Medical Cannabis in Australia: The view from the Lambert Initiative



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University of Sydney, NSW, Australia 2006



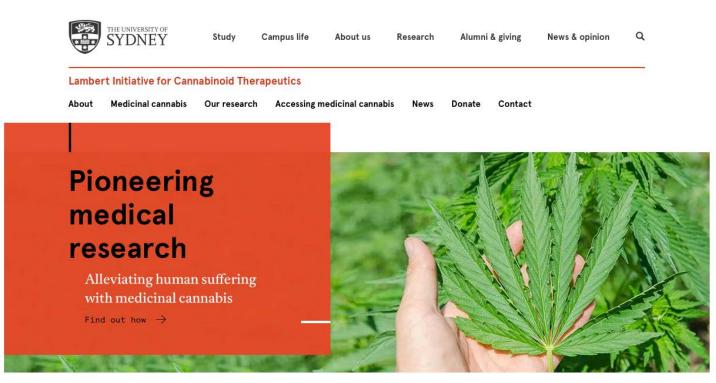


COI Declarations

- I receive and/or have received research and salary funding from the NHMRC, ARC and the Lambert Initiative.
- I am an investigator in clinical trials and other scientific projects involving products manufactured by GW Pharmaceuticals, Tilray, Bedrocan and Ecofibre Industries but have no pecuniary interests in any of the above companies and have received no direct research funding from them.
- I hold patents for a variety of non-cannabinoid therapeutics that are not discussed in this talk.



sydney.edu.au/lambert



Centres and institutes_

Lambert Initiative for Cannabinoid Therapeutics

Advancing cannabinoid-based treatments in mainstream medicine

In 2015, Barry and Joy Lambert made an unprecedented donation of \$33.7 million to the University of Sydney for research into the therapeutic use of medicinal cannabis. This resulted in the Lambert Initiative.

The Lambert initiative is an Australian first in the field of medicinal cannabinoids – both in its breadth and depth of research innovation.

We are targeting a range of conditions including paediatric epilepsy, cancer, chronic pain, obesity, neurological, and mental health disorders.

Our approach involves using medicinal chemistry, cellular and preclinical research, early human testing and clinical trials in patients to identify and develop novel cannabinoid-based therapeutics.

Our research, changing lives Share

Origins of the Lambert Initiative



Michael Lambert

Katelyn Lambert





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Medicinal cannabis: Father of 5yo Katelyn Lambert gave daughter drug out of necessity, court told

By Emma Simkin Updated about an hour ago



VIDEO: Katelyn Lambert is featuring in a campaign advocating for medicinal cannabis (ABC News)

The father of a poster-child for medicinal MAP: Gosford 2250 cannabis was in tears as police confiscated the drug from their home, according to a video shown in court as he answers charges of cultivation and possession.

Michael Lambert entered the court surrounded by his family, including his five-year-old daughter Katelyn and his father, BRW rich-lister Barry Lambert.

Katelyn has a severe form of epilepsy known as Dravet syndrome.

Mr Lambert does not deny possessing or cultivating cannabis, but argued he did it out of necessity for his daughter.

The prosecution argued there were alternatives available to Mr Lambert.

The magistrate has questioned whether home-produced cannabis oil has the same effectiveness as oil produced under clinical conditions.

TOP STORIES

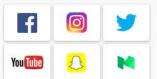
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- 'Every seizure a kick in the head for my daughter': Father of 5yo pleads with police as cannabis taken
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Origins of the Lambert Initiative



Michael Lambert





Barry Lambert

Katelyn Lambert

Michael Spence

Joy Lambert



Lambert Initiative laboratories, Brain and Mind Centre, Camperdown

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The Lambert Initiative Weekly Digest

Aug 21, 2017 11:37 am | Australian



Despite legalisation medicinal cannabis remains confusing for Australian doctors and patients

Frustrated Australian patients could still be several years away from their GPs prescribing medicinal cannabis, the Australian Medical Association's (AMA) vice president has warned.

View »

Aug 21, 2017 12:00 am | Scientific



Medical cannabis may promote good heart health

There has been talk for years regarding the relationship between cannabis use and heart health, but what do the medical studies suggest?

View »

Aug 19, 2017 12:03 pm | Australian



First medical cannabis crop harvested in Vic

Sky News is given exclusive access to the first commercially produced cannabis plants in Victoria.

View »

Aug 11, 2017 02:30 am | Community



Aug 11, 2017 01:22 am | Business



Aug 09, 2017 11:18 am | Australian



Senior citizens embrace medicinal cannabis: use up 250%

Far from a gateway drug, marijuana helps today's senior citizens exit the vicious cycle of pharmaceuticals and addiction. Although marijuana was once considered a dangerous recreational drug by many senior citizens, today's elderly are among the fastest growing demographic within the industry.

View »

Tremendous opportunity in legal cannabis market

Companies need to start thinking about the therapeutic benefits

View »

Medical cannabis licence granted to WA company AusCann

AUSTRALIAN drug regulators have granted what is believed to be the first licence to manufacture and supply medical cannabis in WA.

