

Dr Graham Gulbransen

General Practitioner

Kingsland Family Health Centre

Auckland

Friday, August 11, 2017

17:45 - 18:10 Medicinal Cannabis 101

‘...almost everybody knows that cannabis is either essentially harmless or else necessarily toxic.

Yet, like most arguments, the truth is between these extremes, depending on the ages of use, and frequency and chronicity of use.’

Richard P Mattick,
Drug and Alcohol Review, July 2017

You may find this presentation

challenging...

1. Is it safe?
2. Is it legal?
3. Is it snake oil?
4. Why haven't we been taught about ECS?
5. Should GPs be recommending herbs?
6. How do GPs recommend/prescribe?
7. Remember medicinal cannabis is here now!

Themes

After this talk you will be better placed to support your patients who use medicinal cannabis.

My messages:

- Medicinal vs recreational cannabis
- Case histories
- Evidence for cannabis benefits
- Evidence for harms
- Compassion
- Current NZ situation – how you can prescribe.

Cannabis plant

- Thousands of strains – like tomatoes!
- THC & CBD main active compounds
- Continuum from
 - THC Dominant
 - Balanced
 - CBD Dominant

Sativex

Each spray THC 2.7mg, CBD 2.5mg, ethanol, peppermint oil



Peter 58 (MS)

- MULTIPLE SCLEROSIS
- Left hemiparesis
- Disease modifying therapy: tecfidera
- Muscle spasms: baclofen inadequate.

- Prescribe Sativex with neurologist recommendation.

Prescription pathways at the end of this presentation.

Lynda 67 (Palliative care)

- Terminal pancreatic cancer
- Palliative care; chemotherapy nothing more to offer
- Smoked cannabis during chemo
 - Less nausea
 - Better appetite, but lost weight
 - Less pain
 - But – hated smoking, illegal
- Sativex approved – easy to take, control dose, no choking, eases abdo discomfort, huge appetite stimulant, regained weight!

Barbara 35 (Chronic pain)

- Severe endometriosis, 18 surgeries, full pelvic clearance
- Chronic pain, central sensitisation disorder
- Past misuse of prescription and illicit drugs to manage chronic endometriosis pain (pseudoaddiction)
- Was using cannabis most evenings for analgesia.
- Sativex approved. 1-2 sprays per week effective.

Nick 20 (Knobloch Syndrome)

- Autism spectrum disorder, global development delay, blind, epilepsy with uncontrolled prolonged seizures about twice a week.

Anticonvulsants ineffective with intolerable adverse effects.

- Hemp extract drops taken with unbroken sleep for the first time in his life and calmer during the day! Rapid recovery from seizures.

Jo 61 (MSA)

- Multiple systems atrophy, cerebellar type
- (chronic progressive debilitating neurological condition)
- Quadraparesis, confined to bed, dystonia, muscle spasms, contractures, depressed
- Clonazepam, levodopa/benserazide: minimal relief
- Sativex approved, difficult to use, short trial ineffective.

Eddie 30 (Chronic pain)

- Unexplained chronic facial pain 10 years
- Several surgeries without benefit
- 3 weeks after taking 10 drops of hemp extract tid:
 - Reduced oxycodone from 70mg → 40mg daily
 - Stopped gabapentin 600mg daily
 - Stopped nitrazepam 10mg nocte for sleep
- Continues hemp extract, feels hope for the first time in 10 years.

‘Stuck Patients’ – Compassion

Have you any patients
who are ‘stuck’?

Conventional medicines
just not working?

Cannabis as Medicine in Australia

Presented at
International Medicine in Addiction
Conference, Sydney 26/3/17

Prof Nicholas Lintzeris MBBS, PhD, FACHAM

Director D&A Services, SESLHD



University of Sydney, Division Addiction Medicine



[HOME](#) [ABOUT](#) [EXHIBITORS](#)



2017 HHI EXPO & SYMPOSIUM

Medical Practitioners

2017 Medicinal Cannabis Course

22 June 2017 Melbourne Crowne Plaza



Assoc Prof
David Caldicott
Canberra



The First Australian Medicinal Cannabis Course designed for health care practitioners for health care practitioners.

A comprehensive introduction to:

- The Australian history of medicinal cannabis
- The endocannabinoid system
- The pharmacology of cannabinoid medicine
- The practicalities of dosing
- Conditions amenable to treatment
- Up to date literature
- International perspectives
- ...& much more!



united
IN COMPASSION
for the dignified alleviation of suffering with compassion & empathy

UIC AUSTRALIAN MEDICINAL CANNABIS SYMPOSIUM PROGRAM

23, 24, 25 JUNE 2017 • MELBOURNE, VICTORIA

This is a catered event with morning/afternoon tea & lunch provided

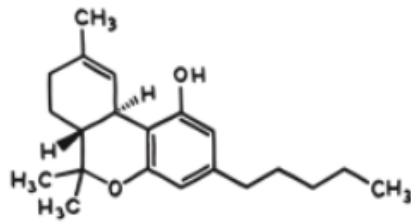


HELP US PUT
the focus back on
PATIENTS

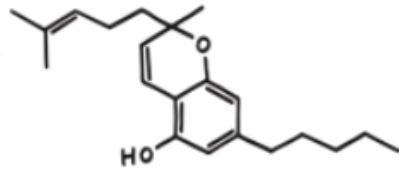
when ACTION meets
compassion
lives can
CHANGE

www.unitedincompassion.com.au

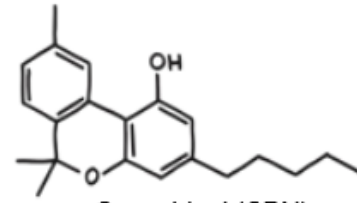




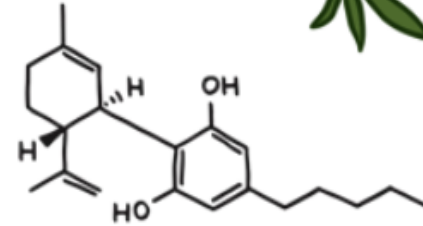
Tetrahydrocannabinol (THC)



Cannabichromene (CBC)

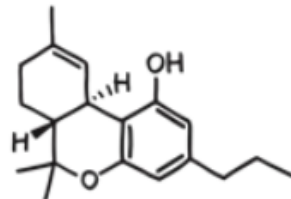


Cannabinol (CBN)



Cannabidiol (CBD)

Cannabis use risk analysis & an introduction to the Endocannabinoid System



(THCV)

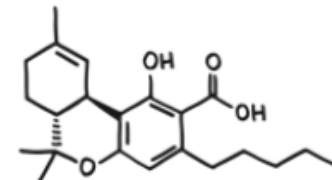
Justin Sinclair (MHerbMed BHSc ND)

Research Fellow - NICM

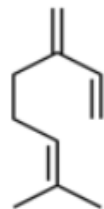
Scientific Advisory Council - United in Compassion

Scientific Advisory Board member - BioCeuticals

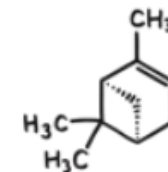
j.sinclair@tmconsultancy.com.au or J.Sinclair@westernsydney.edu.au



(THCA)



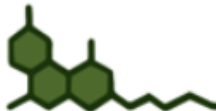
Beta-myrcene



Alpha-pinene

NICM

The science of integrative medicine



History of medical cannabis

- >2000 years therapeutic use
- Widely used until early 20th century
 - bronchitis, epilepsy, hypnotic, analgesia, 'nerve tonic'
- Prohibition: abandoned as therapeutic agent
- Interest rekindled since 1990's
 - Consumer advocacy
 - Scientific developments




CANNABIS AMERICANA
U. S. P.
Physiologically Tested

OUR American variety is the answer to the question which has so long troubled manufacturers. With our material a finished product can be turned out at a reasonable cost.

IT is no longer necessary to depend on the foreign variety which is of high cost and slightly superior. The uncertainty of further supplies of it is another factor favoring the American product.

