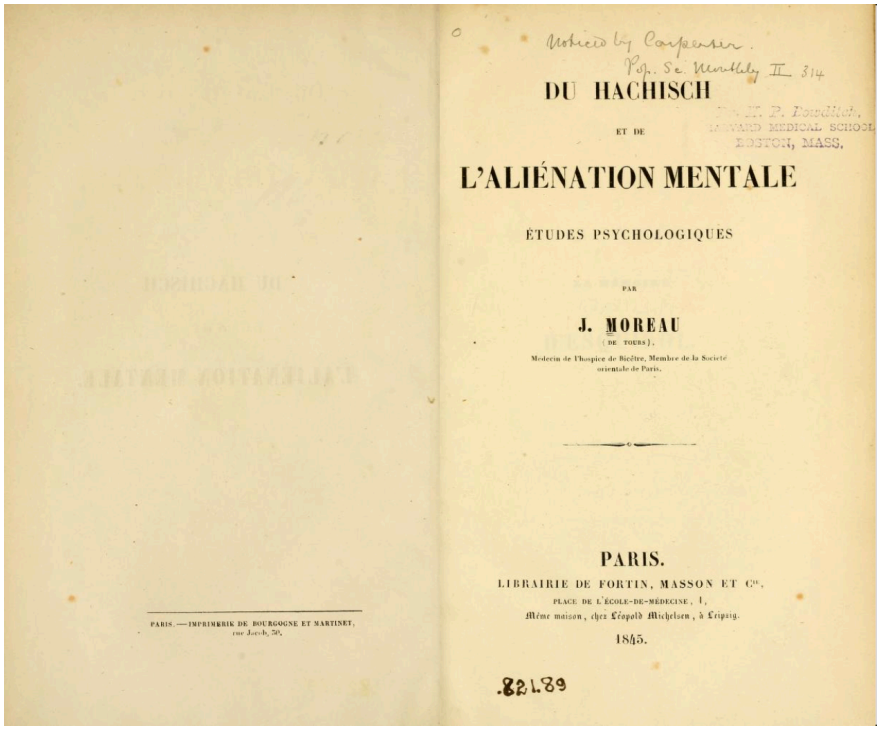
- **Views expressed herein do not represent the views of KCL or my funders**
- My research has been supported by grants from the Medical Research Council, UK; NIHR, UK; Wellcome trust; European Commission; Dowager Countess Eleanor Peel trust; Psychiatry Research trust; Parkinson's UK; Rosetrees Trust; Alzheimer's Research UK.
- Have participated in advisory boards for or received honoraria as a speaker from Reckitt Benckiser, EmpowerPharm/SanteCannabis and Britannia Pharmaceuticals. All of these honoraria were received as contributions toward research support through King's College London, and not personally.
- Collaborated with Beckley Canopy Therapeutics/ Canopy Growth (investigator-initiated research) and ongoing collaboration with NW PharmaTech Ltd.

Outline

- Caveat
- What (mechanisms) might underlie the therapeutic potential of cannabidiol (CBD)?
- How effective is CBD as treatment for psychosis and potentially anxiety?
- How well are CBD (and other CBMs) tolerated as a treatment?

Different Strains - Different Effects

- Cannabis for pain relief- Chinese have been using from 3rd Millennium BCE (Mechoulam, 1986)
- Bhang (Cannabis drink) for the relief of anxiety- known in India from 1st Millennium BCE
- Jacques-Joseph Moreau



Noticed by Carpenter.
Pop. Sc. Monthly II 314

DU HACHISCH

ET DE

L'ALIÉNATION MENTALE

ÉTUDES PSYCHOLOGIQUES

PAR

J. MOREAU

(DE TOURS),

Médecin de l'hospice de Bicêtre, Membre de la Société orientale de Paris.

PARIS.

LIBRAIRIE DE FORTIN, MASSON ET Cie,

PLACE DE L'ÉCOLE-DE-MÉDECINE, 1,

Même maison, chez Léopold Michelsen, à Leipzig.

1845.

.82L89

PARIS. — IMPRIMERIE DE BOURGOGNE ET MARTINET,

Perhaps a familiar experience for many clinicians !

The question here is not so much why are people inclined to use drugs. Joe333, You are assuming people that use drugs are already more inclined to suffer a psychotic episode, which is in fact never been proved. The question is if there is a relation between light drugs consumption and the posterior development of psychosis. Lets assume that some people are more propense to develop some kind of psychosis than others, which is already a big assumption. If you are somehow inclined to develop mental disorders and you frequently and excessively take psychoactive substances, even coffee can trigger panic attacks. I was a friendly happy kid. As many do, i started smoking light drugs at 16. By 21, I used to smoke 10 joints a day when a similar thing happened. I had to level up, i stopped smoking drugs and did medication (risperidone) for 2 years. i Drank alchool and the paranoia did not return. 5 years later i decided to smoke weed again routinely, and after half a year: bam! Panic attacks and paranoia again. I have met many potheads that have experienced similar things.
I'm not saying weed will make you go nuts but i am saying, do take care. With perception and emotions, when things get blurry it's

"….I was a friendly happy kid. As many do, i started smoking light drugs at 16. By 21, I used to smoke 10 joints a day when a similar thing happened. I had to level up, i stopped smoking drugs and did medication (risperidone) for 2 years. I drank alcohol and the paranoia did not return. 5 years later i decided to smoke weed again routinely, and after half a year: bam! Panic attacks and paranoia again. I have met many potheads that have experienced similar things……"

-Vice News

Psychiatry Research 331 (2024) 115626

Contents lists available at ScienceDirect

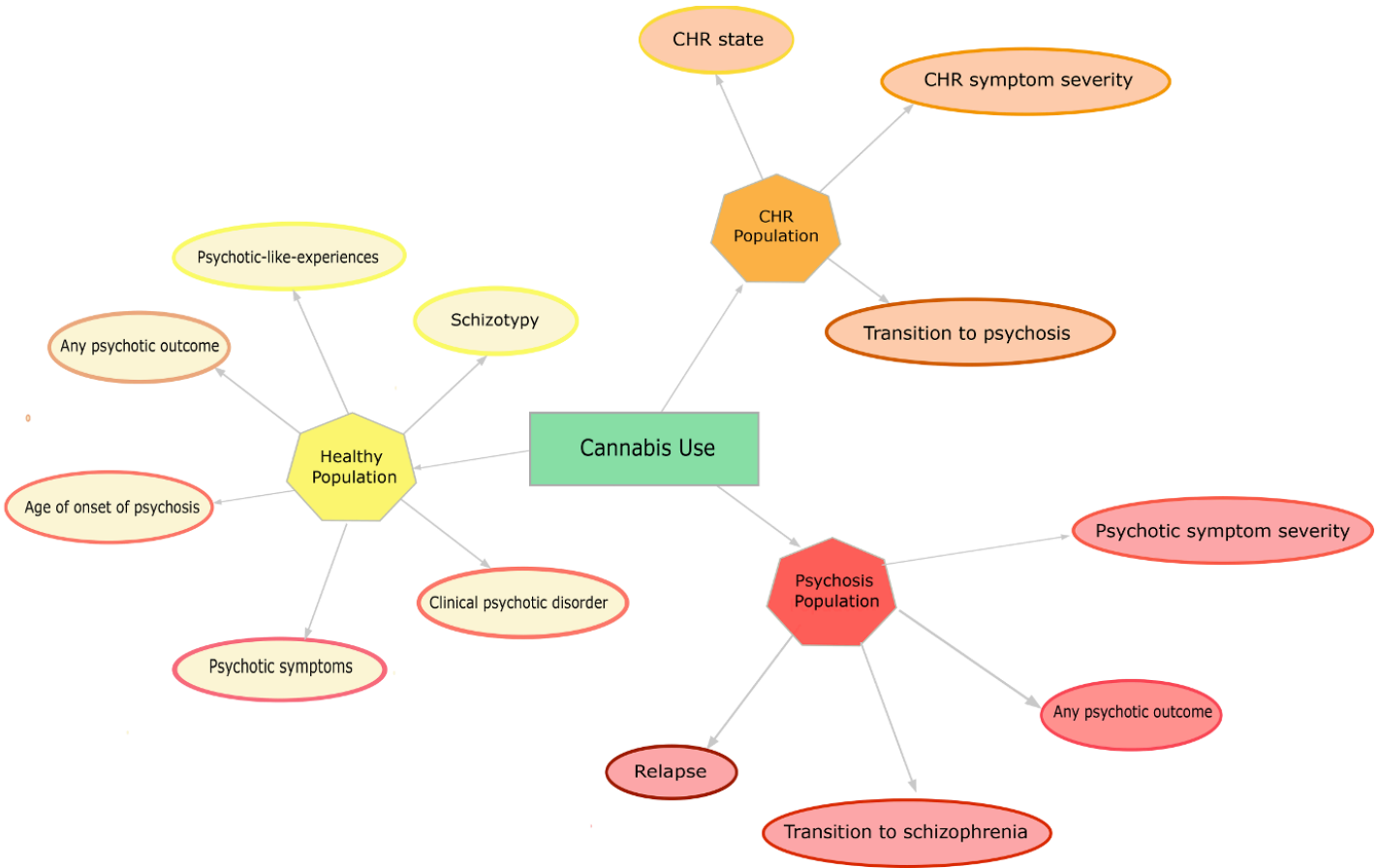
Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Review article

A systematic evidence map of the association between cannabis use and psychosis-related outcomes across the psychosis continuum: An umbrella review of systematic reviews and meta-analyses

Johanna Manja Groening, Emma Denton, Rimsha Parvaiz, David Losada Brunet, Aisha Von Daniken, Yiling Shi, Sagnik Bhattacharyya *



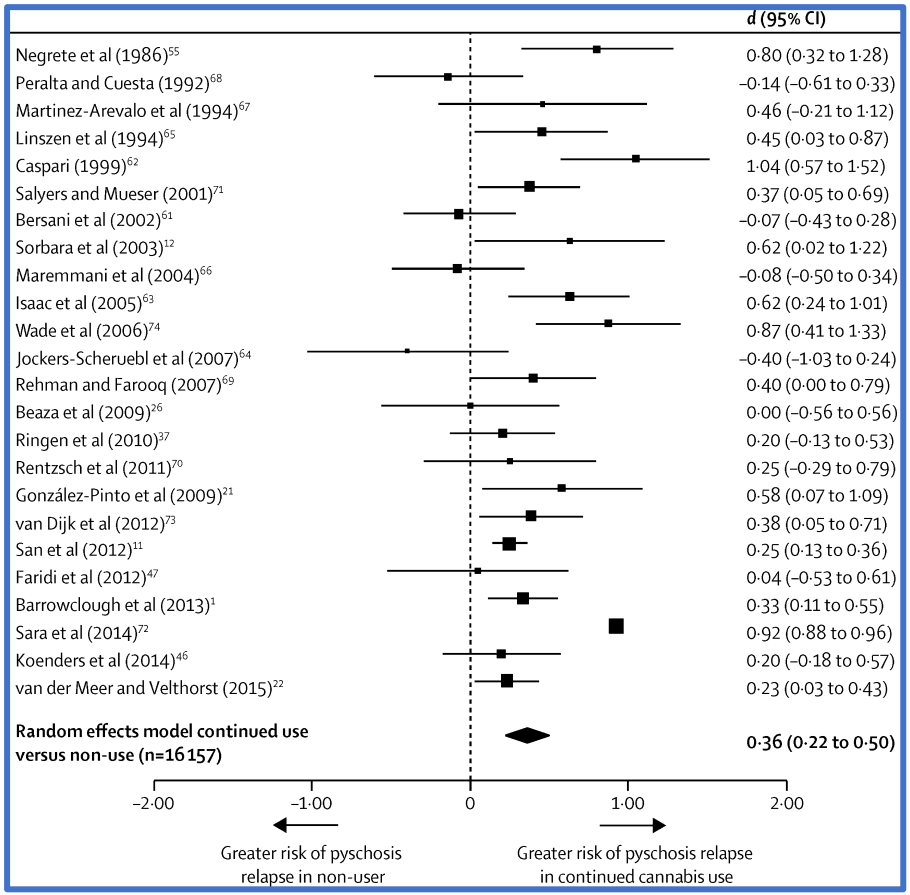
Continued versus discontinued cannabis use in patients with psychosis: a systematic review and meta-analysis

Tabea Schoeler, Anna Monk, Musa B Sami, Ewa Klamerus, Enrico Foglia, Ruth Brown, Giulia Camuri, A Carlo Altamura, Robin Murray, Sagnik Bhattacharyya

Summary

Background Although the link between cannabis use and development of psychosis is well established, less is known about the effect of continued versus discontinued cannabis use after the onset of psychosis. We aimed to summarise available evidence focusing on the relationship between continued and discontinued cannabis use after onset of psychosis and its relapse.

