

The Panel with Nexus: Cannabis and Mental Health – What Role does Medicinal Cannabis play?

Kah-Seong Loke, Nexus

Friday 4/3/2022 – 12.00-12.45pm



We respectfully acknowledge the Traditional custodians of the land on which we meet today, the Wurundjeri people of the Kulin Nation, and we pay respect to all Aboriginal Community Elders, past and present.





We recognise and value the knowledge and wisdom of people with lived/living experience, their supporters and the practitioners who work with them. We celebrate their strengths and acknowledge the important contribution that they make to the development and delivery of health and community services.



Nexus Team

Chris Hynan – Manager Victorian Dual Diagnosis Initiative Kevan Myers – Team leader Kah-Seong Loke – Psychiatrist **Simon Kroes** – Dual diagnosis clinician **Ange Wallace** – Dual diagnosis clinician Mirella Rao – Dual diagnosis clinician **Annie Dolan**– Administrative assistant



Dual Diagnosis

Declaration of Interest - Nil

- Medicinal cannabis and Driving •
- •
- TGA/DHS permit application process ۲

TGA-approved clinical indications

Other clinical uses [harm reduction]

Contraindications and Drug interactions

- Case examples
- ٠ Department of Addiction Medicine (DoAM) trial •
- Suppliers and formulations

Pharmacology • Formulations •

Medicinal Cannabis

Cannabis • **Synthetic Cannabinoids** •

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OUTLINE









CANNABIS TYPE

Drugs like cannabis and derived products have been used throughout history, and modern prevalence is spread around the world.



Effects of Cannabis Use – Short Term



Physical

- Sedation, Confusion
- Motor impairment (driving)
- Increased appetite
- Dry mouth, N&V
- Bloodshot eyes
- Tachycardia, Hypotension
- Respiratory (cough, wheeze)

Cannabis (THC) Intoxication/Overdose

- Rare following administration by smoke inhalation
- More common following oral administration and with synthetic cannabinoids

Neuropsychological

- Sedation, Confusion
- Euphoria, Disinhibition
- Impairment
- Amotivation, Anergia
- Anxiety, Depression
- Paranoia \rightarrow Psychosis

Effects of Cannabis Use – Long Term



Physical

- Impairment (driving, etc.)
- Respiratory: sore throat, cough, lung disease (COPD)
- Amotivation, Dysphoria
- Hormonal: \downarrow libido, \downarrow sperm count, \updownarrow menstruation
- Cannabis hyperemesis syndrome

Cannabis hyperemesis syndrome (CHS)

- frequent, recurring episodes of severe nausea, vomiting, dehydration and abdominal pain; may avoid certain foods (→vomiting) ± LOW; hot baths or showers to relieve symptoms
- frequent visits to the emergency department
- higher risk if: use at least once a week; used since adolescence
- delay of several years in the onset of CHS from commencement

Social: cost, dependence + complications, legal

Other: Barrier to Tx, pharmaco-interactions (CYP-450;1A2,2D6,3A4)

Neuropsychological

- Cognitive: \downarrow STM, Δ time perception;
 - \downarrow p/motor speed, working memory in adol.
- Anxiety, Panic attacks
- Amotivation, Dysphoria
- Paranoia, Perceptual abnormalities
- Psychosis (vulnerability)

FIG. 27 Potency of cannabis and perception of risk from cannabis use among adolescents, Europe and United States, 1995–2019

Europe

United states

risk/harm of smoking cannabis regularly 80 70 60 50 40 30 20 10 0 1999 2001 2005 2005 2009 2011 2013 2013 2013 2013 2013 1995 1997

Perception among adolescents of



Linear trend (Europe) Linear Trend (United States)

Percentage

Endocannabinoid System

CANNABINOID RECEPTOR

The cannabinoid receptors are G protein-coupled receptors that are activated by endocannabinoids or exogenous agonists such as tetrahydrocannabinol. CBD does not directly fit CB1 or CB2 rceptors but has powerful indirect effects still being studied.