J. L. HOPKINS & CO., 100 William St., New York



Cannabis Prohibition in NZ

1965 Narcotics Act

Cannabis oil Class B Misuse of Drugs Act (MoDA) 1975

[Definition: Class B drugs pose a high risk of harm]

Cannabis plant Class C, moderate risk of harm.

Varieties of Cannabinoids

Endocannabinoids

In our brain and body



*AEA (Anandamide),
2-AG (Noladin ether)
etc.*

Phytocannabinoids

In plants



*THC, CBD, CBG, CBDV,
THCV, CBC, CBN, THCVA
etc.*

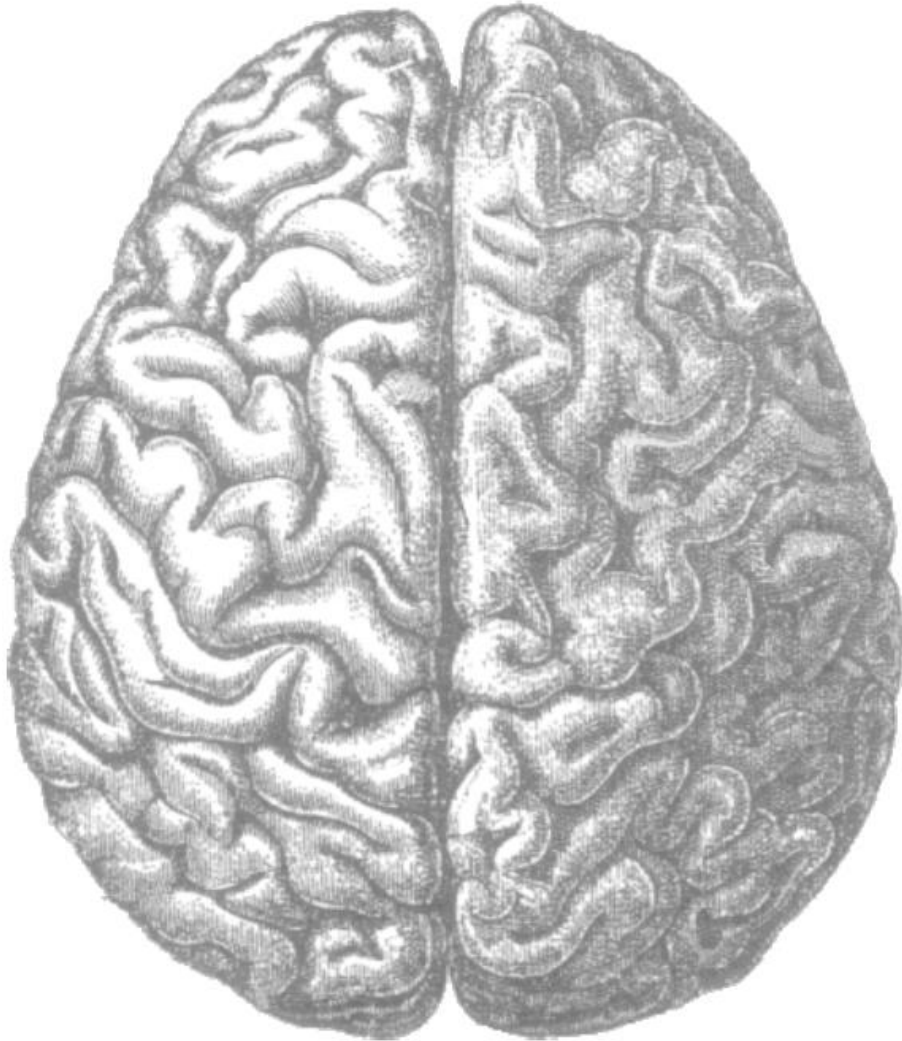
Synthetic
cannabinoids

From the lab



*Nabilone, HU-210, AB-
PINACA, JWH-018,
Includes K2, Kronik etc*

The Endocannabinoid System (ECS)



- ✓ The ECS has evolved over 500 million years in mammals, birds & fish

(McGeeney 2013; Grotenhermen 2006; McPartland *et al.* 2007; Elphick *et al.* 2003; McPartland *et al.* 2006).

- ✓ It is a major neuromodulatory system involved in the regulation of homeostasis.

- ✓ The ECS was originally found by researchers investigating how Cannabis interacted with human physiology

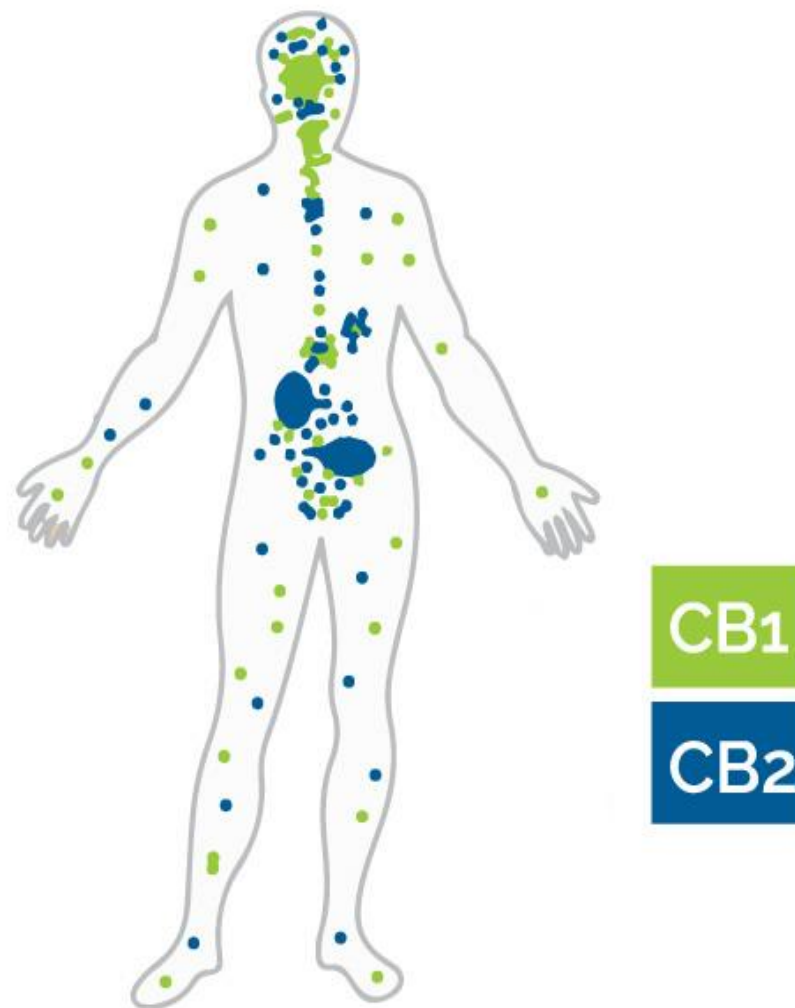
(Herkenham *et al.* 1990; Pertwee 1997; Devane *et al.* 1992; Galiegue *et al.* 1995).

- ✓ The ECS is not a focus of teaching in current medical or health science curriculums.