View »



Phytocannabinoids

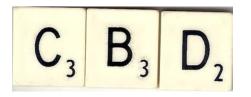
Referral to cannabis as though it were one type of drug is unhelpful and misleading; researchers, clinicians, and policy makers need to start differentiating the various forms that cannabis takes in their various endeavours.





From Lancet (2016)





 $C_3 B_3 N_1$

B₃

D,

>100 cannabinoids in the plant. Many do **not** interact with CB1 receptors and are not intoxicating.



Many have therapeutic potential.

Different cannabis **strains** (> 2000) have different cannabinoid profiles.

Additional components include terpenoids and flavonoids.

Heating/burning the plant material changes the profile of cannabinoids

Our preclinical research program has identified to date:

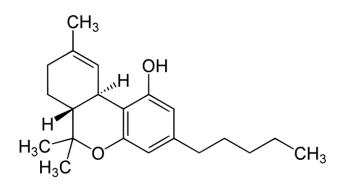
- Four novel phytocannabinoids with anticonvulsant effects in Dravet mice
- **One** phytocannabinoid that restores function in specific types of mutant GABA receptors prevalent in some forms of epilepsy.
- **Two** novel phytocannabinoids with powerful anti-cancer effects (using cellular and *in vivo* models).
- **One** phytocannabinoid with powerful therapeutic effects in PTSD animal models





The two most important cannabinoids: THC and CBD

THC





- The main intoxicating compound in cannabis.
- A moderate affinity agonist at CB1 and CB2 receptors.
- In synthetic form has been available for decades as Marinol (Dronabinol).
- Schedule 8 compound in Australia but no TGA-registered product is currently marketed.
- Available: On prescription in the U.S, Canada, Germany and New Zealand.
- Indications: Chemotherapy-induced nausea and vomiting, cachexia, anorexia.
- Emerging Indications include: Pain, spasticity, insomnia, dementia, Tourette's etc.

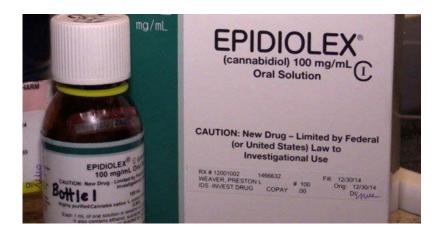


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- A non-intoxicating cannabinoid.
- Largely inactive at CB1 and CB2 cannabinoid receptors but has diverse other actions e.g. TRPV1, 5-HT1A, GPR-55.
- May increase endocannabinoid levels by inhibiting **FAAH**.
- A schedule 4 medicine in Australia, but no TGA-registered products currently available.
- Small numbers of children have compassionate access in NSW/QLD epilepsy trials.
- Emerging Indications: Epilepsy, psychosis, anxiety, dementia, addictions, acne.

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VOL. 376 NO. 21

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

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

RESULTS

The median frequency of convulsive seizures per month decreased from 12.4 to 5.9 with cannabidiol, as compared with a decrease from 14.9 to 14.1 with placebo (adjusted median difference between the cannabidiol group and the placebo group in change in seizure frequency, -22.8 percentage points; 95% confidence interval [CI], -41.1 to -5.4; P=0.01). The percentage of patients who had at least a 50% reduction in convulsiveseizure frequency was 43% with cannabidiol and 27% with placebo (odds ratio, 2.00; 95% CI, 0.93 to 4.30; P=0.08). The patient's overall condition improved by at least one category on the seven-category Caregiver Global Impression of Change scale in 62% of the cannabidiol group as compared with 34% of the placebo group (P=0.02). The frequency of total seizures of all types was significantly reduced with cannabidiol (P=0.03), but there was no significant reduction in nonconvulsive seizures. The percentage of patients who became seizure-free was 5% with cannabidiol and 0% with placebo (P=0.08). Adverse events that occurred more frequently in the cannabidiol group than in the placebo group included diarrhea, vomiting, fatigue, pyrexia, somnolence, and abnormal results on liver-function tests. There were more withdrawals from the trial in the cannabidiol group.

The first published RCT of CBD in pediatric epilepsy (May 2017) showed reasonable efficacy.

Question mark over role of pharmacokinetic interactions with clobazam......

Typical Victorian Cannabis Grower



www.nature.com/tp

Cannabidiol enhances anandamide signaling and alleviates psychotic symptoms of schizophrenia

FM Leweke^{1,2}, D Piomelli^{3,4}, F Pahlisch^{1,3}, D Muhl^{2,3}, CW Gerth², C Hoyer^{1,2}, J Klosterkötter², M Hellmich⁵ and D Koethe^{1,2}