Lancet Psychiatry 2016
Published Online
January 14, 2016
http://dx.doi.org/10.1016/S2215-0366(15)00363-6



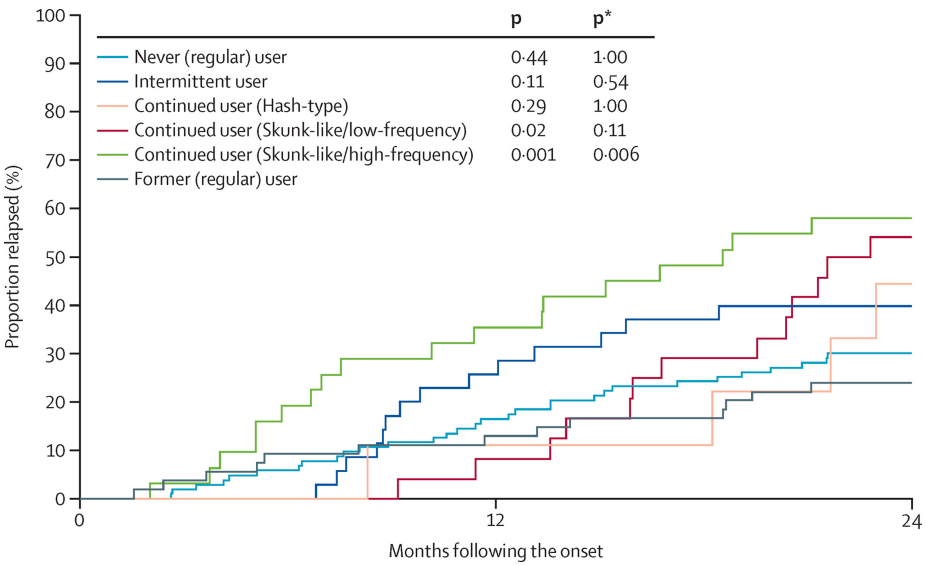
Effects of continuation, frequency, and type of cannabis use on relapse in the first 2 years after onset of psychosis: an observational study

Tabea Schoeler, Natalia Petros, Marta Di Forti, Ewa Klamerus, Enrico Foglia, Olesya Ajnakina, Charlotte Gayer-Anderson, Marco Colizzi, Diego Quattrone, Irena Behlke, Sachin Shetty, Philip McGuire, Anthony S David, Robin Murray, Sagnik Bhattacharyya

Summary

Background Although cannabis use after a first episode of psychosis has been associated with relapse, little is known about the determinants of this most preventable risk factor for relapse of psychosis. Here we aimed to study whether

Lancet Psychiatry 2016; 3: 947–53



Continued heavy skunk user vs former user: OR 3·28

Joe333 · 8 months ago

"he wrote that the results "all but eliminate the possibility that pre-existing group differences between users and non-users account for the differences in observed outcomes.""

What a crackpot. It doesn't do that at all. People who use drugs often do it to cope with problems. This is incredibly basic. I guarantee you could do the same study for any drug including alcohol or even tobacco. Patients who continued using drugs are statistically more likely to have any kind of problem than people who stopped using drugs. .

23 ^ | v · Reply · Share ›

"….What a crackpot. People who use drugs often do it to cope with problems. You would find the effect for any drug……."

"…….This is like saying park benches cause homelessness. Or that tall buildings cause terrorism……."

-***Vice News***

JAMA Psychiatry | Original Investigation

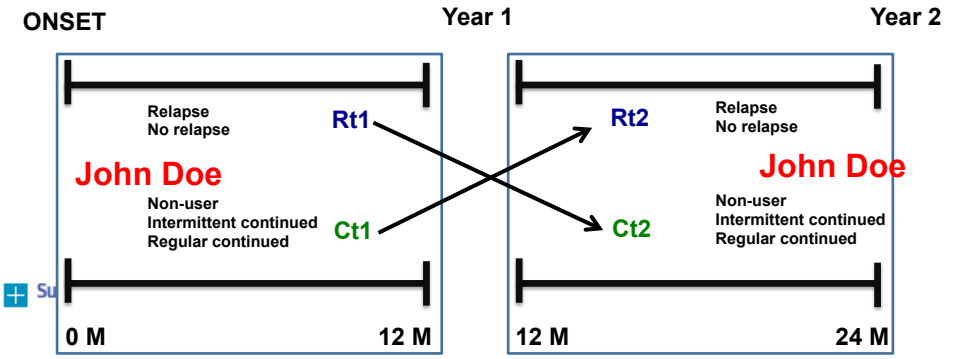
2016;73(11):1173-1179

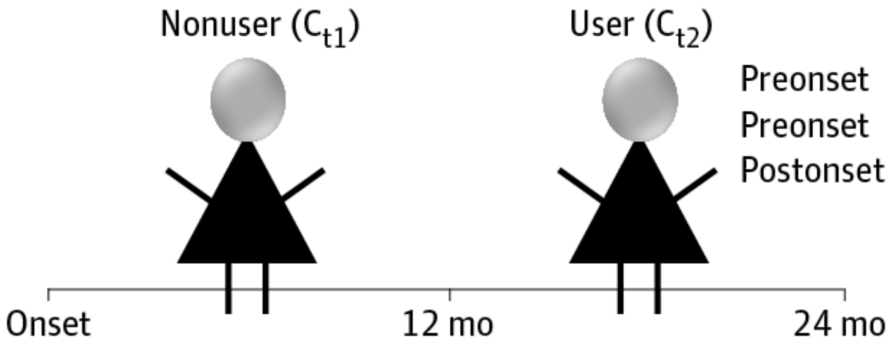
Association Between Continued Cannabis Use and Risk of Relapse in First-Episode Psychosis

A Quasi-Experimental Investigation Within an Observational Study

Tabea Schoeler, MSc; Natalia Petros, MSc; Marta Di Forti, PhD; Jean-Baptiste Pingault, PhD; Ewa Klamerus, BSc; Enrico Foglia, BSc; Amanda Small, BSc; Robin Murray, FRS; Sagnik Bhattacharyya, PhD

IMPORTANCE Cannabis use after first-episode psychosis is associated with poor outcomes, but the causal nature of this association is unclear.





Preonset Genetic profile: 100%
Preonset Environment: 100%
Postonset Time-varying environment: 0%

Association of cannabis use and psychosis relapse unlikely because of shared predisposition increasing the risk of both

Cannabis use status and pattern of use after onset of psychosis predict subsequent relapse but not vice versa.

Developmental sensitivity to cannabis use patterns and risk for major depressive disorder in mid-life: findings from 40 years of follow-up

Tabea Schoeler[1,*], Delphine Theobald[2,*], Jean-Baptiste Pingault[1], David P. Farrington[3], Jeremy W. Coid[4] and Sagnik Bhattacharyya[5]

***Psychological Medicine* 2018; 48, 2169-2176**

	OR	95% CI	*p*
Multiple logistic regression (N = 284)			
Cannabis late onset – low frequency	0.68	0.10–2.65	0.63
Cannabis late onset – high frequency	2.23	0.26–14.94	0.42
Cannabis early onset – low frequency	2.41	1.22–4.76	**0.01**
Cannabis early onset – high frequency	8.83	1.29–70.79	**0.03**

	Univariate			Multivariate[a]		
	OR	95% CI	*p*	OR	95% CI	*p*
Effect of cannabis frequency on MDD in young adolescence (age 18–32)						
Cannabis frequency (age 14–18)	1.08	(1.04–1.13)	**0.0002**	1.08	(1.03–1.12)	**0.0008**
Cannabis frequency (age 18–32)	1.02	(1.00–1.05)	0.07	1.01	(0.99–1.05)	0.32
Effect of cannabis frequency on MDD in adulthood (age 32–48)						
Cannabis frequency (age 14–18)	1.22	(1.12–1.33)	**<0.0001**	1.20	(1.10–1.31)	**<0.0001**
Cannabis frequency (age 18–32)	1.07	(1.02–1.13)	**0.007**	1.05	(0.99–1.11)	0.10
Cannabis frequency (age 32–48)	1.04	(0.99–1.09)	0.17	1.01	(0.95–1.07)	0.76
	Univariate			Multivariate[a]		
	Est.	95% CI		Est.	95% CI	
Effect of MDD on cannabis frequency in adulthood (age 32–48)						
MDD (age 18–32)	0.77	(0.59–0.99)	**0.05**	0.72	(0.57–0.92)	**0.009**
MDD (age 32–48)	1.07	(0.94–1.21)	0.33	1.02	(0.90–1.15)	0.77

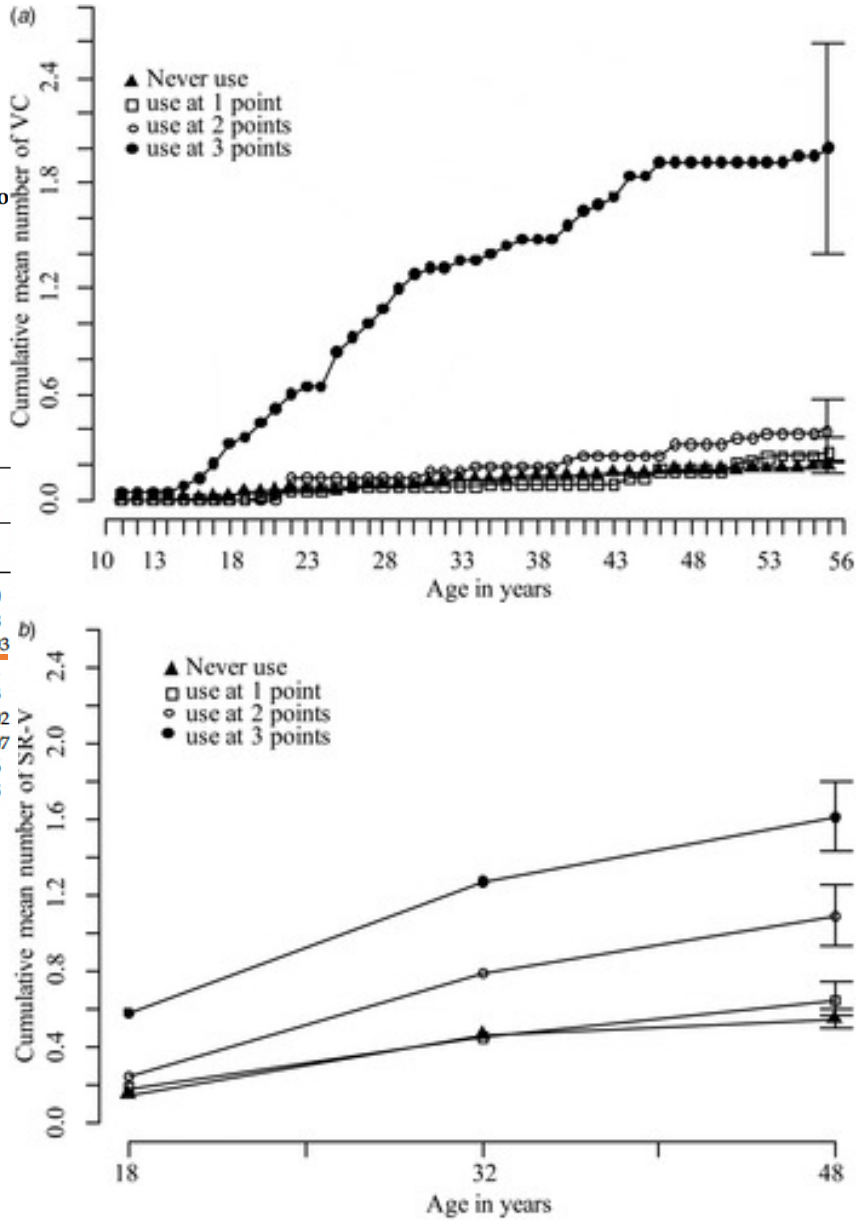
Psychological Medicine, Page 1 of 15. © Cambridge University Press 2016
doi:10.1017/S0033291715003001