Endocannabinoid System - Homeostasis

- CB1 receptors:
 - Brain: cortex, basal ganglia, hippocampus, cerebellum
 - Modulate: memory, mood, executive function, cognition, analgesia, movement
 - GI: appetite, lipolysis
 - Respiratory
- CB2 receptors
 - Immune system: regulate inflammation, neuropathic pain
- CB3 & other receptors under investigation





THE ENDOCANNABINOID SYSTEM GUARDS LIFE'S MOST CRITICAL FUNCTIONS

CELL CYCLE

Repair / Pro-
apoptotic

METABOLISM

Sleeping / eating

CANNABINOIDS
PROMOTE
BALANCE

IMMUNE SYSTEM

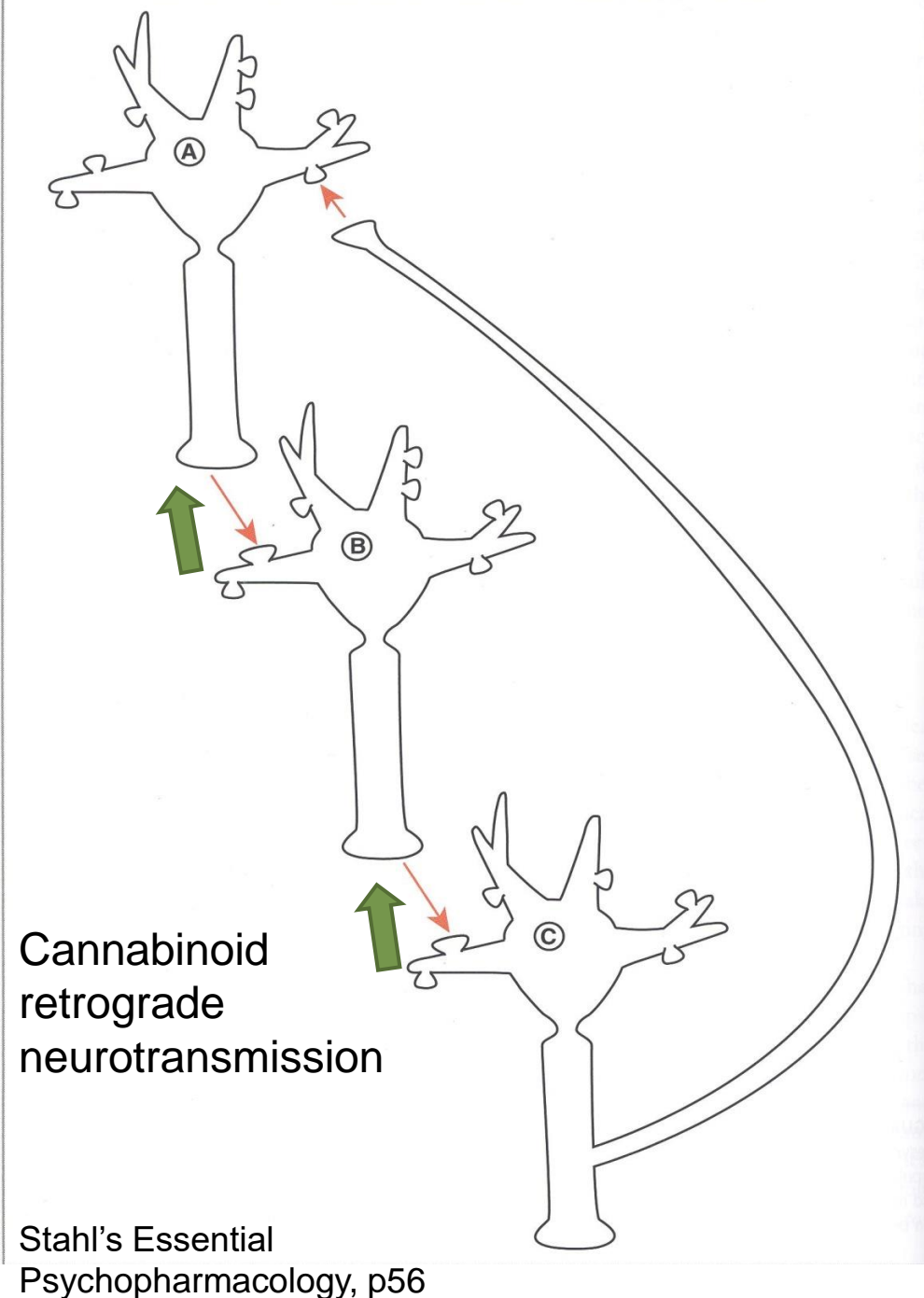
Anti-inflammatory

BRAIN ACTIVITY

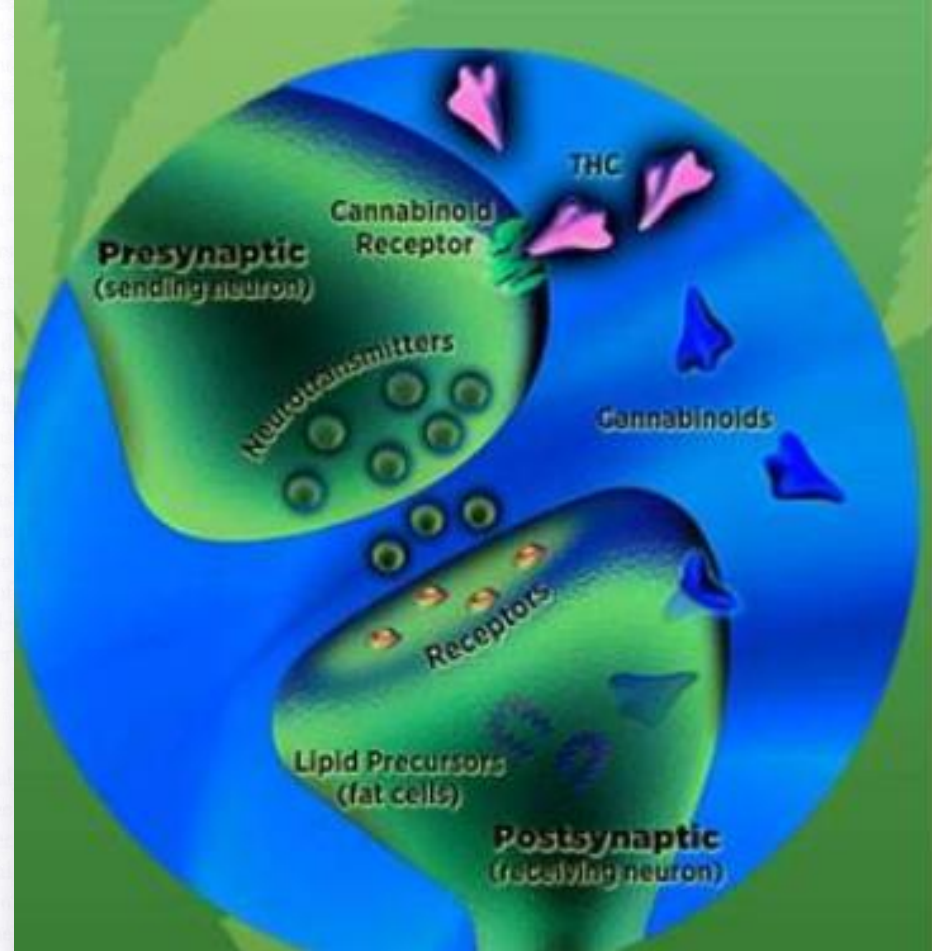
Neuromodulators / analgesia



Slide by Viola Brugnattelli



Stahl's Essential
Psychopharmacology, p56



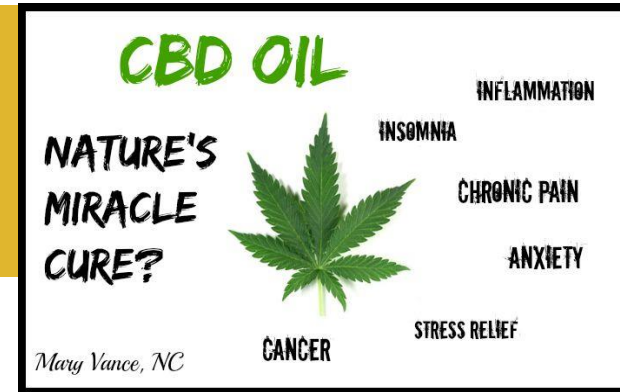
Viola Brugnattelli, neuroscientist,
<https://naturegoingsmart.com/understanding-endocannabinoid-system/> 2017

Cannabinoids regulate neurotransmission

- Pain
- Epilepsy
- Anxiety, PTSD

Cannabidiol (CBD)

- **A non-intoxicating cannabinoid**
 - Anticonvulsant effects
 - Anxiolytic, antipsychotic
 - Neuroprotective: ?dementia
 - Analgesia: THC+CBD > THC or CBD alone; synergistic
- Hepatic metabolism:
 - CYP 3A4, 2D9 inhibition: ?clinically relevant
- Doses:
 - ?200-1200mg oral / day prescribed
 - 10-50mg oral / day OTC for 'wellness'