Endocannabinoids

- 2-arachidonoylglycerol (2-AG)
- anandamide (N-arachidonoylethanolamide)

Cannabis

- Derived from Indian hemp plants (Cannabis sativa, indica, ruderalis)
- 3 main ingredients:
 - Δ^9 -tetrahydrocannabinol (THC); dronabinol synthetic Δ^9 -THC
 - cannabidiol (CBD)
 - cannabinol (CBN) [25% potency of THC]
- MoA agonist at CB1 receptors in CNS
 - agonist at CB2 receptors in PNS
- CNS depressant; Hallucinogenic effects in large doses
- Most commonly & frequently used illicit drug amongst Australians aged over 14*
 - 36% have used in their lifetime
 - 11.6% have used in the last 12 months
 - 37% of cannabis users using it weekly or more often

*National Drug Strategy Household Survey 2019





Cannabinol (CBN)



Marijuana usually mixed with tobacco (& very occ'ly speed/ice/cocaine/heroin) in a "mull bowl" \rightarrow "mull" or "mix"



Cannabis Misuse in Mental Illness



Why do people with severe mental illness (SMI) use cannabis?

Main reasons given:

- reduce boredom
- to socialise
- to enjoy positive mood from intoxication

Nearly half of patients use cannabis:

- to get relief from dysphoria & agitation
- to sleep better

A minority use it to reduce their suspiciousness

Self-medication has been proposed as a reason (yet to be supported by research evidence)

The CBD in cannabis has anti-anxiety & anti-psychotic effects

(but street cannabis contains very small quantity of CBD & high quantity of THC)

None of the models proposed explain the interaction b/SMI & substance use disorder nor has a satisfactory evidence base & it is thought that a multiple risk factor model is needed.

Reasons For Use Scale ()

Which drug do you use the most or causes most concern for you? (Write drug name here): Manyung

Considering your current use of that substance, how often do you use that drug for the following reasons? (Tick a box for each reason)

		1 Almost never never	2 Some of the time	3 Half of the time	4 Most of the time	5 Almost always/ always			Abnost never/ never	2 Some of the time	3 Half of the time	4 Most of the time	5 Almost always/ always
10	To relieve boredom				V		14	To get away from the voices	~				
2	To make it easier to sleep		1				15	Because you feel more self confident and sure	. /				
3	To slow down racing thoughts		V					of yourself	V	-	-		
4	To be sociable	~					10	you feel nervous 7	V				
5	To relax				~		17	Because it's what most of your triends do when you get together		1			
8	To be part of a group	V					18	As a way to celebrate	1				
7	To get high			~	WA		.19	To decrease restlessnosa (America		-	~		
8	To decrease ()) suspiciousness / paranola		V				20	Help me concentrate	~				
9	To forget your worries	V					21	Because your friends	1				
10	Because it's fun	1					22	To be liked	~		-		
11	To reduce side effects of medication	V	191				23	So you won't feel left out	~	-			
12	Because it makes a social gathering more enjoyable	V					24	It helps when you feel	- /	-			
13	To help you talk to others	1			-			depressed interm	V			-	
-						1	25	To feel more motivated	と深		2		
	Spenter, Caxle, Michie, 197	2 based on D	MQ Cloper	1994 (with a	del terrat River	0	26	Because it makes you feel good		V			

Synthetic cannabinoids



• CB-1 and CB-2 agonists

- Synthetic cannabinoid families (e.g. AM-xxx, CP-xx,xxx, HU-xx, JWH-xxx) which are classified by the creator of the substance; e.g. benzoylindole, cyclohexylphenol, naphthoylindole, phenylacetylindole
- aka Kronic, K2, Karma, Spice, Voodoo, Aroma and Dream (sold with herbal substances)
- most synthetic cannabinoid receptor agonists shohigher affinity for CB1 (and CB2) receptors than THC (**† toxicity risk**)
- not able to be detected by most pathology labs ⇒ use in occupations where mandatory drug testing occurs





Endocannabinoids	Natural cannabinoids	Synthetic cannabinoids
Arachidonylethanolamide	Δ^9 -tetrahydrobannbinol	JWH-133
	H CH	
2-arachidonoylglycerol	Cannabidiol	WIN55,212-2
К С С С С С С С С С С С С С С С С С С С		aspo