ORIGINAL ARTICLE

Continuity of cannabis use and violent offending over the life course

T. Schoeler[1]†, D. Theobald[1,2]†, J.-B. Pingault[3], D. P. Farrington[4], W. G. Jennings[5], A. R. Piquero[6], J. W. Coid[7] and S. Bhattacharyya[1]*

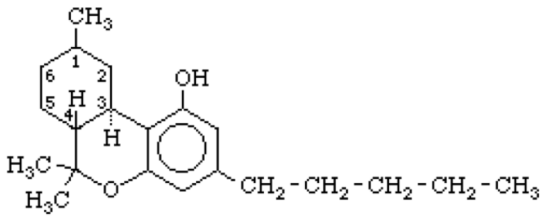
	Risk of VC (n = 327)[a]		Risk of SR-V (n = 332)	
Multivariate logistic regression	OR (95% CI)	p	OR (95% CI)	p
Cannabis use at one time point[d]	0.91 (0.31–2.38)	0.85	1.08 (0.59–1.98)	0.80
Cannabis use at two time points	1.91 (0.60–5.68)	0.25	2.26 (0.93–5.79)	0.08
Cannabis use at three time points	7.08 (2.19–23.59)	0.001	8.94 (2.37–46.21)	0.003
Antisocial personality, yes[e]	3.43 (1.59–7.52)	0.002	2.15 (1.19–3.91)	0.01
Family history of crime, yes[e]	2.51 (1.22–5.22)	0.01	1.38 (0.82–2.33)	0.23
Alcohol use[f]	1.34 (0.90–1.97)	0.14	1.65 (1.21–2.27)	0.002
Cigarette use[f]	1.36 (0.97–1.91)	0.07	1.40 (1.10–1.79)	0.007
Other illicit drug use, yes[e]	1.88 (0.59–5.71)	0.27	0.79 (0.26–2.34)	0.66
Low social class, yes[e]	2.05 (0.90–4.55)	0.08	1.35 (0.72–2.52)	0.35



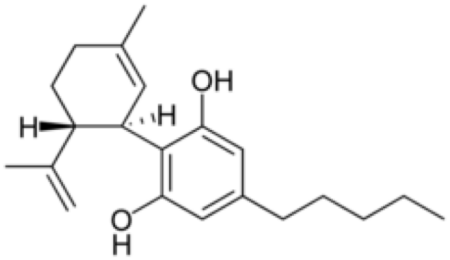
What (mechanisms) might underlie the therapeutic potential of cannabidiol (CBD)?

Different Strains - Different Effects

Extract of the cannabis plant has over 150 different cannabinoids



Delta-9-tetrahydrocannabinol (THC)



Cannabidiol (CBD)

What do they do?

- THC can induce psychotic symptoms and impair memory *(D'Souza et al., 2004, Bhattacharyya et al., 2009)* in healthy individuals; worsen them in Schizophrenia *(D'Souza et al., 2005)*
- CBD does not induce psychotic symptoms (*Bhattacharyya et al., 2009)* may have anxiolytic (*Crippa et al., 2004*) and possible antipsychotic effects (*Zuardi et al., 2006*)
- CBD does not impair memory (*Fadda et al., 2004; Ilan et al.l, 2005*); may have neuroprotective effects (*Mechoulam et al, 2002; Lastres-Becker et al., 2005*)

Why cannabidiol?

Neuropsychopharmacology (2010) 35, 764–774

www.neuropsychopharmacology.org

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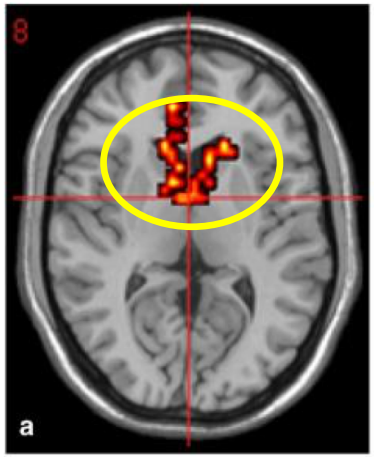
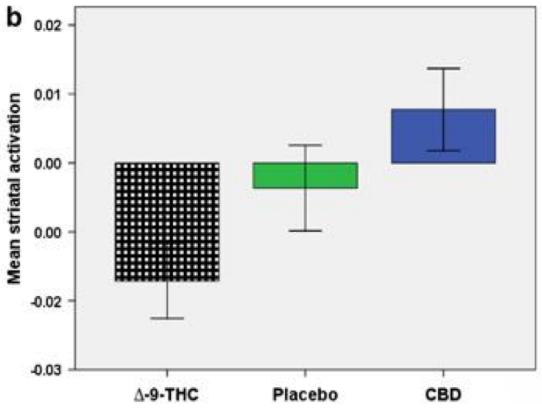
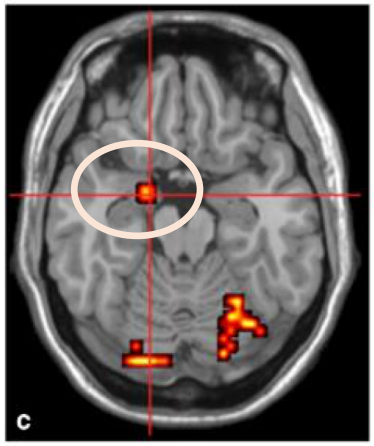
Opposite Effects of Δ-9-Tetrahydrocannabinol and Cannabidiol on Human Brain Function and Psychopathology

Sagnik Bhattacharyya[1], Paul D Morrison[2], Paolo Fusar-Poli[1,3], Rocio Martin-Santos[1,4], Stefan Borgwardt[1,5],