OTHER COMPONENTS

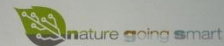
- ▶ 120 terpenes
- ▶ 50 hydrocarbons
- ▶ 34 sugars
- ▶ 20 alkaloids
- ▶ 19 flavonoid-glycosides
- ▶ 16 phenols
- ▶ 13 ketones
- ▶ 12 aldehydes
- ▶ 11 steroids
- ▶ 7 alcohols
- ▶ 2 pigments

> 500



CANNABIS RESEARCH
ONE PLANT, MANY MOLECULES

Viola Brugatelli
Founder & Chief Editor

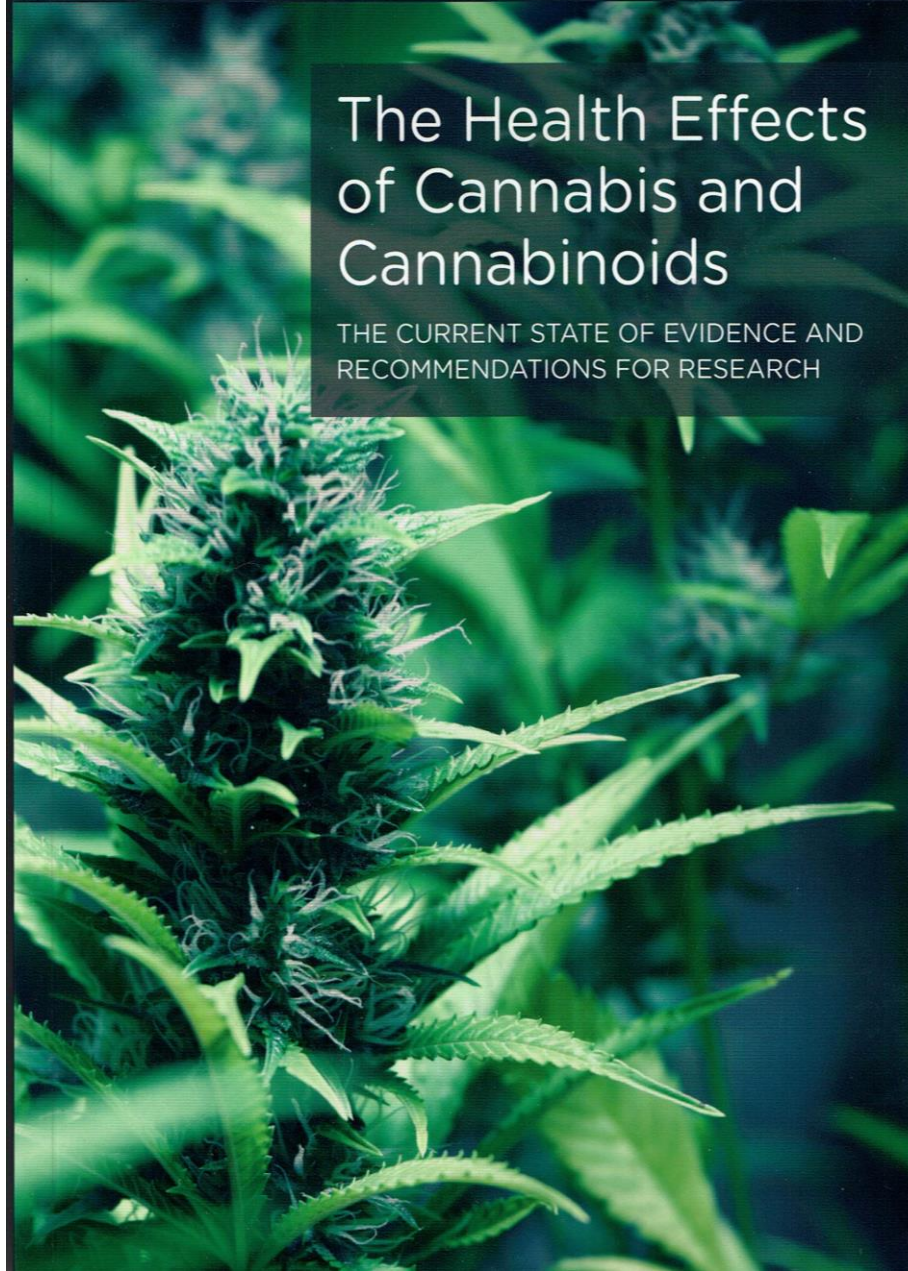


The National Academies of
SCIENCES • ENGINEERING • MEDICINE

REPORT

The Health Effects of Cannabis and Cannabinoids

THE CURRENT STATE OF EVIDENCE AND
RECOMMENDATIONS FOR RESEARCH



Evidence of Benefit

- 2017 National Academies of Science, Engineering, Medicine, USA reviewed 10,700 clinical studies
- Few high quality RCTs available:
 - Prohibition restricts supply and standardisation of cannabis
 - Cannabis plant has hundreds of compounds to study separately and individually, different ratios
 - Plants cant be patented, reduces funding sources
- EBM vs Personalised Medicine: GPs know RCTs are a guide but not real-world, we personalise Rx
- Neuroscientists have huge research data-base
- Patients' experience of illicit cannabis useful guide.