Cannabidiol is a component of marijuana that does not activate cannabinoid receptors, but moderately inhibits the degradation of the endocannabinoid anandamide. We previously reported that an elevation of anandamide levels in cerebrospinal fluid inversely correlated to psychotic symptoms. Furthermore, enhanced anandamide signaling let to a lower transition rate from initial prodromal states into frank psychosis as well as postponed transition. In our translational approach, we performed a double-blind, randomized clinical trial of cannabidiol vs amisulpride, a potent antipsychotic, in acute schizophrenia to evaluate the clinical relevance of our initial findings. Either treatment was safe and led to significant clinical improvement, but cannabidiol displayed a markedly superior side-effect profile. Moreover, cannabidiol treatment was accompanied by a significant increase in serum anandamide levels, which was significantly associated with clinical improvement. The results suggest that inhibition of anandamide deactivation may contribute to the antipsychotic effects of cannabidiol potentially representing a completely new mechanism in the treatment of schizophrenia. *Translational Psychiatry* (2012) **2**, e94; doi:10.1038/tp.2012.15; published online 20 March 2012

CBD shown to be as effective as amisulpiride (Solian) in treating schizophrenia but has a better side effect profile. A larger trial is underway.

Mythbuster: cannabis causes schizophrenia



Markus Leweke



Young children with mental health issues could be treated with medicinal cannabis

LANAI SCARR, Senior Writer, News Corp Australia Network March 3, 2017 10:28am Subscriber only

EXCLUSIVE

CHILDREN as young as twelve suffering anxiety and severe mental health issues could be treated with medicinal cannabis, as part of a world first study by former Australian of The Year, psychiatrist Patrick McGorry.

Professor McGorry has received private philanthropic funding through the Lambert Initiative to start medicinal cannabis trials in mentally ill young people aged 12–25 through Headspace centres from June.

Patients with anxiety and depression who have had trouble with traditional therapies will receive two to four powder capsules daily of cannabidiol, a nonpsychoactive component of cannabis. Those taking part will receive the medication for twelve weeks to see the impact of the drug on their condition. If successful patients could receive access to the drug longer term.

Professor McGorry's study will be the first in the world to look at the use of cannabidiol in youth.

RELATED: How medicinal cannabis might help



D Former Australian of the Year Professor Patrick McGorry.

Current trial of CBD for anxiety in teenagers through VIC headspace centres and Lambert Initiative.



How would you like your cannabis?



SMOKED



VAPORISED



OIL / TINCTURE



CAPSULES



BUCCAL SPRAY



LOZENGE



CHEWING GUM



DAB (RESIN)



EDIBLES



INFUSED TEA



TOPICAL GEL



TRANSDERMAL PATCH



CREAM



SUPPOSITORY



Evidence of efficacy?



http://nationalacademies.org/hmd/reports/2017/health-effects-of-cannabis-and-cannabinoids.aspx

Conclusions from NAS review (2017)

Conclusive or substantial evidence

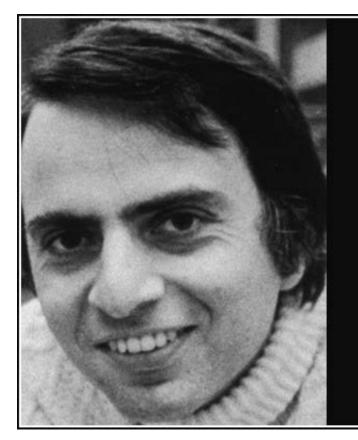
- For the treatment of chronic pain in adults (*cannabis*)
- As anti-emetics for chemotherapy-induced nausea and vomiting (oral cannabinoids)
- For improving patient-reported multiple sclerosis spasticity symptoms (*oral cannabinoids*)

Moderate evidence

• Improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis (*cannabinoids*, primarily *Nabiximols*)

Limited evidence

- Increasing appetite and decreasing weight loss in HIV/AIDS (cannabis and oral cannabinoids)
- Improving clinician-measured multiple sclerosis spasticity symptoms (oral cannabinoids)
- Improving symptoms of Tourette syndrome (*THC capsules*)
- Improving anxiety symptoms in a public speaking test, in individuals with social anxiety (CBD)
- Improving symptoms of PTSD (nabilone; one single, small fair-quality trial)
- Better outcomes after a traumatic brain injury or intracranial hemorrhage



The absence of evidence is not the evidence of absence.

— Carl Sagan —

AZQUOTES

Other Issues with Clinical Trial Evidence

- Dissociation between the products being used in *clinical trials* (e.g. Sativex) and those being used in the *community* (oils, smoked and vaped cannabis).
- Clinical trials may not capture spectacular n=1 effects that are anecdotally reported e.g. in epilepsy and tumour regression.
- Already 100 million users of cannabis products worldwide each year. No mortality, unprecedented safety signal already present.
- Doubt that the "gold standard" clinical trial approach is sustainable in general medicine, let alone cannabis research.
- Smartphone and cloud approach may be more suited.