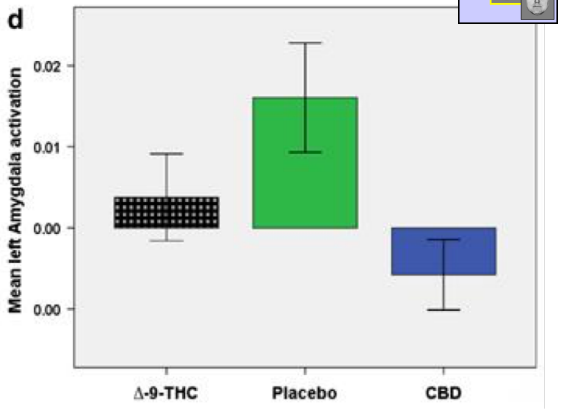
Memory



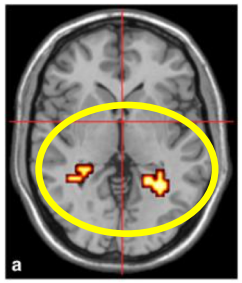


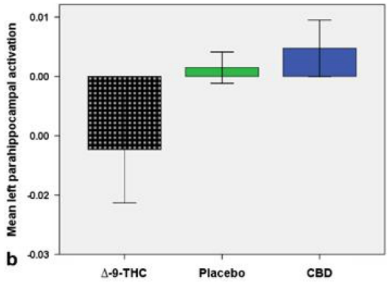


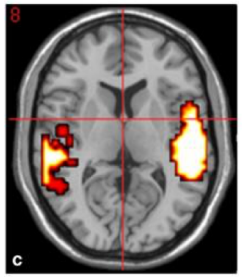
Anxiety

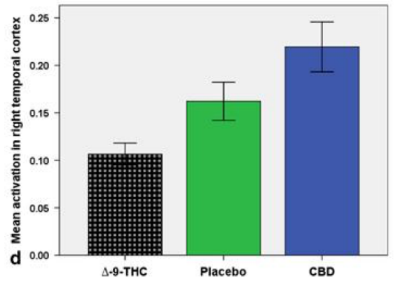


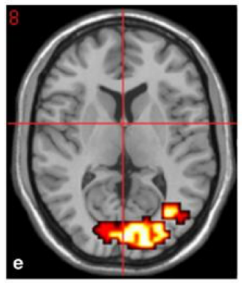
Go/ No-Go

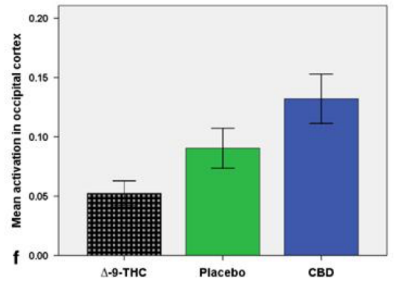


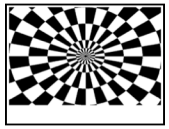




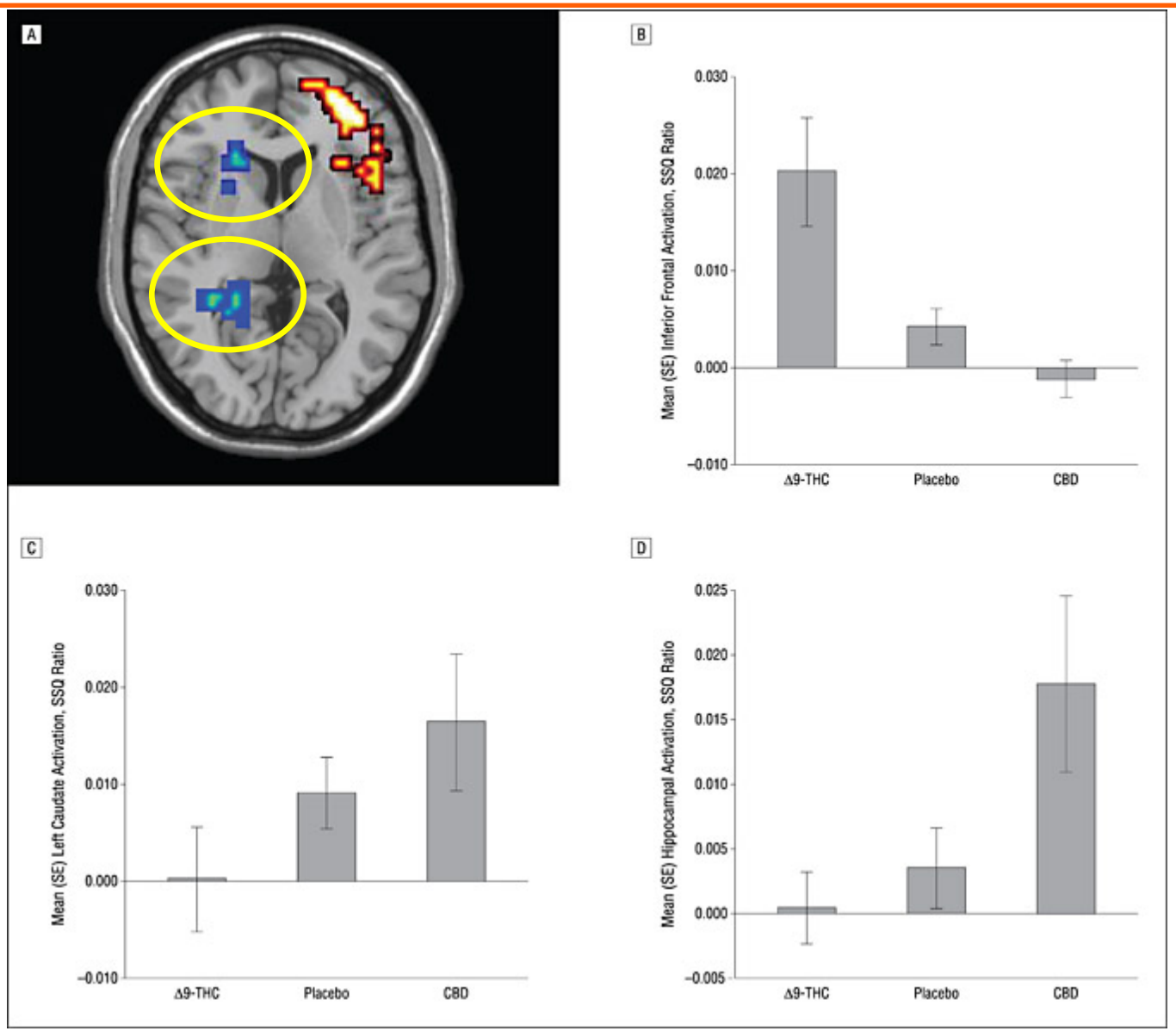








Opposite effects of delta-9-THC & CBD during salience processing



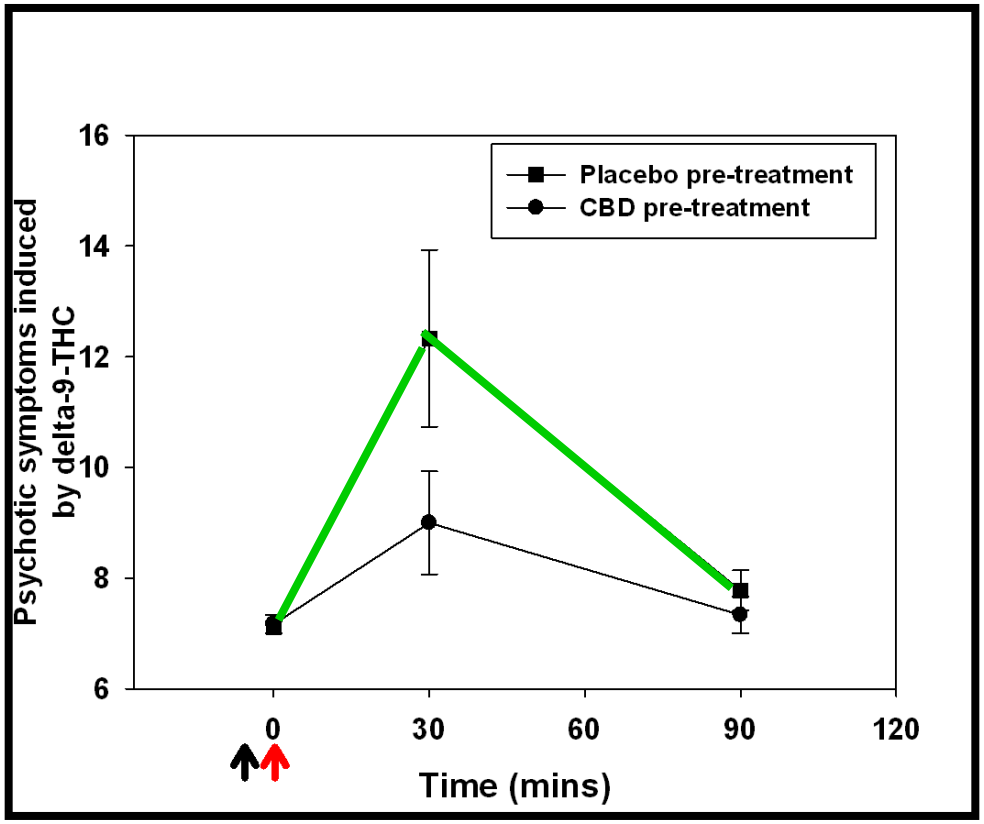
ARCHIVES OF GENERAL PSYCHIATRY

Bhattacharyya, S. et al. 2012; 69(1):27-36.

www.neuropsychopharmacology.org

Opposite Effects of Δ-9-Tetrahydrocannabinol and Cannabidiol on Human Brain Function and Psychopathology

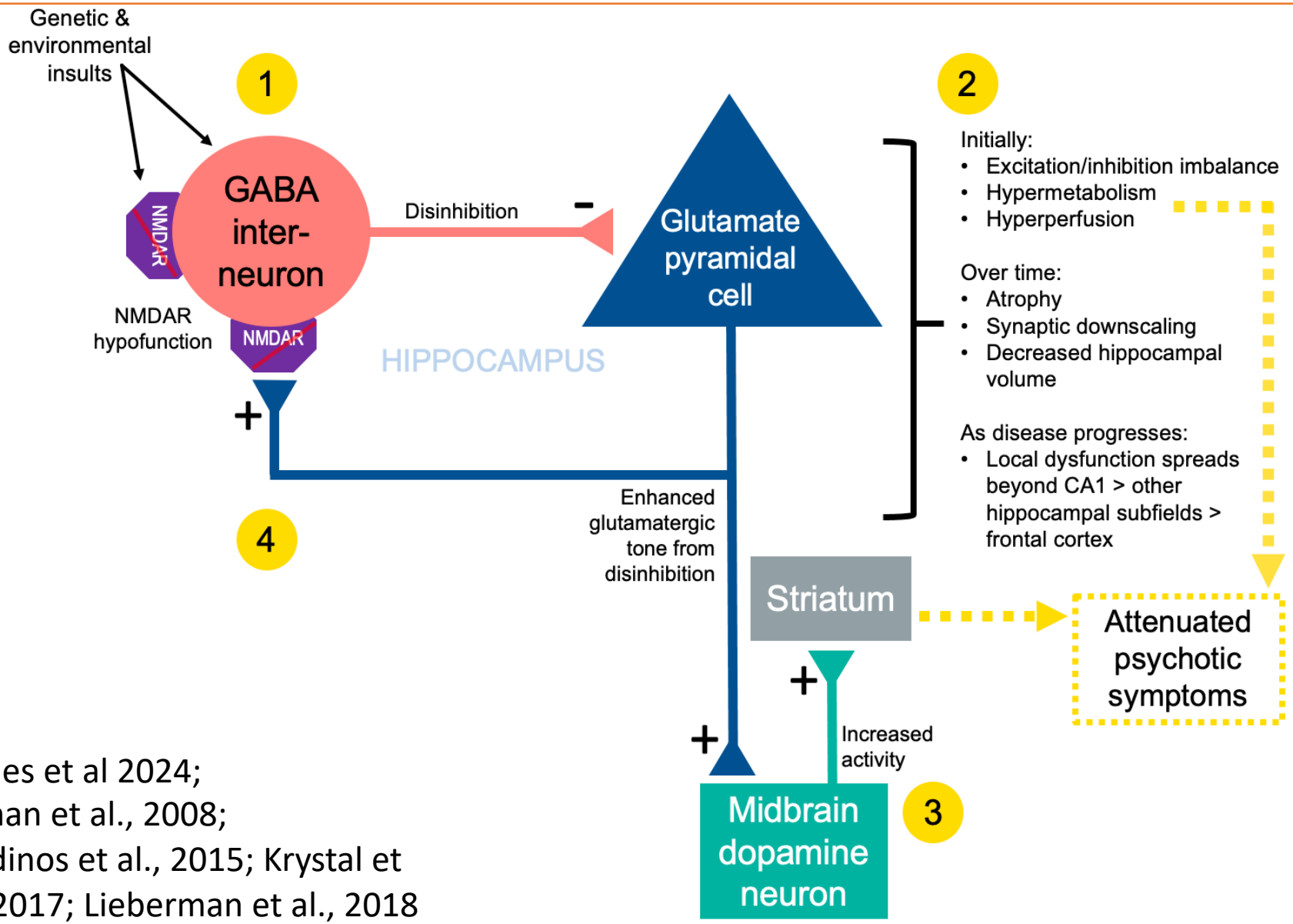
Sagnik Bhattacharyya[1], Paul D Morrison[2], Paolo Fusar-Poli[1,3], Rocio Martin-Santos[1,4], Stefan Borgwardt[1,5],



- CBD has some effects on brain function and psychotic symptoms in **healthy individuals** that are opposite to those of the psychotomimetic effects of delta-9-THC and its neural underpinnings

- *Does CBD also target brain regions implicated in schizophrenia and are these effects consistent with its antipsychotic and/or anti-anxiety potential*

Medial temporal dysfunction in the pathophysiology of Psychosis onset- a simplified schematic



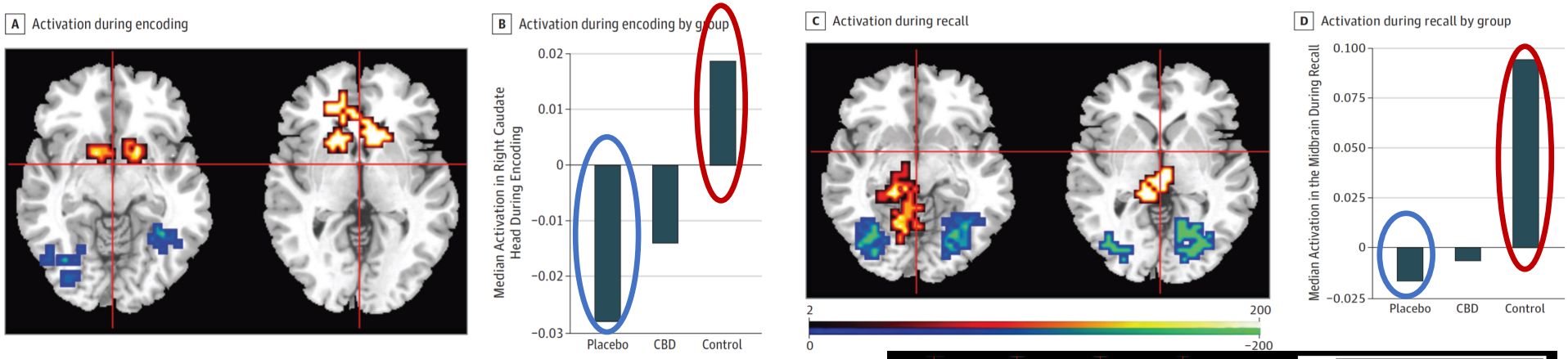
Davies et al 2024;
Lisman et al., 2008;
Modinos et al., 2015; Krystal et al., 2017; Lieberman et al., 2018

Acute effect of CBD treatment on brain activation in patients with established psychosis and those at clinical high-risk

JAMA Psychiatry | Original Investigation

Effect of Cannabidiol on Medial Temporal, Midbrain, and Striatal Dysfunction in People at Clinical High Risk of Psychosis
A Randomized Clinical Trial

Sagnik Bhattacharyya, MBBS, MD, PhD; Robin Wilson, MBBS, MRCPsych; Elizabeth Appiah-Kusi, MSc; Aisling O'Neill, MSc; Michael Brammer, PhD; Jesus Perez, MBBS, MD, PhD; Robin Murray, DSc, FRCPsych, FRS; Paul Allen, PhD; Matthijs G. Bossong, PhD; Philip McGuire, MD, PhD, FRCPsych



Psychological Medicine

cambridge.org/psm

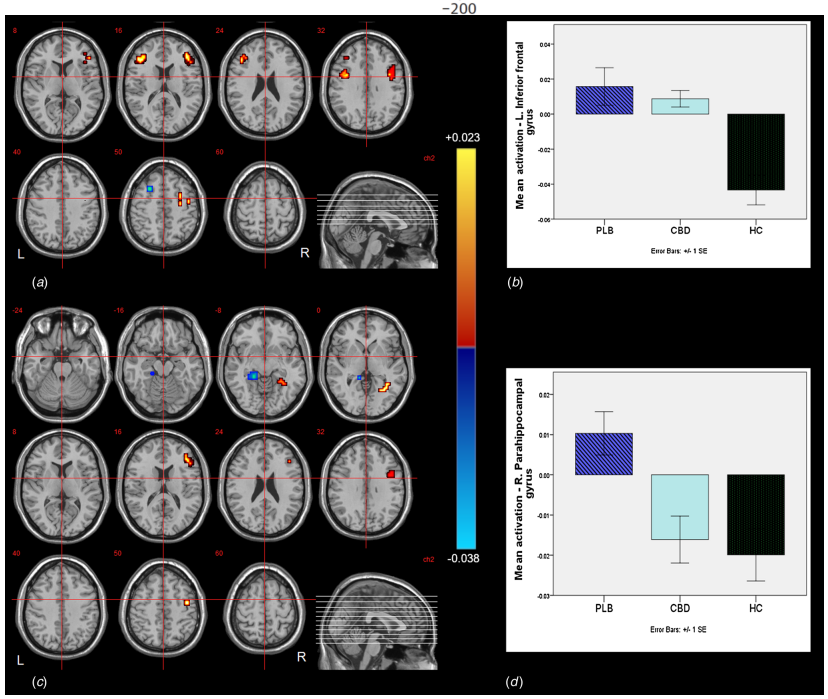
Normalization of mediotemporal and prefrontal activity, and mediotemporal-striatal connectivity, may underlie antipsychotic effects of cannabidiol in psychosis