Systematic review Cannabinoids

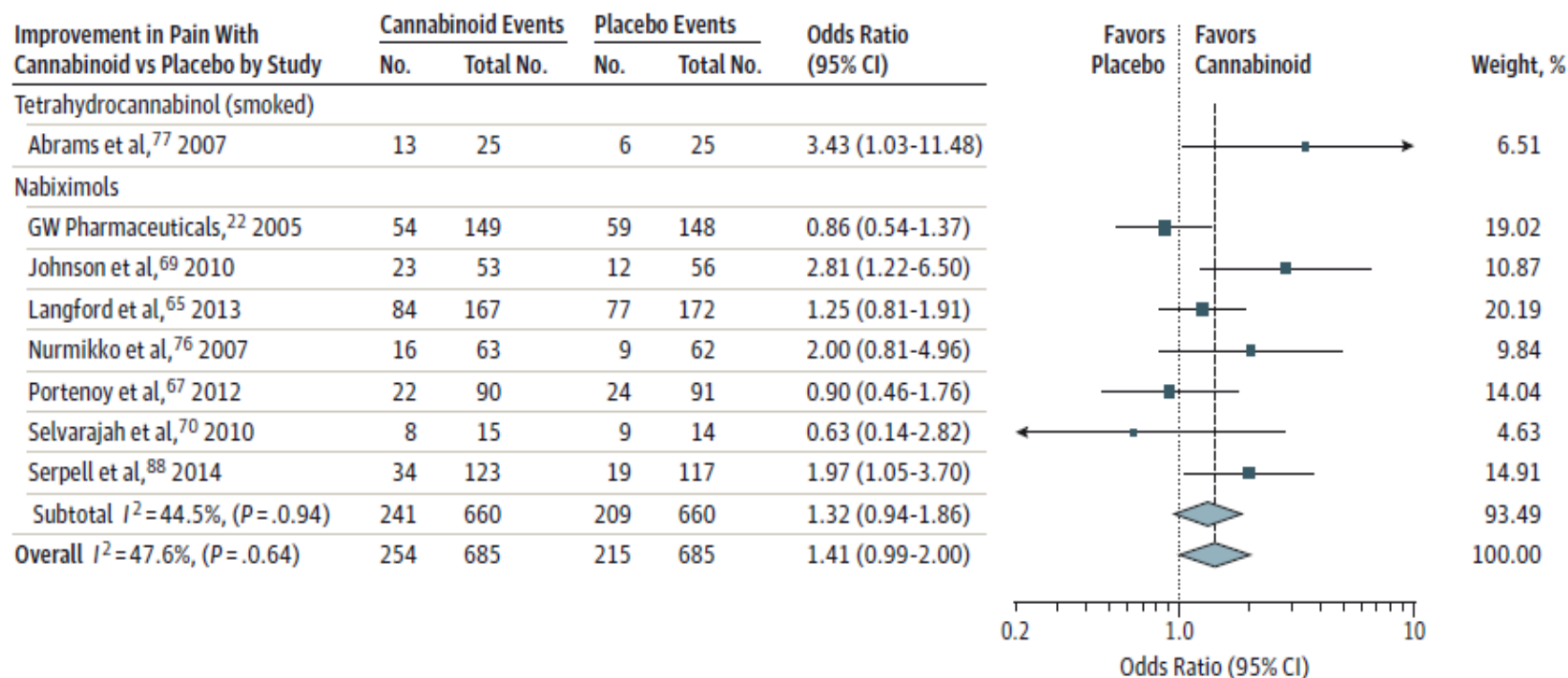
Whiting et al JAMA June 2015

Condition	# studies	Strength of evidence	Conclusion
Nausea & vomiting	3 RCTs	Low	THC or THC/CBD > placebo
Weight gain in HIV/AIDS	1 RCT	Low	THC > placebo
Spasticity in MS / paraplegia	14 RCTs	Moderate	THC/CBD > placebo
Depression	3 RCTs	Low	Placebo > THC/CBD
Anxiety	1 RCT	Low	CBD>placebo
Sleep	12 RCTs	Low	THC/CBD, THC > Placebo
Psychosis	1 RCT	Low	CBD = amisulpiride
Tourette Syndrome	1 RCT	Low	THC > placebo
Glaucoma	1 RCT	Low	THC=CBD=placebo
Epilepsy	Not completed	N/A	CBD

Cannabinoids in chronic pain

Systematic review: Whiting et al JAMA June 2015

Figure 2. Improvement in Pain



Odds indicate 30% or greater improvement in pain with cannabinoid compared with placebo, stratified according to cannabinoid. The square data markers indicate odds ratios (ORs) from primary studies, with sizes reflecting the statistical weight of the study using random-effects meta-analysis. The

horizontal lines indicate 95% CIs. The blue diamond data markers represent the subtotal and overall OR and 95% CI. The vertical dashed line shows the summary effect estimate, the dotted shows the line of no effect (OR = 1).

Compared to other medicines we use to treat pain

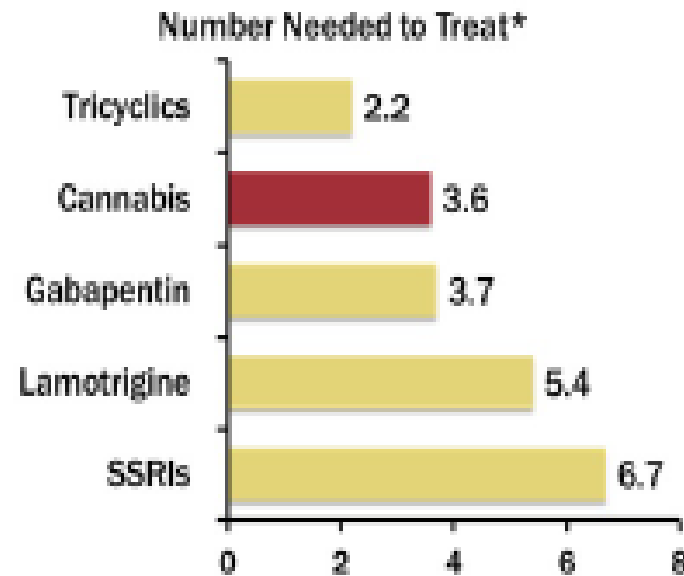


Figure 1. Common analgesics for neuropathic pain.

*to achieve a 30% reduction in pain.

Number needed to treat (NNT) = $1/(E-P)$, where E is the proportion improved in experimental condition and P is the proportion improved on placebo. Example: If 60% “improve” (according to a given definition) in the experimental condition, while 30% “improve” in the placebo condition, then $NNT = 1/(.6-.3) = 3.3$. Data adapted from Abrams et al. [3] and Ellis et al. [4].

Targeting cannabinoids for people with CNCP

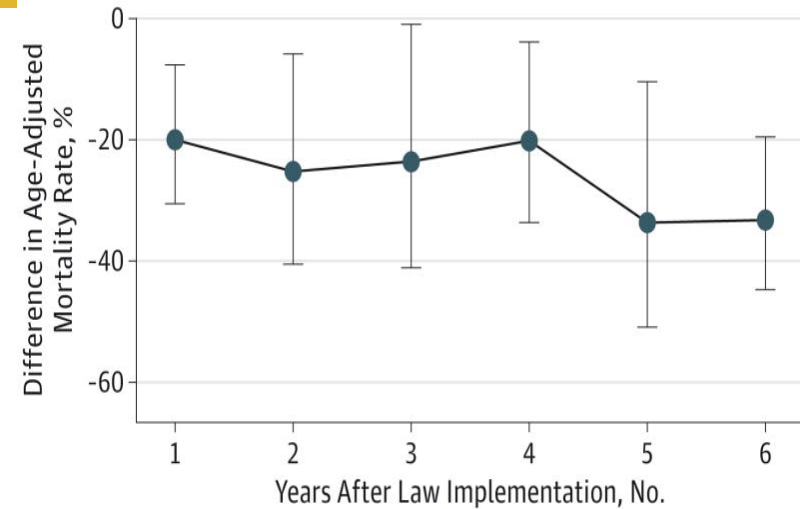
- Pain, substance use, mood and sleep disorders often co-occur, and individually difficult to address
- Childhood trauma is a common link
- Role of cannabinoids for this population?
 - Cannabinoids target the 'distress' of pain > pain 'severity'
 - Cannabinoids involved with mood, sleep, substance use
 - Safer profile than many other medicines used by pain patients
- Could cannabinoids be a useful strategy in addressing 'high risk' medication in pain patients - or will they contribute to the problem?
 - All CB RCTs for pain to date have excluded 'addiction comorbidities'

Medical cannabis & opioid related deaths

Bachhuber et al 2014. Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999-2010. JAMA Int Med 174:1668-73.

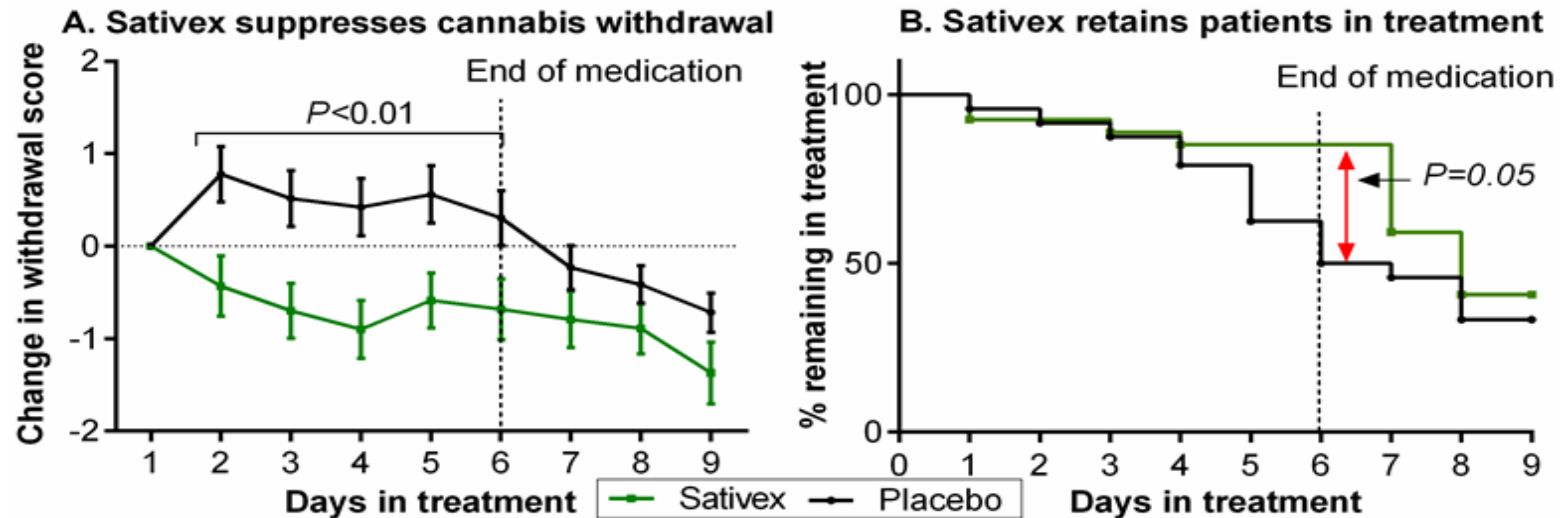
- “Medical cannabis laws are associated with significantly **lower state-level opioid overdose mortality** rates. Further investigation is required to ...”