Current community use of medicinal cannabis

Cannabis and Medicine Survey (CAMS)

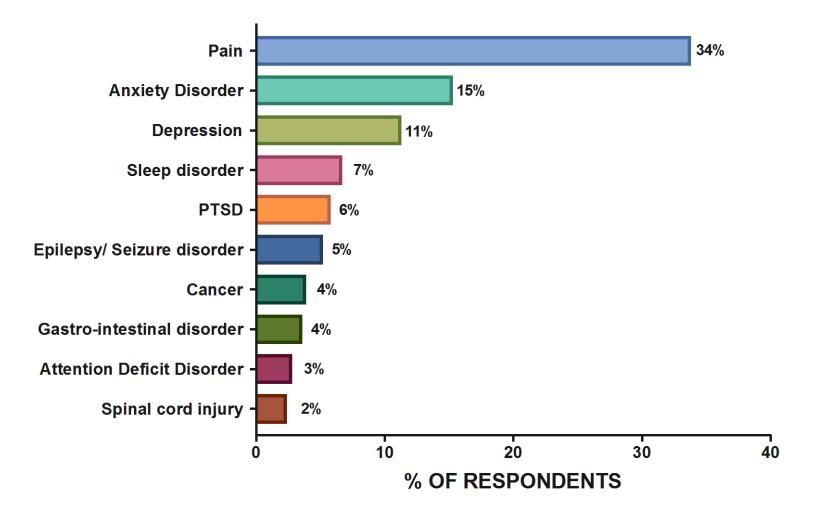
(Lintzeris, McGregor, Elias, Allsop et al unpublished)

- On-line survey using REDcap with over 1700 respondents.
- Recruited mostly via social media.
- 54% of survey respondents indicated they had used cannabis for nonmedical reasons prior to medicinal use.



Top 10 Indications Treated

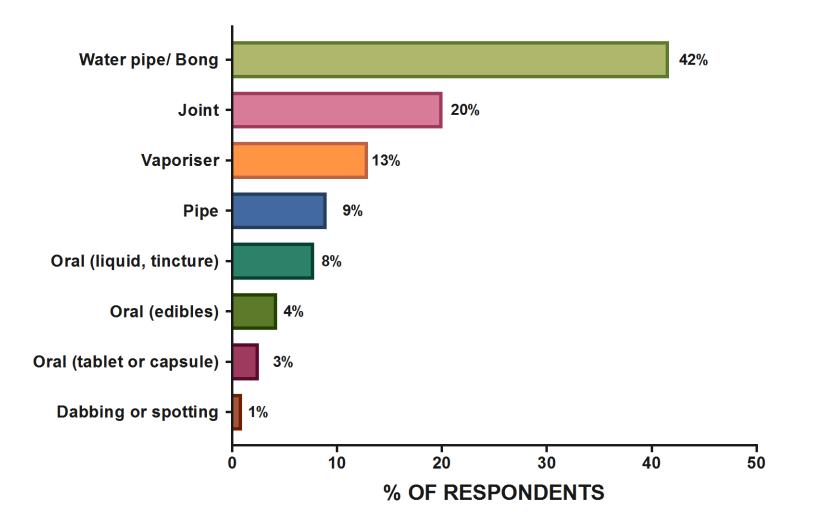
(n=1468)



*Pain combines back pain, neck pain, arthritis, neuropathy, migraines and fibromyalgia