Original Article

Cite this article: O'Neill A, Wilson R, Blest-Hopley G, Annibale L, Colizzi M, Brammer M, Giampietro V, Bhattacharyya S (2020). Normalization of mediotemporal and prefrontal activity, and mediotemporal striatal connectivity, may underlie antipsycho effects of cannabidiol in psychosis. *Psychological Medicine* 1–11. https://d 10.1017/S0033291719003519

Aisling O'Neill[1], Robin Wilson[1], Grace Blest-Hopley[1], Luciano Annibale[1], Marco Colizzi[1,2], Mick Brammer[3], Vincent Giampietro[3] and Sagnik Bhattacharyya[1]

[1]Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London,



Hippocampal- striatal connectivity:
PLB>HC
CBD<PLB

Psychological Medicine

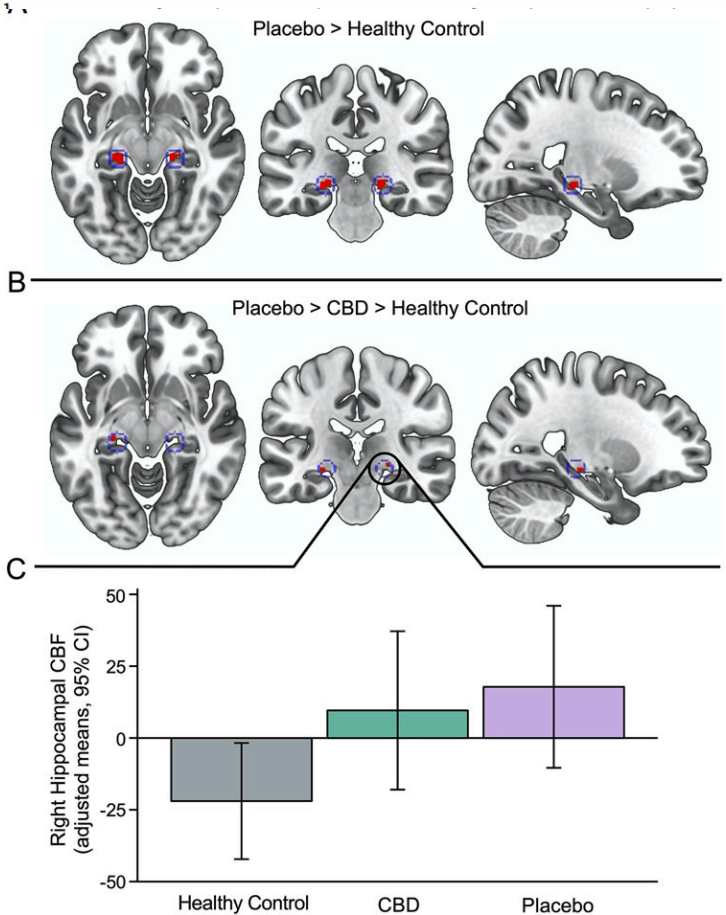
cambridge.org/psm

Increased hippocampal blood flow in people at clinical high risk for psychosis and effects of cannabidiol

Cathy Davies[1,2], Matthijs G Bossong[3], Daniel Martins[2,4], Robin Wilson[1], Elizabeth Appiah-Kusi[1], Grace Blest-Hopley[1], Fernando Zelaya[2], Paul Allen[1,2], Michael Brammer[2], Jesus Perez[5,6], Philip McGuire[7,8,9] and Sagnik Bhattacharyya[1]

Original Article

Cite this article: Davies C *et al* (2023). Increased hippocampal blood flow in people at clinical high risk for psychosis and effects of cannabidiol. *Psychological Medicine* 1–11. https://doi.org/10.1017/S0033291723002775



Effects of CBD on hippocampal glutamate in clinical high-risk

Cannabidiol modulation of hippocampal glutamate in early psychosis

Aisling O'Neill[1,2], Luciano Annibale[1], Grace Blest-Hopley[1], Robin Wilson[1], Vincent Giampietro[3] and Sagnik Bhattacharyya[1]

Psychopharm

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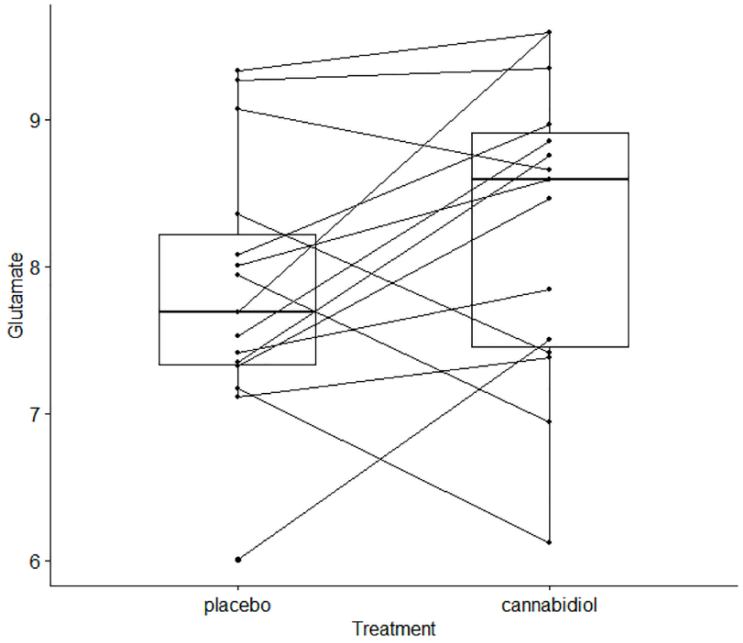
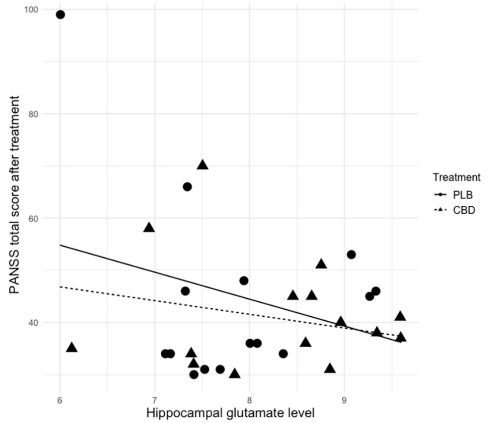
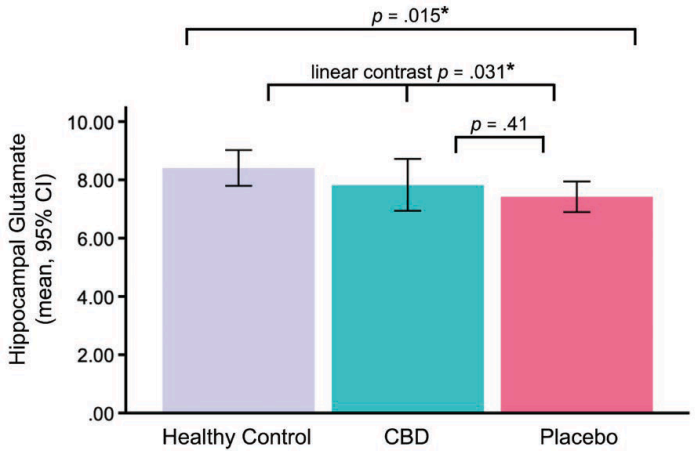
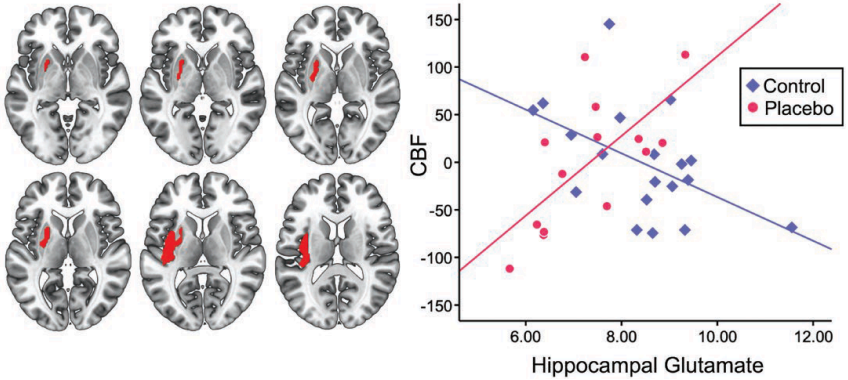




A Hippocampal Glutamate: Healthy Control > CBD > Placebo

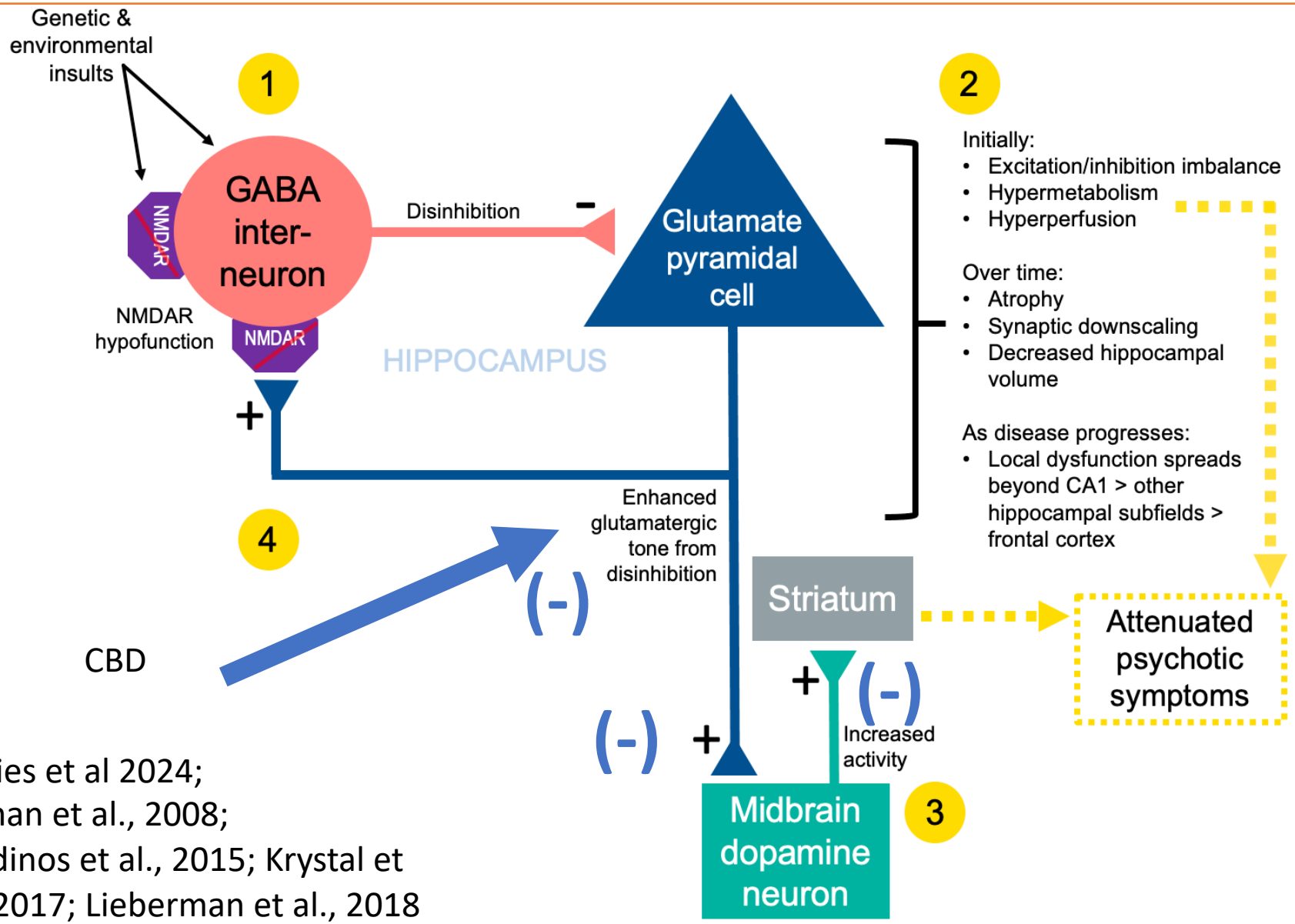


B Glutamate x CBF x Group (Placebo vs Control) Interaction



Davies et al., Schiz Bull Open 2023

Medial temporal dysfunction in the pathophysiology of Psychosis onset- a simplified schematic



Davies et al 2024;
Lisman et al., 2008;
Modinos et al., 2015; Krystal et al., 2017; Lieberman et al., 2018

Salience – Psychosis- Insula

- Aberrant attribution of salience leading to psychotic symptoms (Kapur, Corlett and others……..)
- Insula- acts as salience detector to guide behaviour
- Facilitates task-related information processing by signals to brains regions involved in attentional, working memory and higher-order cognitive processes and disengaging the default mode network to facilitate goal-directed behaviour (Uddin, 2015)
- Aberrant insular activation in Psychosis (Palaniyappan & Liddle 2012; Walter et al 2016; Thusius et al., 2018……..)