Review of **opioid-sparing role** of cannabinoids – animal and clinical studies: suggestive but not conclusive
(Nielsen et al Neuropsychopharmacology accepted)



CBs for cannabis withdrawal

- Nabiximols (Sativex) effective in treating cannabis withdrawal
(Allsop *JAMA Psychiatry* 2015)



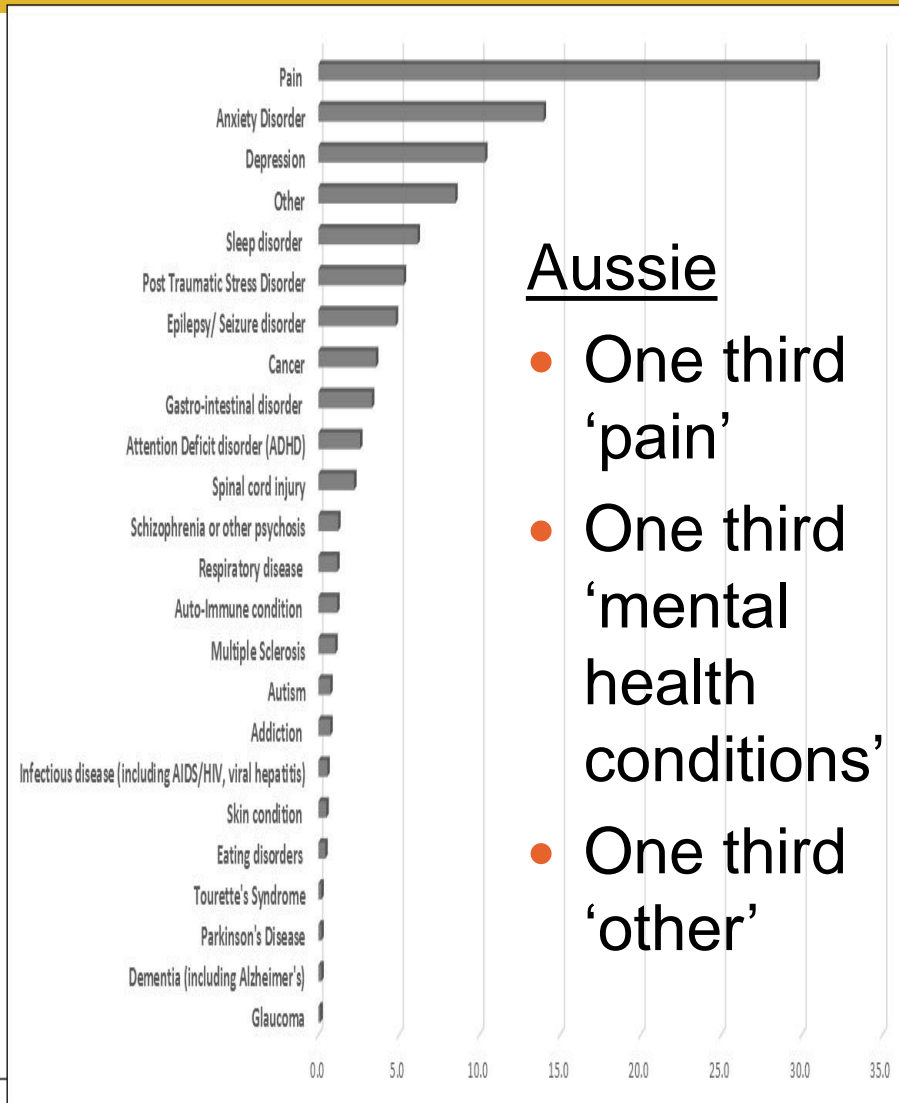
- Similar positive findings with **synthetic THC** (dronabinol, nabilone)
- BUT ... withdrawal alone rarely results in better long term outcomes ...

Cannabinoids for other addictions: 'exit drug'

- Alcohol
 - CBD (and other CBs) for alcohol withdrawal, relapse prevention, cravings
- Opioids
 - CBs (THC) for opioid withdrawal
 - Opioid sparing in pain management
- Amphetamines
 - Promising animal research re: CBD

CAMS-16: Reason for use (n=1624)

NZ Health Survey 2012/13 (n=13,009)



Aussie

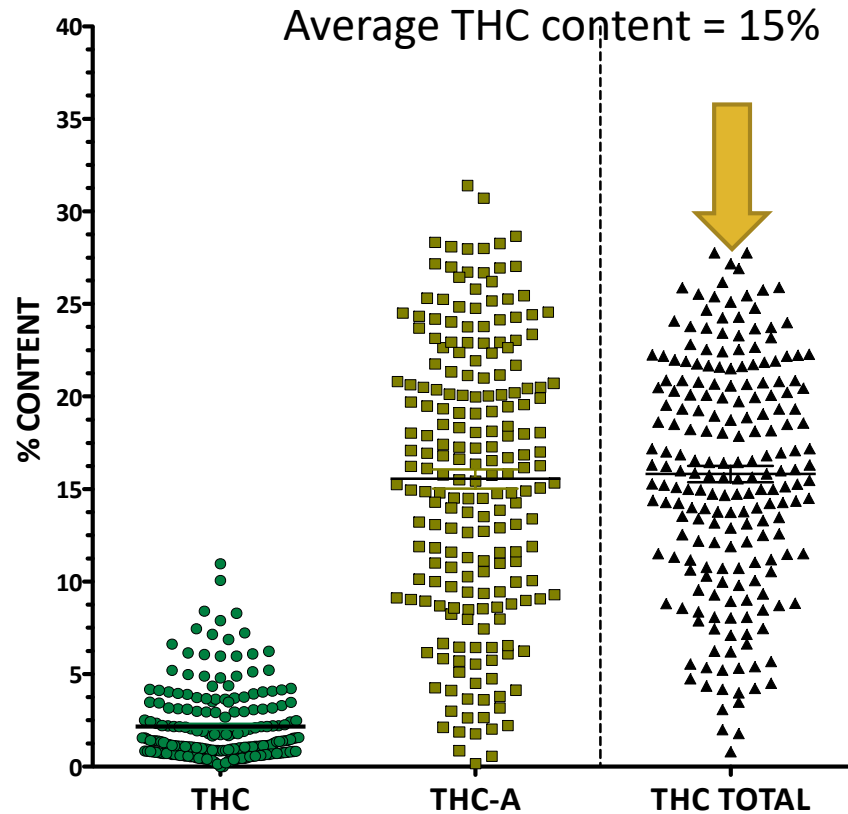
- One third 'pain'
- One third 'mental health conditions'
- One third 'other'