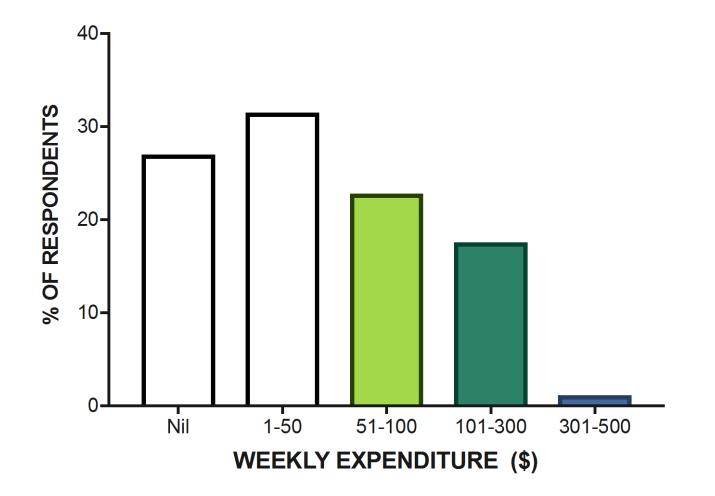
Route of Administration

n=1456

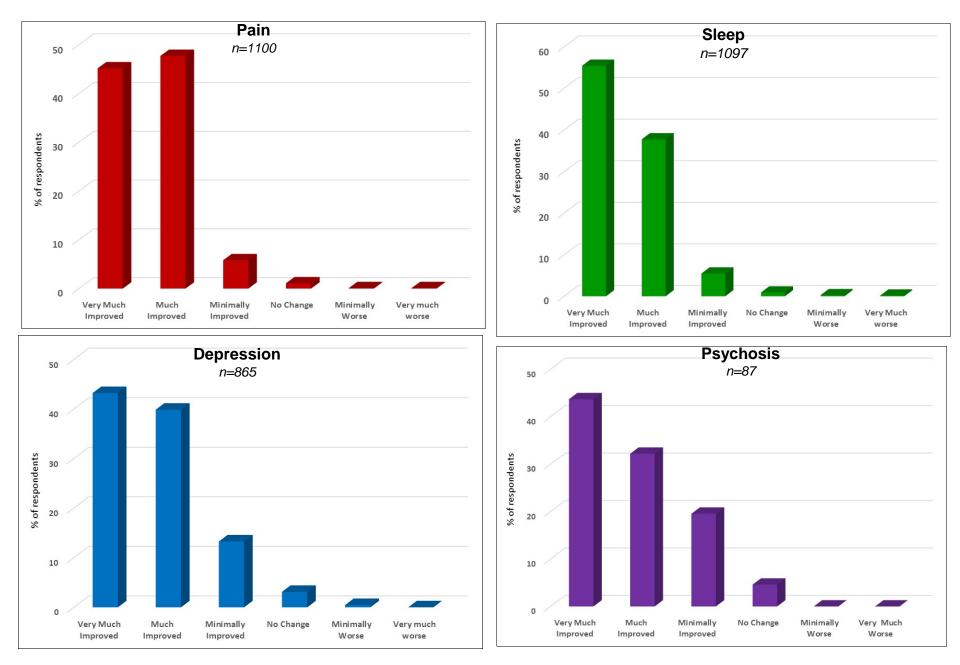


Estimation of Weekly Expenditure on Medical Cannabis

n=1236



Self-rated Improvement







THE PELICAN STUDY

Paediatric **E**pilepsy **L**ambert Initiative **C**annabinoid **AN**alysis

AIM: To analyse the cannabinoid content and effectiveness of artisanal cannabis products used as treatment for childhood epilepsy in Australia.



High variability in the content of illicit cannabis oils rated as "effective" by parents

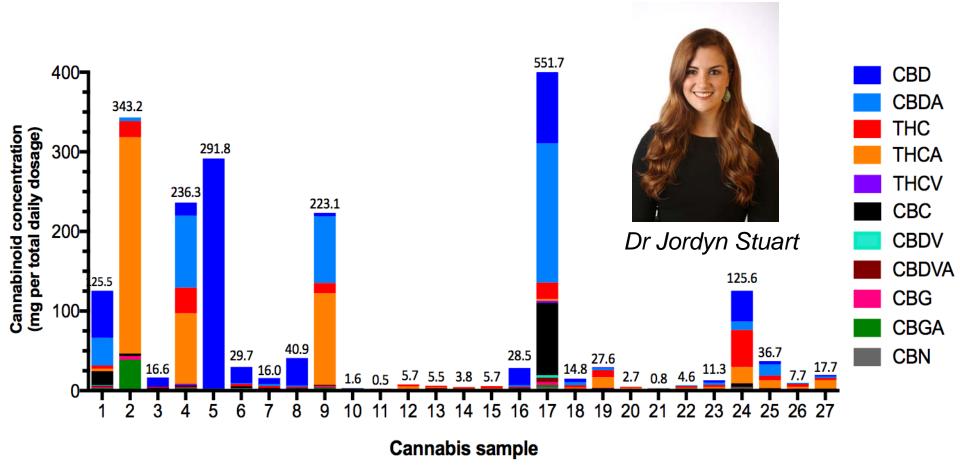


Figure 1. Cannabinoid concentration in milligrams (mg) per daily dosage in all 27 cannabis samples perceived "effective" i.e. ≥50% seizure reduction according to parent self-report. Numbers above each bar indicate total cannabinoid content.

These children need a reliable supply of medicines containing stable, fixed doses



How do Australian GPs feel about medicinal cannabis?

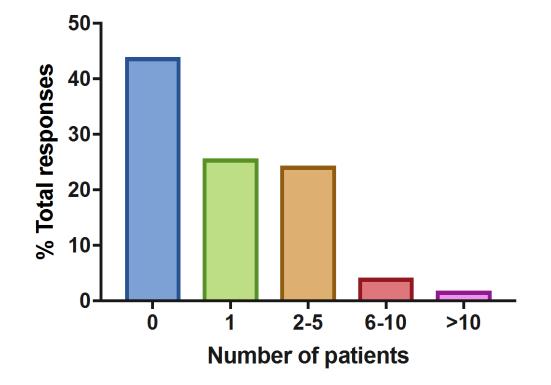
Survey of Australian GPs around Medicinal Cannabis