Wilson et al. *Translational Psychiatry* (2019)9:203
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Translational Psychiatry

ARTICLE Open Access

Cannabidiol attenuates insular dysfunction during motivational salience processing in subjects at clinical high risk for psychosis

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Psychological Medicine

cambridge.org/psm

Original Article

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Cannabidiol attenuates insular activity during motivational salience processing in patients with early psychosis

Brandon Gunasekera[1], Robin Wilson[1], Aisling O'Neill[1], Grace Blest-Hopley[1], Owen O'Daly[2] and Sagnik Bhattacharyya[1]

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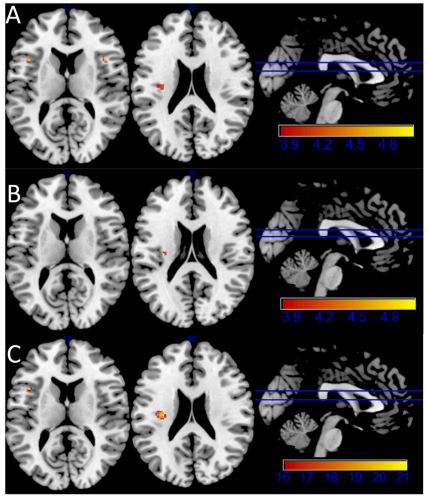
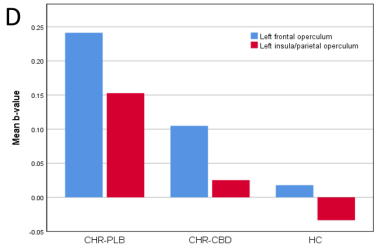
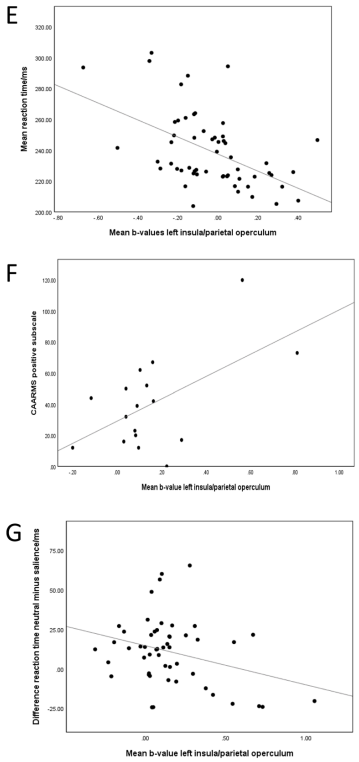
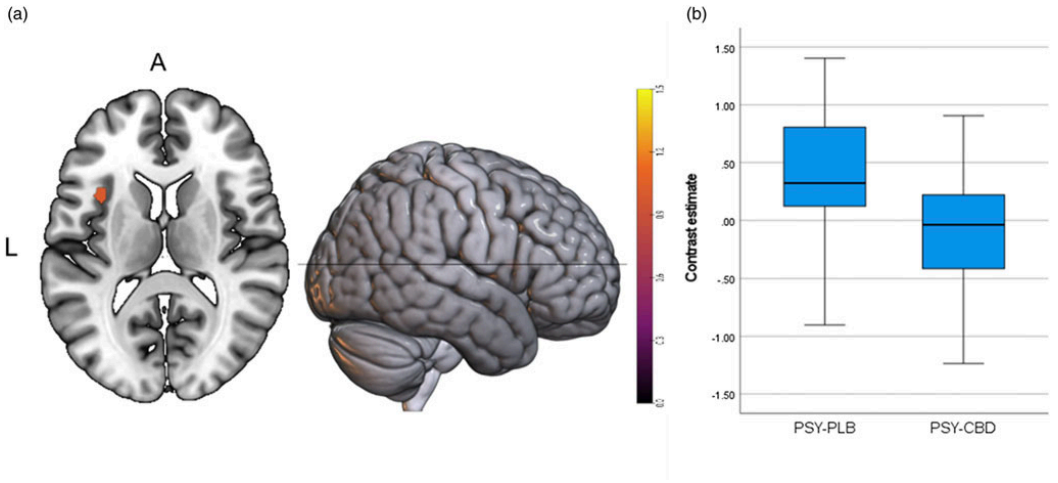








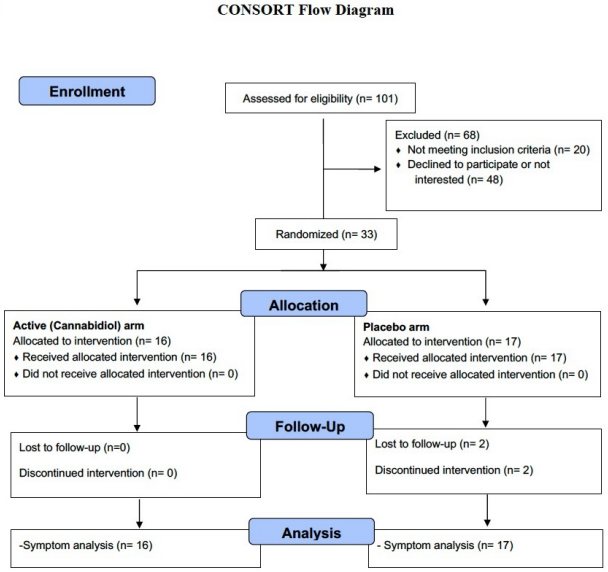
What might this mean?

- A single dose of CBD seems to modulate the key neurophysiological and neurochemical substrates that may be implicated in psychosis

- Might these effects underlie its antipsychotic potential?

How effective is CBD as treatment for psychosis and potentially anxiety related indications?

Effects of cannabidiol on symptoms in people at clinical high risk for psychosis



Sagnik Bhattacharyya[1,2], Elizabeth Appiah-Kusi[1], Robin Wilson[1], Aisling O'Neill[1], Michael Brammer[3], Steven Williams[3], Jesus Perez[4], Matthijs G. Bossong[5], Philip McGuire[6]

World Psychiatry 23:3 - October 2024

Supplementary Table 2. Clinical measures at 21 days (last observation carried forward)

Clinical Measures at 21 days (mean±SD)			
	CHR-PLB (n=17)	CHR-CBD (n=16)	*Statistics*
Total CAARMS score (change from baseline*)	174.94±105.21 (26.00±65.29)	114.88±74.37 (58.56±54.41)	$F_{1,30}$=7.168, *p= 0.012*
CAARMS positive symptoms (change from baseline*)	35.29±24.71 (7.64±12.61)	27.31±19.48 (12.87±12.89)	$F_{1,30}$=2.24, *p= 0.144*
CAARMS negative symptoms (change from baseline*)	26.59±20.08 (1.82±5.90)	16.37±11.13 (6.87±12.50)	$F_{1,30}$=4.37, *p= 0.045*
CAARMS distress (change from baseline*)	39.93±32.49 (-2.10±23.30)	26.31±24.46 (14.70±19.73)	$F_{1,30}$=4.66, *p=0.039*
PANSS total score** (change from baseline*)	48.17±15.12 (0.17±13.52)	35.91±4.72 (5.91±8.31)	$F_{1,20}$=4.71, *p=0.042*
STAI-S (change from baseline*)	42.0± 11.70 (-3.06±12.51)	42.0±10.12 (-1.69±9.94)	$F_{1,30}$=0.03, *p= 0.862*

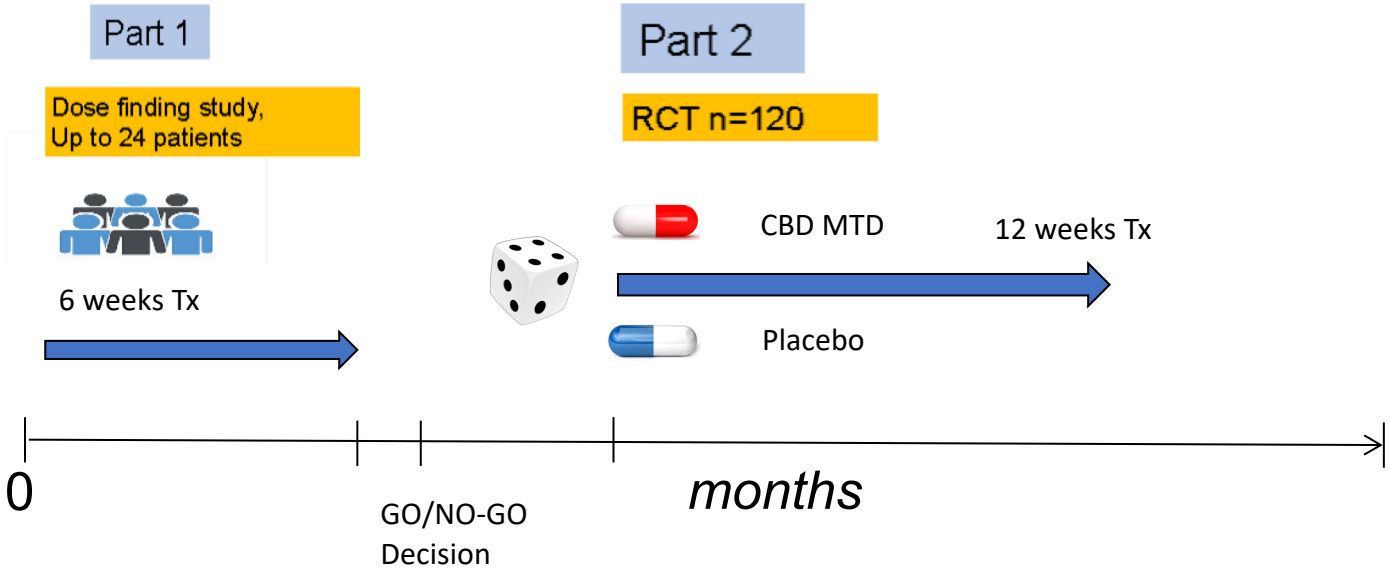
CBD: RCTs in established psychosis

- CBD (n=20; 800 mg/ day) was non-inferior to Amisulpiride (n=19) following 4 weeks treatment in patients with acute schizophrenia (Leweke et al., 2012)

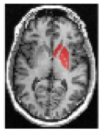
- CBD (n=43; 1000mg/day; 6 weeks) as an add-on to existing antipsychotics caused significantly greater reduction in psychotic symptoms compared to placebo (n=45) in patients with chronic psychosis (McGuire et al., 2018)

- CBD (n=21; 600mg/ day ; 6 weeks) augmentation of existing antipsychotics was associated with comparable reduction in psychotic symptoms as placebo (n=20) in chronic psychosis patients (Boggs et al., 2018)