NZ

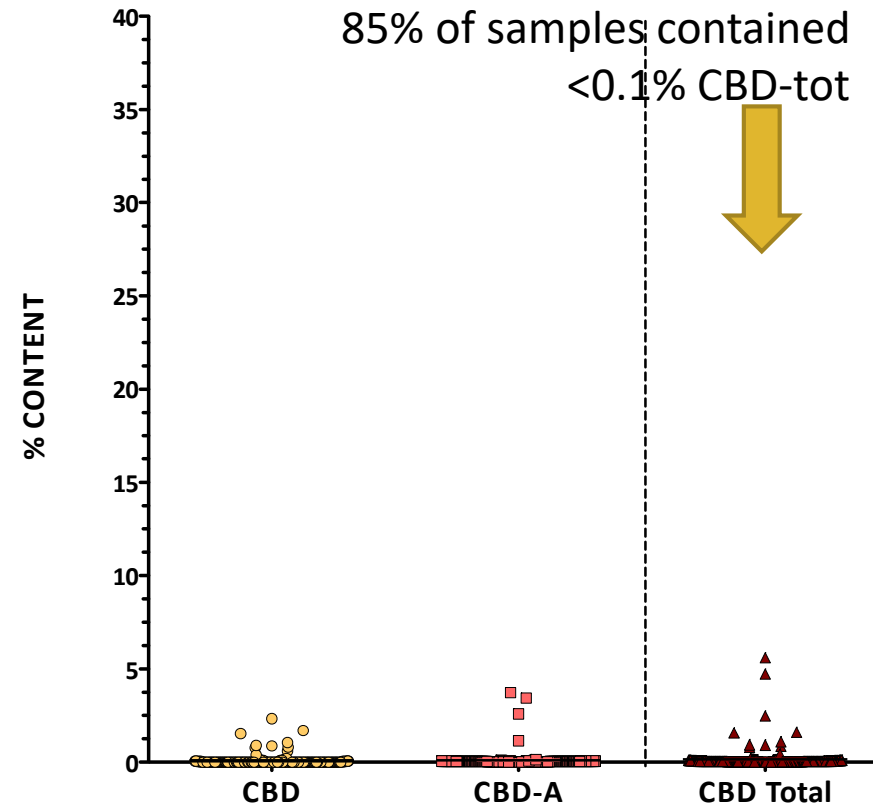
- 11% used cannabis in past year
- 5% used cannabis medicinally
- Of those
 - 40% for pain
 - 27% for anxiety
 - 26% for depression
 - 11% for nausea

Potency of NSW police seized cannabis: high THC and low CBD

Swift et al PLoS One 2013



THC: psychoactive, sedation, analgesia, antiemesis, antispasmodic

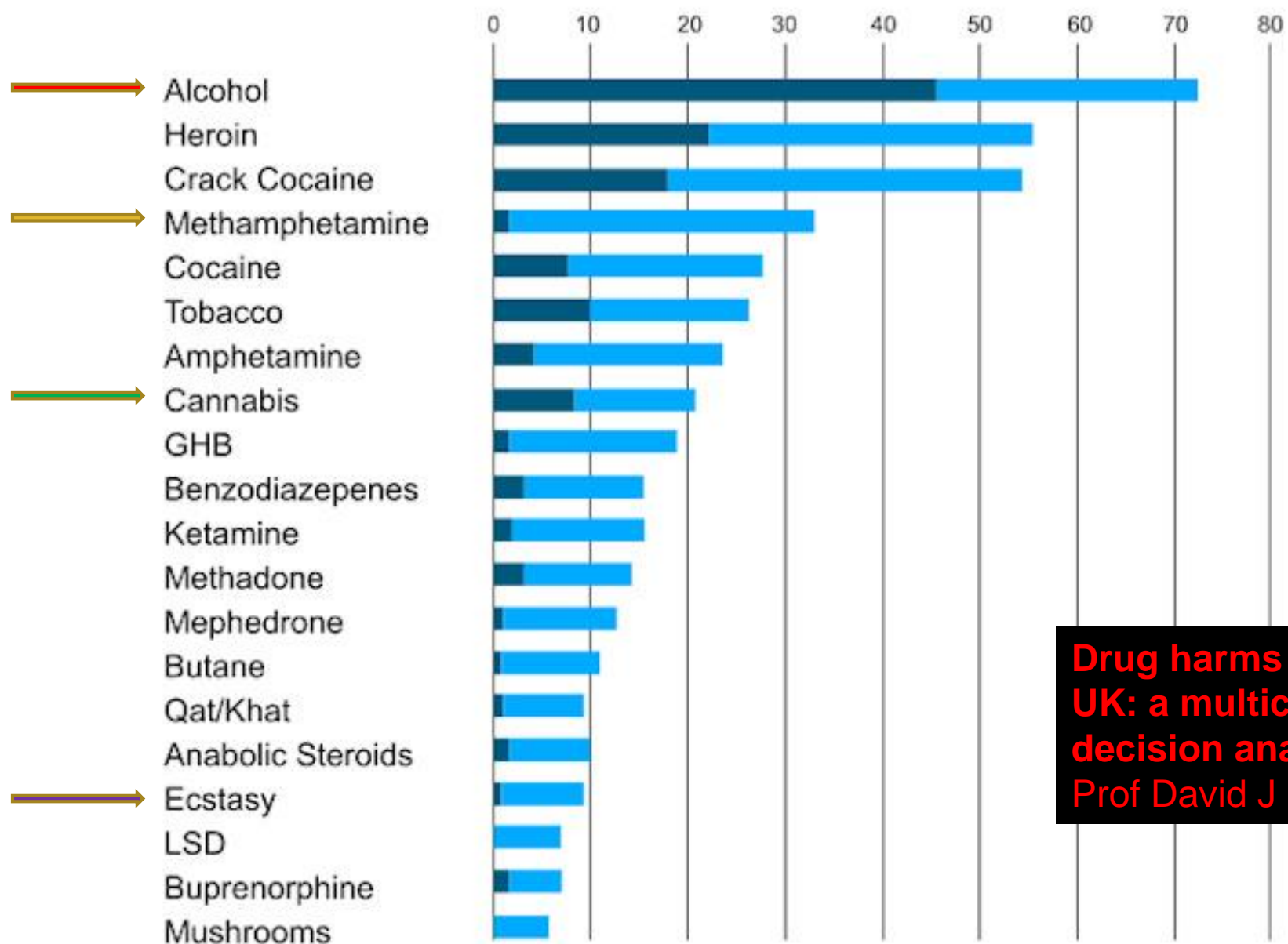


CBD: not psychoactive, anxiolytic, antipsychotic, anticonvulsant, protective against memory loss

Harm Caused by Drugs

■ Harm to others
■ Harm to users

*With a maximum possible harm rating of 100



Drug harms in the UK: a multicriteria decision analysis
Prof David J Nutt. 2010

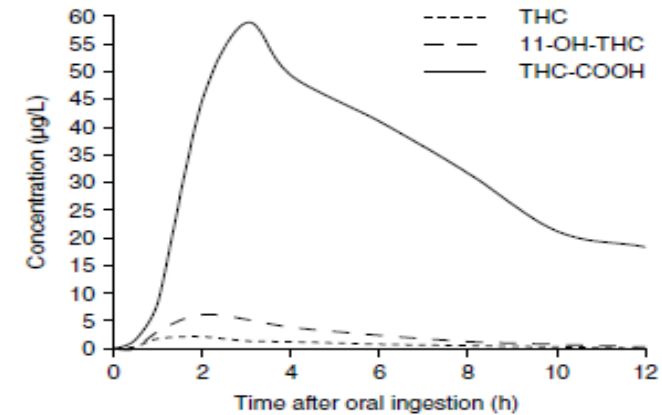
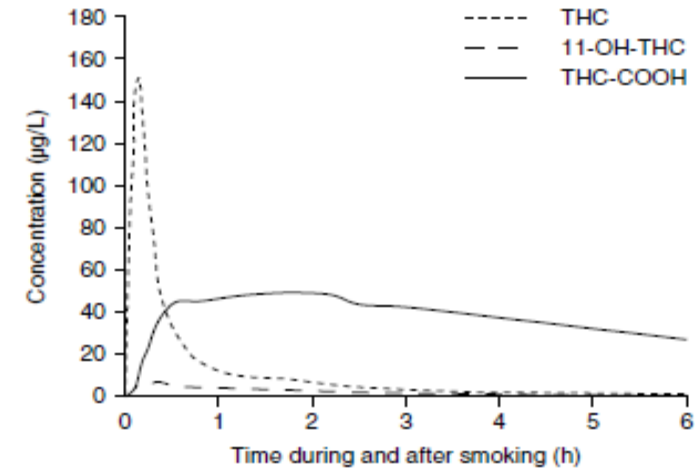
Sativex Adverse Effects

See New Zealand Data Sheet for full list

- Very common $\geq 10\%$: dizziness & fatigue during titration
- Common: 1 – 10%: appetite changes, depression, disorientation, dissociation, euphoria, asthenia, feeling drunk, malaise, blurred vision, vertigo, constipation, diarrhoea, dry mouth, mouth ulcers, nausea, vomiting
- Uncommon: 0.1 – 1%: hallucination, paranoia, suicidal thoughts, syncope, tachycardia, abdo pain etc

Using THC

- Higher bioavailability inhaled
 - 10-35% inhaled
 - 5-15% oral (hepatic CYP 2C8/9/19)
- Peak effects:
 - Inhaled: 10-90 minutes after use
 - Oral: 60- 240 minutes after use
- **Vaporising**: similar to 'e-cigarettes'
 - heats cannabis at lower temperature
 - fewer 'toxins', higher bioavailability
 - no side stream smoke (fewer concern re: passive smoking)
 - TGA-compliant devices: Volcano, Mighty Medic



Vaporisers: The Hemp Store

www.hempstore.co.nz

Vaporite digital desktop

Herb chamber



mouthpiece

Focus handheld



Arizer Air handheld



BEDROCAN®



Bedrocan is featuring 22% THC, with a CBD-level below 1%.