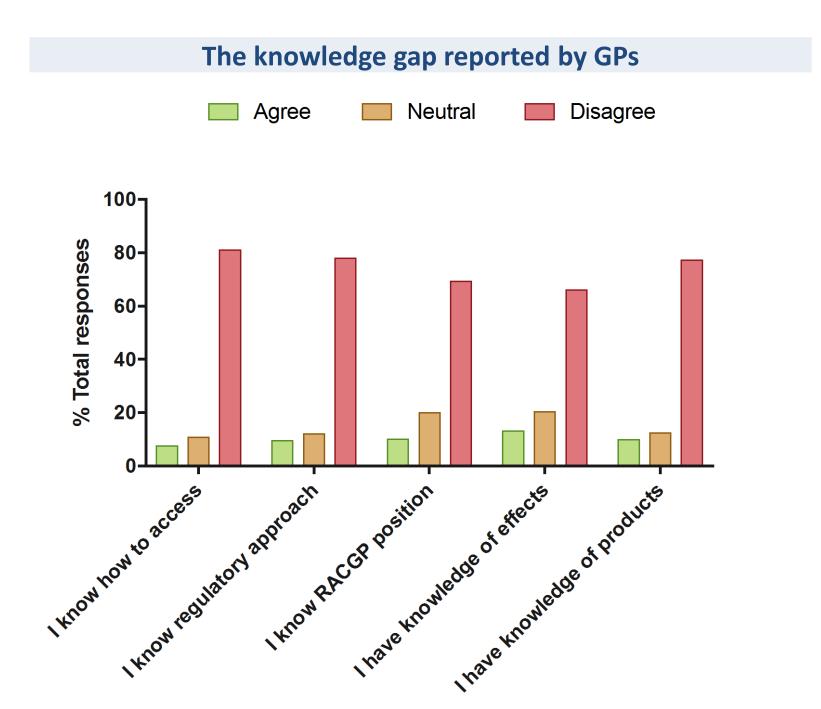
(McGregor, Karanges, Suraev, Elias, Manocha et al unpublished)

- Pen and paper survey delivered at *HealthEd* educational events (August-November 2017).
- A work in progress: responses so far from Sydney, Adelaide and Melbourne events. Brisbane and Adelaide yet to come. Total responses to date = **459**.
- GPs surveyed to date work at practices in metropolitan (67%), regional (30%) and remote areas (3%).

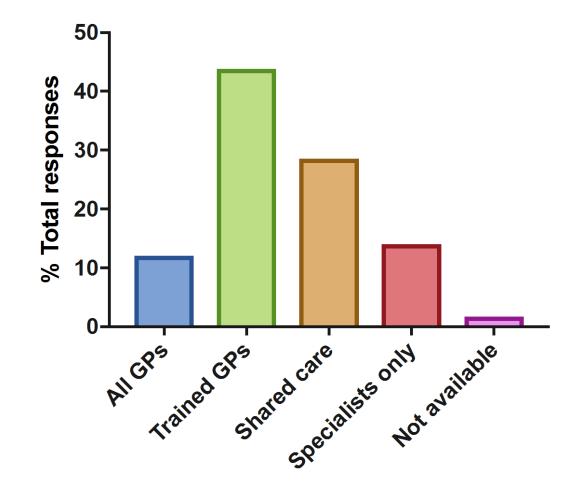


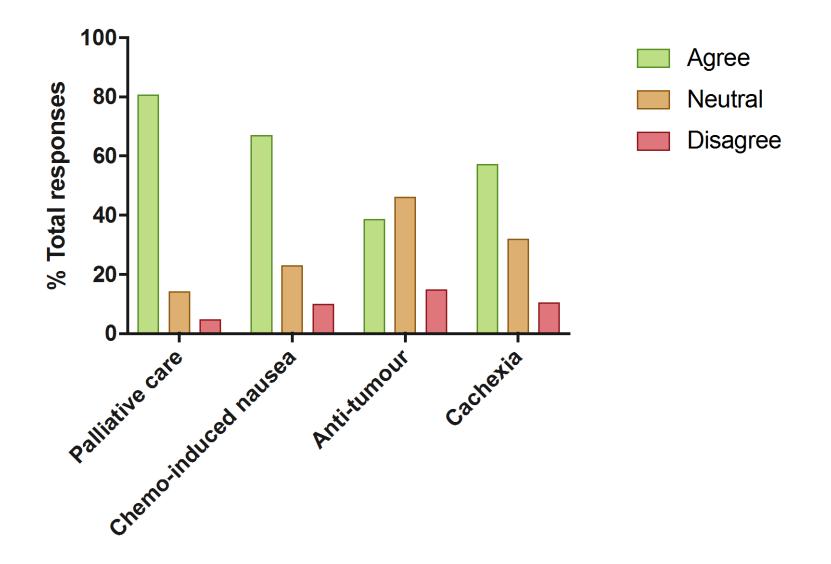
In the past 3 months, how many of your patients have enquired about medicinal cannabis products?