CAN-PDP: Cannabidiol for Parkinson's disease psychosis



Part 3



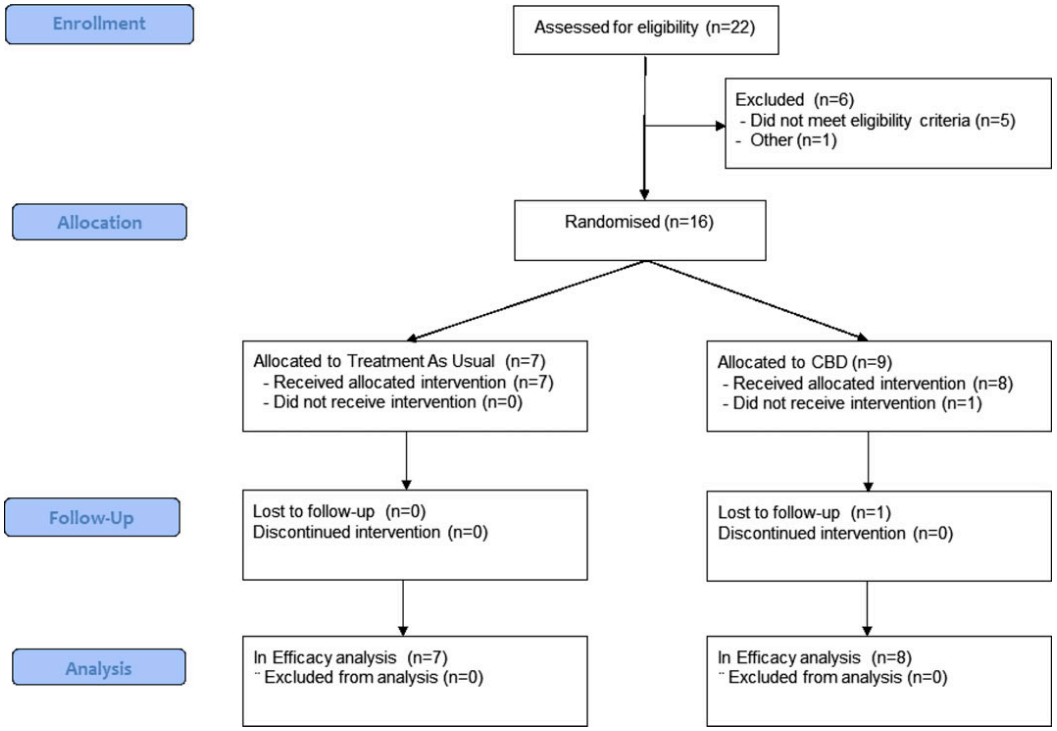
Neuroimaging component
PDP=40
PD=20
Controls=20

doi:10.1017/S1041610224000516

Cannabidiol for behavior symptoms in Alzheimer's disease (CANBiS-AD): a randomized, double-blind, placebo-controlled trial

There are currently no safe and effective approved

with the rest White Caucasians. Participants were randomly assigned to receive either oral capsules of CBD



- People with AD and behavioural and psychological symptoms of dementia
- CBD titrated to 600 mg/day; 6 weeks
- Good acceptability, compliance and retention
- CBD was well tolerated, with no serious adverse events or withdrawal.
- Non-significant reduction in anxiety and agitation under CBD.
- Change in anxiety under CBD was significantly correlated with plasma CBD levels at the end of treatment (r=0.83, p=0.020).

Velayudhan et al., *Int. Psychogeriatrics* 2024

Essential characteristics for a treatment in any population

- Efficacy
- Good safety / tolerability profile

How well are CBD (and other CBMs) tolerated as a treatment?

PLOS MEDICINE

RESEARCH ARTICLE

Safety and tolerability of natural and synthetic cannabinoids in adults aged over 50 years: A systematic review and meta-analysis

Latha Velayudhan[1], Katie McGoohan[1], Sagnik Bhattacharyya[2]*

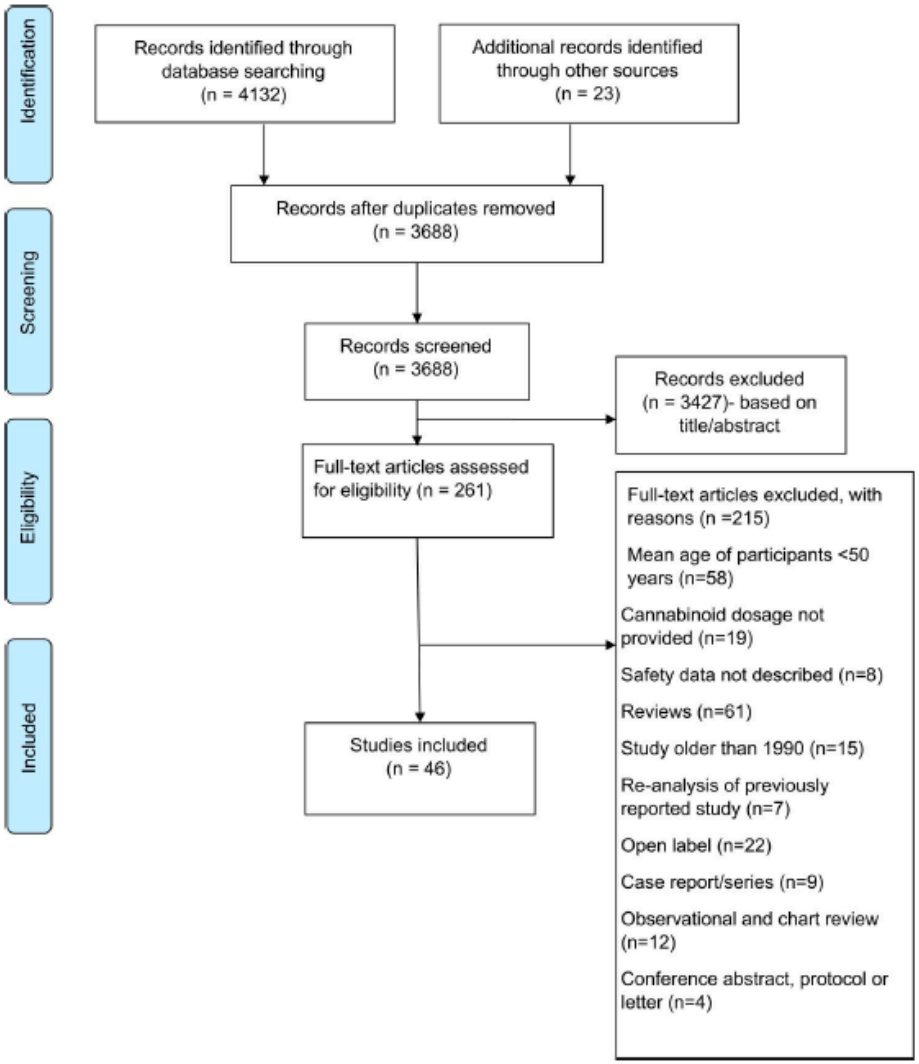


Fig 1. Study disposition.

- N=6216 participants
- n= 3469 received CBMs
- ~1933 person-years of CBM exposure

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Good news!

- Serious adverse events (all cause and treatment-related) and deaths were not greater in THC or THC:CBD studies compared to placebo.

- Withdrawals were also not greater in THC studies.

Treatment-related adverse events- THC

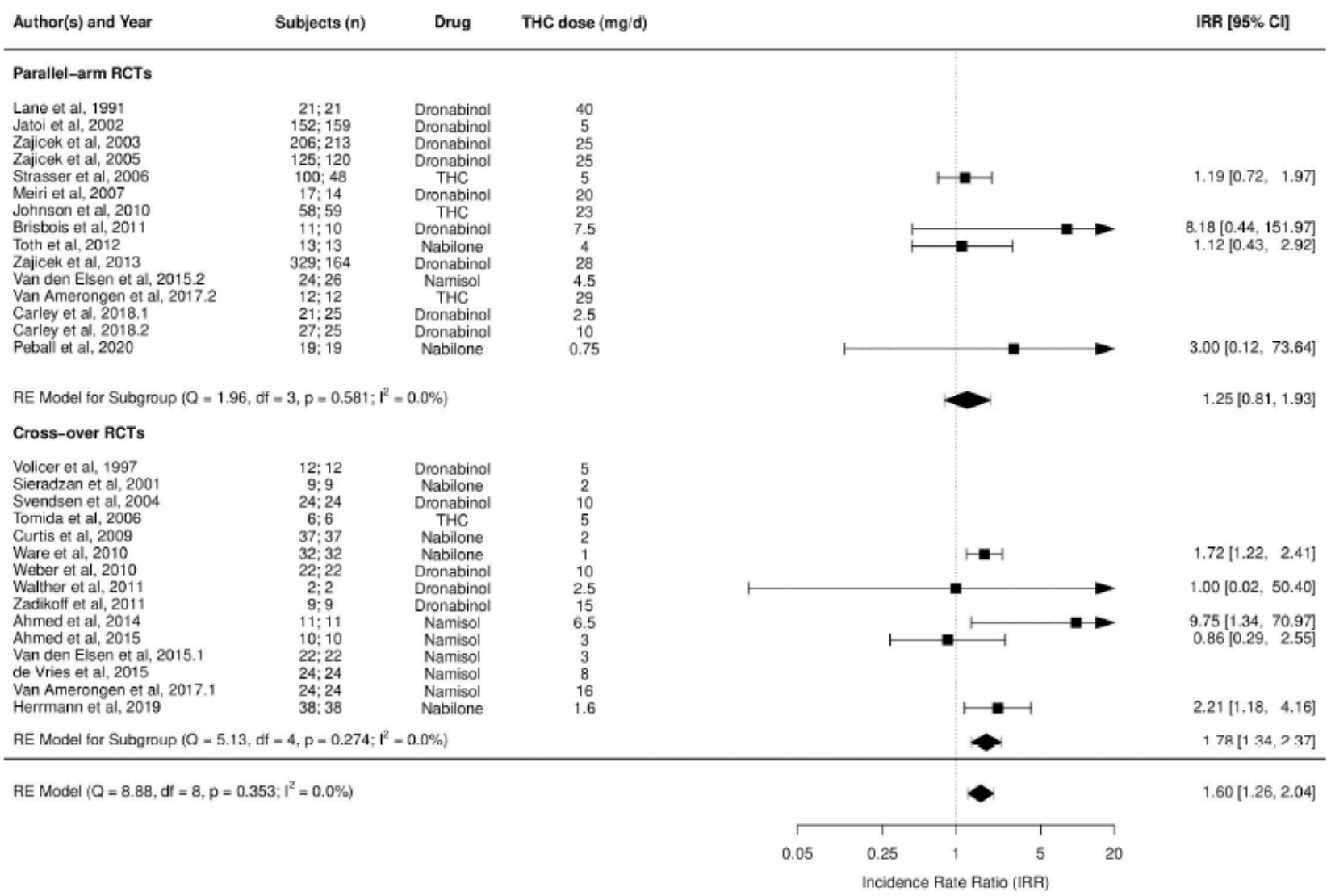

Fig 3. Forest plot of treatment-related adverse events: THC studies. Numbers under the "Subjects (n)" column refer to analysed participants from the active and control intervention arms, respectively. IRR, incident rate ratio; RCT, randomised clinical trial; THC, delta-9-tetrahydrocannabinol.