BEDROBINOL®



Its THC-level is standardised at 13.5%, with a CBD-level below 1%.

BEDIOL®



Bediol has a balanced ratio of THC 6.3% and CBD 8%.

BEDICA®



Bedica contains 14% THC with less than 1% CBD.

BEDROLITE®



Bedrolite is a CBD-only product, with less than 1% THC and 9% CBD.

LIQUID CAPSULES

Available in Sativa, Indica, Hybrid and two varieties of CBD for easy ingestion and precise dosage.



DROPS

Available in Sativa, Indica, Hybrid and two varieties of CBD for convenient ingestion. These products also give patients the option of infusing cannabis into many foods of their choice.



VAPORIZER OIL

Available in two varieties of CBD for inhalation and ease of use via vaporization, which is an alternative to smoking.



ORAL SPRAY

Available in Sativa, Indica, Hybrid and two varieties of CBD for quick onset of relief, both convenient and fast-acting.



TOPICAL OIL

Available in Hybrid and two varieties of CBD for direct skin application and localized use.



50+ STRAINS

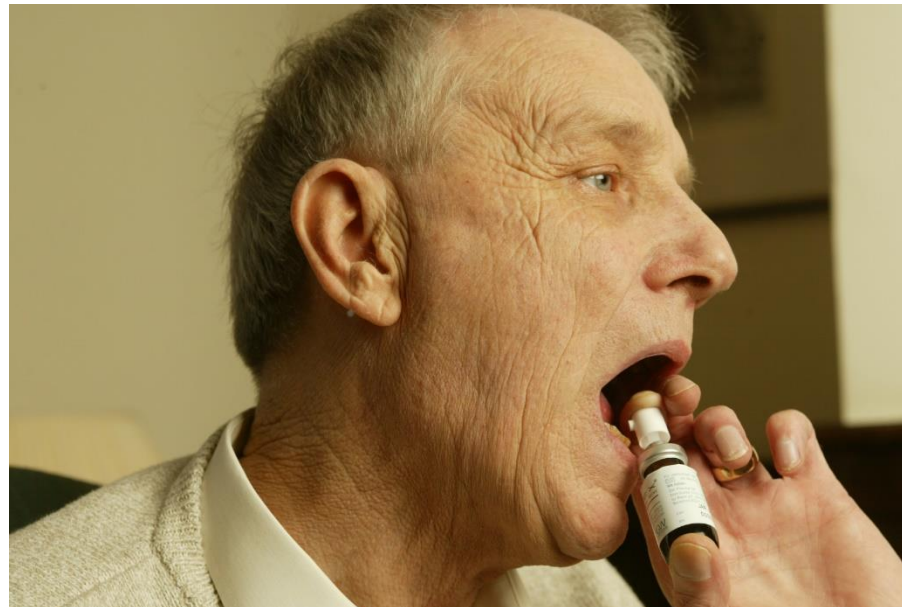
Tilray has sourced 50+ strains of high quality medical cannabis from British Columbia and around the world, with some of the highest concentrations of THC and CBD available on the market.



What is Sativex[®]?

Sativex[®] is a cannabis-based product classified as a Schedule 2, Part 1 (Class B1) controlled drug product under the Misuse of Drugs Act 1975. Sativex[®] is an oromucosal (mouth) spray administering a metered, actuated dose containing the cannabis extracts delta-9-tetrahydrocannabinol (THC) (2.7 mg/spray) and cannabidiol (CBD) (2.5 mg/spray) [+ traces of terpenes and other cannabinoids].

Five Pathways to medicinal cannabis



1. Restriction on the Supply of Sativex—Approval to Prescribe, Supply and Administer (Approval No. 2016/AP305)

- MS: spasms not managed by conventional medicine
- Medical practitioners... acting on the written recommendation... of a Neurologist may prescribe Sativex
- The prescriber is required to state **multiple sclerosis** & Neurologist name on the prescription form.

2. Sativex 'unapproved use'

- Form 2
- 6 pages
- GP & Specialist signatures: oncologist, neurologist, anaesthetist, palliative care specialist.
- Proposed Use
 - Nausea, anorexia, wasting in cancer or AIDS
 - Chronic pain where other treatment ineffective or not tolerated
 - Neuropathic pain
 - Muscle spasm, spasticity from spinal cord injury.
- Process time 1 – 4 weeks.

Form 2

FORM 2

Application for APPROVAL TO PRESCRIBE SATIVEX® FOR AN UNAPPROVED USE under Regulation 22 of the Misuse of Drugs Regulations 1977

A completed and signed copy of this form must be submitted for each application for Ministerial approval to prescribe Sativex® for an **unapproved use** in a specified patient.

Please refer to the current New Zealand Sativex® data sheet when completing this form (see <http://www.medsafe.govt.nz/profs/Datasheet/s/sativexspray.pdf>)

Please note that Sativex® is currently **not** funded by PHARMAC.

3. Application for Ministerial approval to prescribe a pharmaceutical grade cannabis-based product without consent for distribution in New Zealand under Regulation 22 of the Misuse of Drugs Regulations 1977 [SPECIALIST ONLY]

Please note that the Government does not support the use of unprocessed or partially processed cannabis leaf or flower preparations for medicinal use.

<http://www.health.govt.nz/our-work/regulation-health-and-disability-system/medicines-control/prescribing-cannabis-based-products>

Application for Ministerial approval to prescribe a pharmaceutical grade cannabis-based product without consent for distribution in New Zealand under Regulation 22 of the Misuse of Drugs Regulations 1977

A completed and signed copy of this form must be submitted for each application for Ministerial approval to prescribe a pharmaceutical grade cannabis-based product without consent for distribution in New Zealand for a specified patient.

IMPORTANT INFORMATION FOR APPLICANTS

Applications to prescribe pharmaceutical grade cannabis-based products without consent for distribution in New Zealand are considered on a case by case basis. Please review the guidelines used for assessing applications listed on the Medicines Control section of the Ministry of Health website.

1. PRODUCT

Name of the product:



Do you have a Certificate of Analysis?

- No
 Yes – please attach details

Please attach any evidence of potential benefits of the use in the product in the condition(s) to be treated and known adverse effects.

4. Alternatives to Sativex

‘In practical terms the changes mean CBD would be able to be prescribed by a doctor to their patient and supplied in a manner similar to other prescription medicine.’

Peter Dunne, Associate Minister of Health, 2/6/17.

5. Compassionate Cannabidiol

Patients tell me that non-standardised, non-approved, non-medical grade CBD extracts are available.

More information on medicinal cannabis at my workshops tomorrow. You are welcome.

Acknowledgements

- Presenters at the United in Compassion Australian Medicinal Cannabis Course & Symposium, Melbourne June 2017
- Assoc Prof David Caldicott
- Prof Nick Lintzeris
- Dr Jeffrey Hergenrather
- Dr Viola Brugnatelli
- Justin Sinclair

~NGA MIHI NUI~