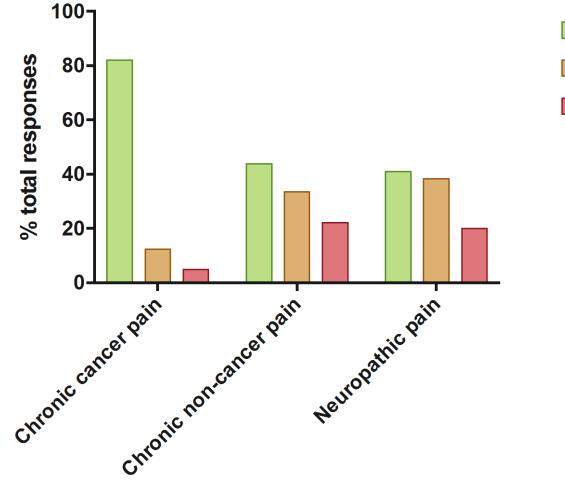


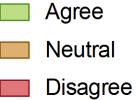


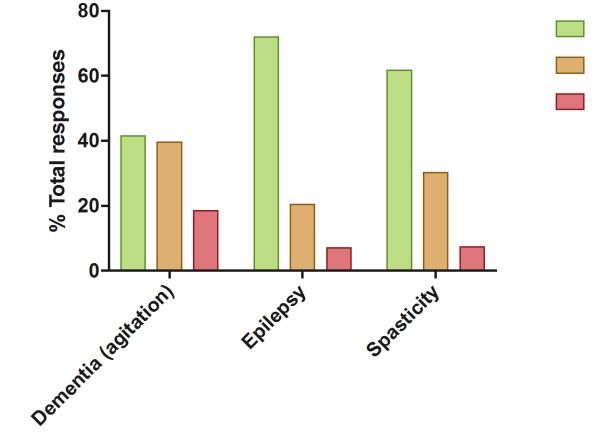
The right to prescribe medicinal cannabis should be available to:

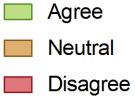


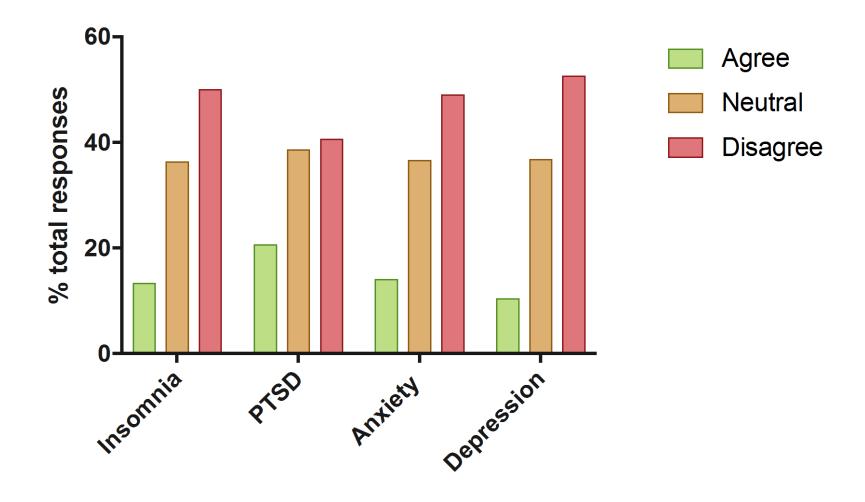




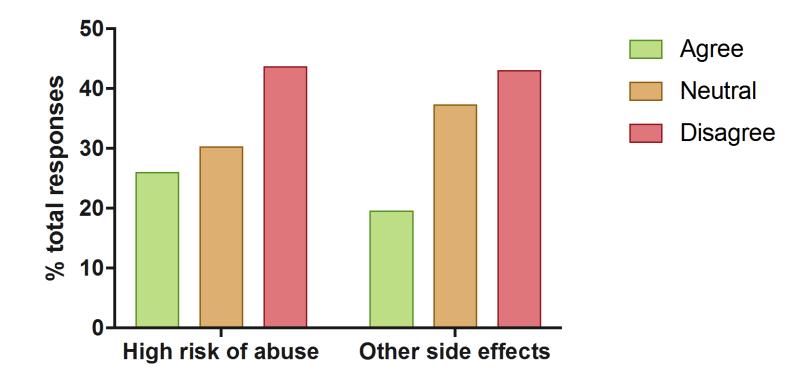




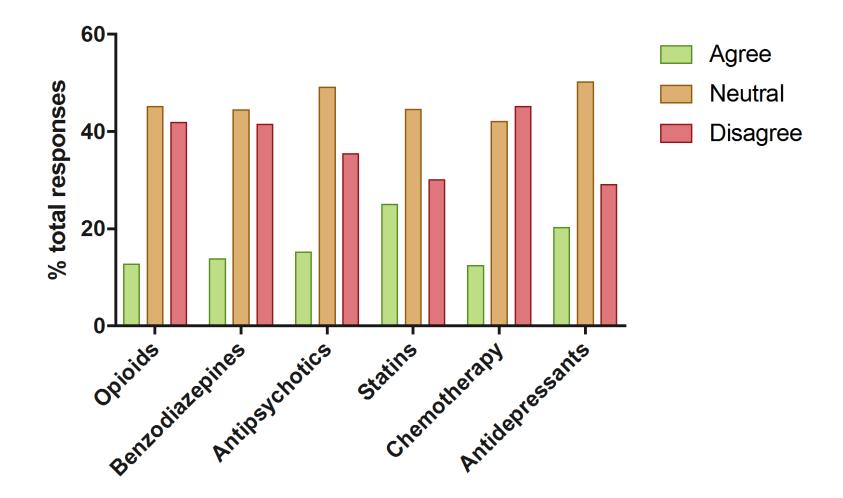




I would not prescribe due to



Medicinal cannabis is generally more hazardous than.....