Treatment-related adverse events- THC:CBD

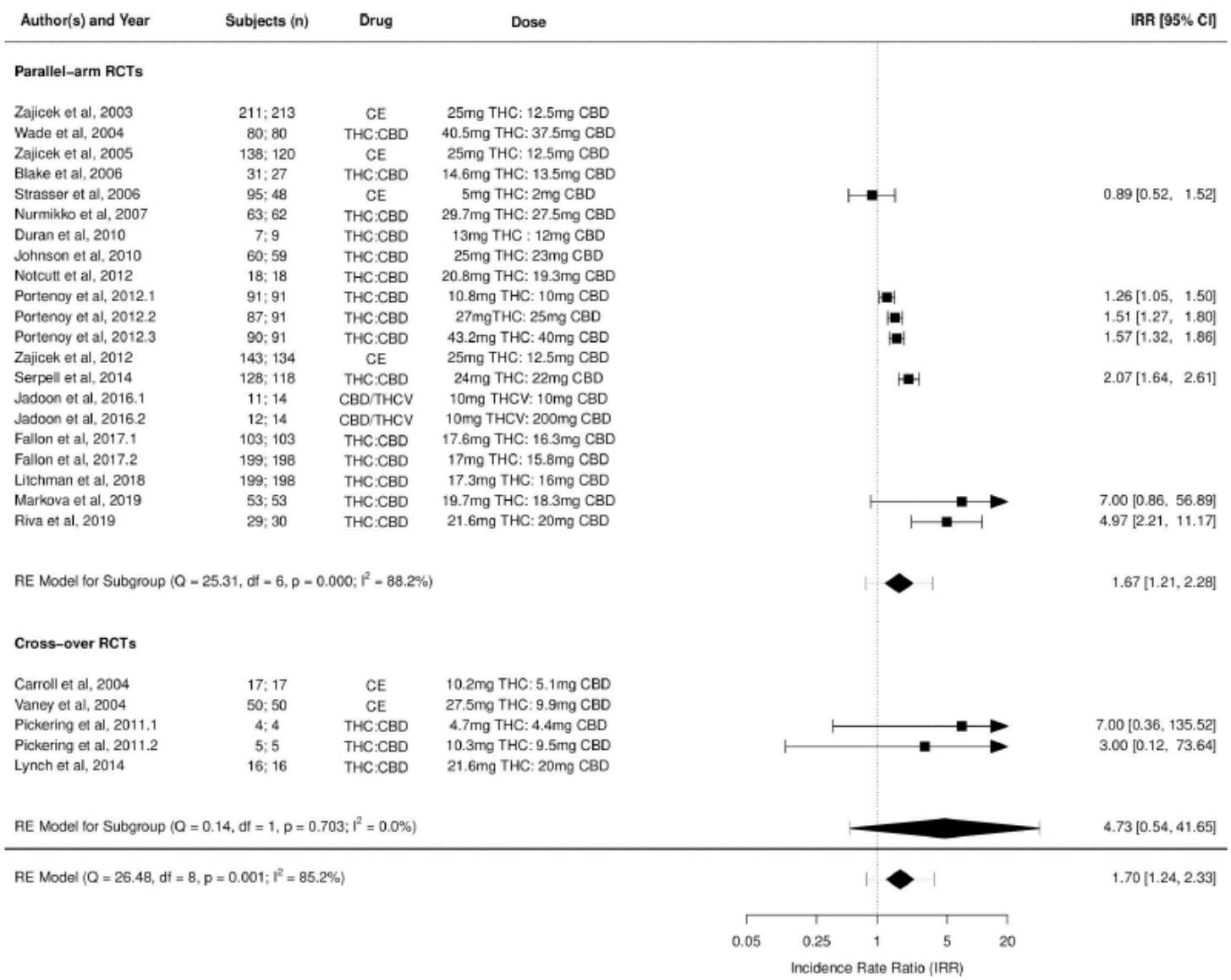

Fig 9. Forest plot of treatment-related adverse events: THC:CBD studies. Numbers under the "Subjects (n)" column refer to analysed participants from the active and control intervention arms, respectively. CBD, cannabidiol; CE, cannabis extract; IRR, incident rate ratio; RCT, randomised clinical trial; THC, delta-9-tetrahydrocannabinol.

Withdrawals- THC:CBD

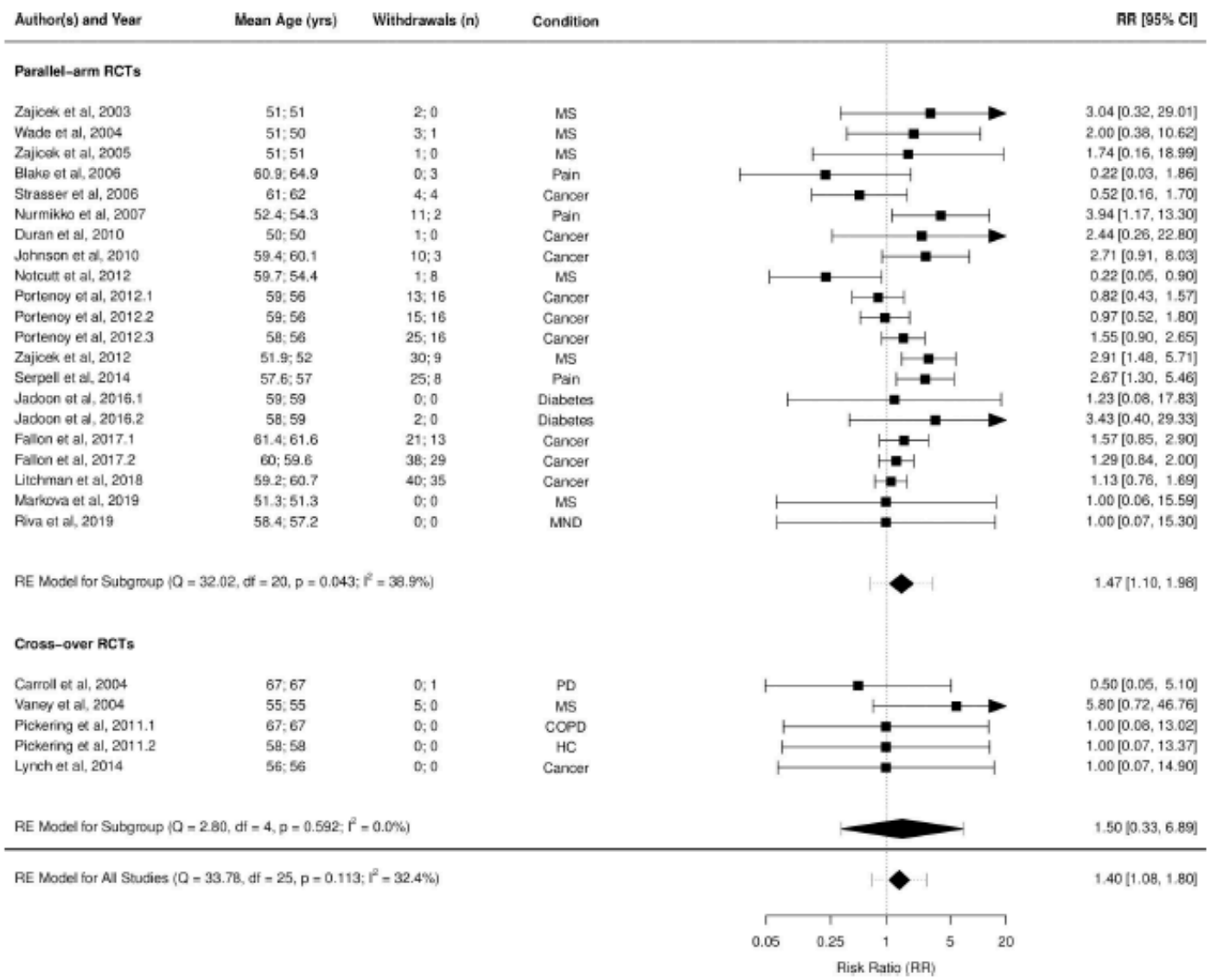

Fig 12. Forest plot of all withdrawals: THC:CBD studies. Numbers under the "Mean Age (yrs)" and "Withdrawals (n)" columns refer to the values in active and control intervention arms, respectively. The conditions listed are the disease conditions subgrouped for meta-regression analyses purposes are: MS; MND; pain (neuropathic pain, rheumatoid arthritis), cancer (cancer or chemotherapy-related anorexia, pain or nausea/vomiting), diabetes mellitus, COPD, HC, levodopa-induced dyskinesia in PD. CBD, cannabidiol; COPD, chronic obstructive pulmonary disease; HC, healthy controls; MS, multiple sclerosis; MND, motor neurone disease; PD, Parkinson disease; RCT, randomised clinical trial; RR, risk ratio; THC, delta-9-tetrahydrocannabinol.

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Research Letter | Pharmacy and Clinical Pharmacology

Evaluation of THC-Related Neuropsychiatric Symptoms Among Adults Aged 50 Years and Older

A Systematic Review and Metaregression Analysis

Latha Velayudhan, MD; Katie Louise McGoohan, PhD; Sagnik Bhattacharyya, MD, PhD

THC *dose-dependently* increased the incidence of dry mouth, dizziness/ light-headedness, mobility /balance / coordination difficulties, dissociative/ thinking/perception problems and somnolence/ drowsiness.

Age and Ageing 2024; **53:** afae261
https://doi.org/10.1093/ageing/afae261

SYSTEMATIC REVIEW

Adverse events caused by cannabinoids in middle aged and older adults for all indications: a meta-analysis of incidence rate difference

Latha Velayudhan, Sara Pisani, Marta Dugonjic, Katie McGoohan, Sagnik Bhattacharyya

KING'S College LONDON

PLOS MEDICINE

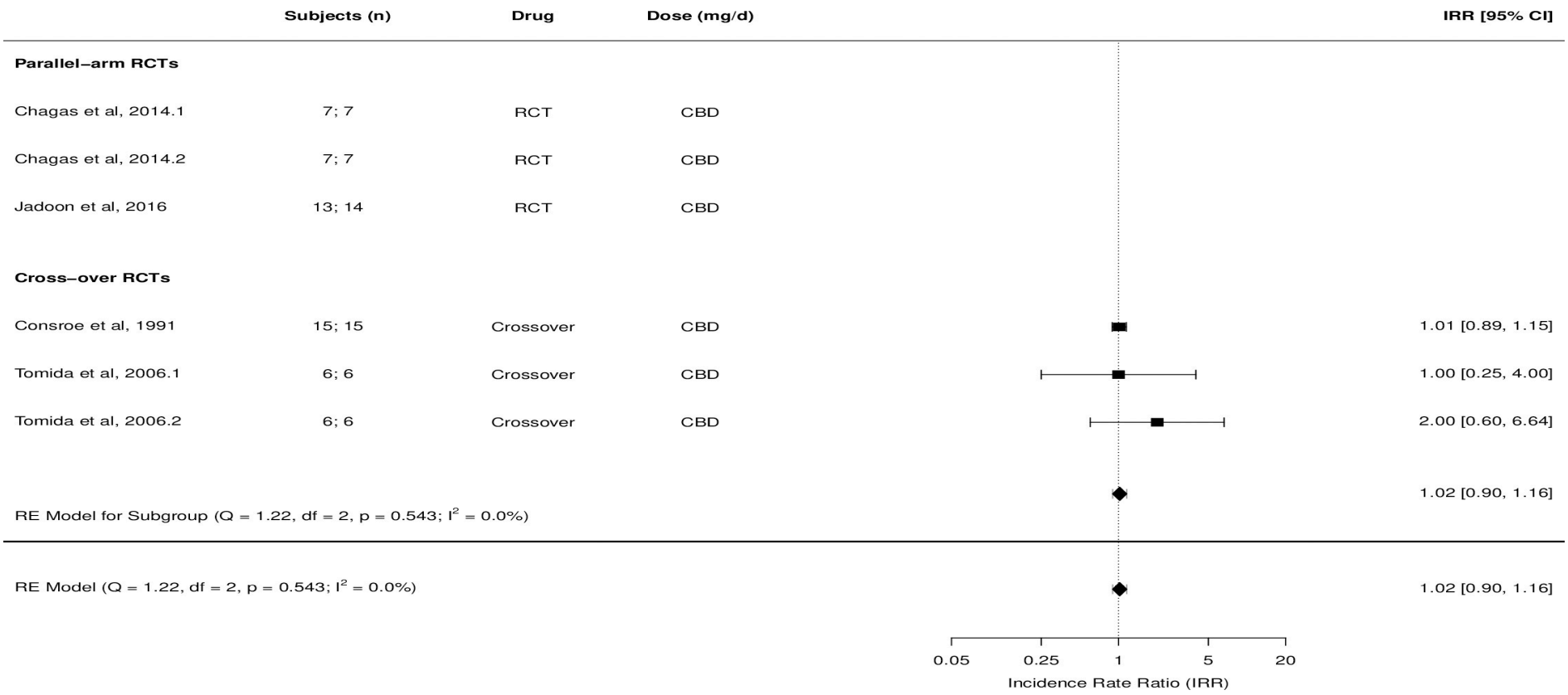
RESEARCH ARTICLE

Safety and tolerability of natural and synthetic cannabinoids in adults aged over 50 years: A systematic review and meta-analysis

Latha Velayudhan[1], Katie McGoohan[1], Sagnik Bhattacharyya[2]*

1 Department of Old age Psychiatry, Division of Academic Psychiatry, Institute of Psychiatry, Psychology and

Forest Plot of all cause Adverse Events: CBD studies



CBD tolerability across all age groups

- 12 trials; 803 participants
- Increased odds of withdrawal, any adverse and serious adverse events
- Increased odds of abnormal liver function test, pneumonia, decreased appetite, diarrhoea and sedation
- Odds of abnormal liver function test, pneumonia, decreased appetite and sedation mainly due to epilepsy trials
- Excluding epilepsy trials, CBD only associated with increased odds of diarrhoea (OR= ~5)

Chesney et al., *Neuropsychopharm* 2020

Future steps

- Pivotal study/ies, planned in discussion with regulators (FDA/ MHRA/ EMA)

- Licensing

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Thank You

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- Elizabeth Appiah-Kusi
- Aisling O'Neill
- Latha Velayudhan

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