Can patients access products?

Patient access

- In general, prescribing medicinal cannabis can only be undertaken by GPs in conjunction with specialists (although see next slide for exceptions).
- Processes require separate Federal and State approvals.
- Three mechanisms:
 - **Special Access A:** only for individual patients with only weeks to live.
 - Special Access B: individual patients, requires evidence based application.
 - Authorised Prescriber: specialist can obtain approval to use a product with class of patients (i.e. multiple patients with same diagnosis). Major current example is prescription of *Epidiolex* in pediatric epilepsy.



https://www.tga.gov.au/access-medicinal-cannabis-products

Are these schemes delivering?

- Only **11** notifications under **SAS-A**: this mechanism only recently possible following Senate disallowance motion.
- TGA "warning off" manufacturers: you are not permitted to supply under SAS-A.
- As of October 2017, **151** applications for medicinal cannabis products approved by TGA under **SAS-B**.
- Only **30 Authorised Prescribers** in Australia: nearly all are pediatric neurologists prescribing *Epidiolex* for a total of **101** patients.
- Lack of **PBS subsidy** for medicinal cannabis products puts them out of the reach of most individuals, particularly those on disability pensions and Centrelink benefits.

Are these schemes delivering?

- Only 4 notifications under **SAS-A**: this mechanism only recently possible following Senate disallowance motion. TGA "warning off" manufacturers.
- As of July 1st 2017, less than 100 (?) applications for medicinal cannabis approved by TGA under **SAS-B**.
- Less than **30 Authorised Prescribers** in Australia: nearly all are pediatric neurologists prescribing *Epidiolex*.
- Note that there is **no PBS subsidy** for medicinal cannabis products, putting them out of the reach of most individuals, particularly those on disability pensions and Centrelink benefits.
- Mismatch between conditions that attract approval ("zebras") and those where illegal medicinal cannabis is most prevalent ("horses").

The community is using medicinal cannabis (illegally) for:



- Back pain
- Arthritis
- Neuropathic pain
- Fibromyalgia
- Migraine
- Insomnia
- Anxiety
- Depression
- PTSD
- Cancer
- Dementia

The TGA and State Health Depts are likely to approve medicinal cannabis applications for:



- Intractable paedatric epilepsy
- Multiple sclerosis
- Chemotherapy-induced nausea

COMMENT OCTOBER 11 2017

lain McGregor

SAVE PRINT LICENSE ARTICLE

Why so few Australians are using medicinal cannabis on prescription

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SHARE 💓 TWEET MORE So often in Australia, we are astounded to discover that good policy has been subverted by political mismanagement. Think NBN, gas supply, the marriage plebiscite and ... medicinal cannabis. A resounding 85 per cent of Australians support legislation permitting the use of cannabis for medical purposes. Find out more > SHARE

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It is increasingly clear that many diseases can be treated by cannabis products that have little, if any, THC, the main psychoactive ingredient. Photo: The Age

And medical specialists can indeed apply to the Therapeutic Goods Administration to prescribe cannabis-based products to their patients under the Special Access and Authorised Prescriber schemes.

However, the most recent figures show that only 153 patients nationwide have been authorised to receive medicinal cannabis products under the Special Access Scheme. And only about 30 Australian doctors have been granted Authorised Prescriber status, prescribing cannabis products to a further 101 patients.

MOST POPULAR

- Forget the issue, it's the political party that counts
- Weinstein: It took a split second for 2 me to glimpse the predator in him
- This is the only way Abbott's vendetta will end

The alternative:



GROW YOUR OWN!

By comparison

Number of patients, Canada (population 36.2M)

As of October 2017, more than 200,000 patients registered.

Number of patients, Israel (population 8.5M)

As of October 2017, more than **30,000** patients.

Estimated of number of potential patients, Australia (population 24M)

50,000-100,000?

A prescription for change

- Risk avoidance *versus* risk management.
- Amnesty for compassionate use with verified conditions (e.g. cancer pain, palliative care, refractory epilepsy).
- Allow appropriately trained/credentialed GPs to prescribe if they want to.
- Reschedule non-intoxicating CBD rich products to Schedule 3 (Pharmacy only medicine).



Premium quality formulas to support energy production



Ricky Ponting Australian Cricket Legend

A prescription for change

- Risk avoidance *versus* risk management.
- Amnesty for compassionate use with verified conditions (e.g. cancer pain, palliative care, refractory epilepsy).
- Allow appropriately trained/credentialed GPs to prescribe if they want to.
- Reschedule non-intoxicating CBD rich products to Schedule 3 (Pharmacy only medicine).
- Reschedule moderate THC products to Schedule 4 (Prescription medicine).
- Formulate national research agenda and training program.



Thank you!



lambert.initiative@sydney.edu.au