Medicinal cannabis



- Varying proportions of CBD: THC
- Formulations: capsule, oil/oral liquid, flower
- Multiple suppliers
- Varying cost / value for \$









Medicinal Cannabis		THC/unit	CBD/unit	Amount/Volume	Total THC content	Total CBD content	Cost	THC cos	/mg	CBD cost/mg	Cost/mg
Brand	Product	(mg)) (mg) (caps)) (mg)	(mg)		\$	\$/mg	ş \$/mj	g \$/mg
Spectrum gel (CBD/THC)	Spectrum Cannabis Yellow Softgels 20mg	<1	20	30)	600		70		0.13	2
Spectrum gel (CBD/THC)	Spectrum Cannabis Blue Softgels 2.5mg	2.5	3.75	5 60	150	225		70	0.47	0.3	1
Spectrum gel (THC/CBD)	Spectrum Cannabis Red Softgels 2.5mg	2.5	i <1	L 60) 150			65	0.5	5	
Spectrum gel (THC/CBD)	Spectrum Cannabis Red Softgels 10mg	10) <	1 30	300			75	0.25	5	
		(mg/mL)) (mg/mL) (mL)) (mg)	(mg)		\$	\$/mg	5	
Spectrum liquid (CBD/THC)	Spectrum Therapeutics Cannabis Oil Yellow Oral Liquid	<1	20	40)	800		95		0.13	2
Spectrum liquid (CBD/THC)	Spectrum Therapeutics Cannabis Oil Blue Oral Liquid	10) 15	5 40	400	600		110	0.28	0.1	8
Spectrum liquid (THC/CBD)	Spectrum Therapeutics Cannabis Oil Red Oral Liquid	26.3	3 <	L 40	1052			110	0.10)	
Spectrum liquid (CBD/THC)	Spectrum Therapeutics Cannabis Oil White Oral Liquid	C	100	50)	5000		295		0.0	6
		(mg)) (mg) (wafers)) (mg)	(mg)		\$	\$/mg	ş \$/m	g
iX Syrinx Pty Ltd (CBD) wfr	iX Biopharma Xativa sublingual wafers 12.5mg S4	C	12.5	5 60) 0	750		89		0.12	2 0.18
iX Syrinx Pty Ltd (CBD) wfr	iX Biopharma Xativa sublingual wafers 25mg S4	C	25	5 60) 0	1500		146		0.10	0.097
Cannatrek (CBD) oil	C25 Sunstone 25mg CBD capsules S8	C) 25	5 60) 0	1500		150		0.1	1 0.1
Cannatrek (CBD) oil	C115 Sunstone CBD oil (115mg/mL) S8	C	115	5 30 mL	. 0	3450		245		0.0	7 0.07
Cannatrek (CBD/THC) oil	C20 (20:1mg/mL) CBD oil S8 (new - C25 - 25:1)	<1	. 20) 25mL	<25	500		105	4.2	0.2	1 0.2
Cannatrek (CBD/THC) oil	C100 Amber (100:4 mg/mL) CBD oil S8	<4	100) 30mL	. 120	3000		255	2.125	0.08	5 0.08
Cannatrek (CBD/THC) oil	C200 Amber (200:8 mg/mL) CBD oil	<8>	3 200) 30mL	. 240	6000		425	1.77	0.0	0.069
Cannatrek (CBD/THC) oil	C20T5 Ruby (20:5 mg/mL) CBD oil S8	5	5 20) 30mL	. 150	600		90	0.6	5 0.1	5 0.12
Cannatrek (CBD/THC) oil	C12T12 Ruby (12.5:12.5 mg/mL) balanced CBD oil S8	12.5	12.5	5 30mL	. 375	375		90	0.24	0.24	4 0.12
Cannatrek (THC) oil	T20 Indica oil (THC 20mg/mL) S8	20) (25	5 500			\$105	0.21	L	0.21
Cannatrek (THC) oil	T25 Ruby oil (THC 25mg/mL) S8	25	i (30	750			90	0.12	2	0.12
								\$			
Beacon	Girl Scout cookies (10g)							150			
Cannatrek flowers (THC)	T15 Flower (Sativa Avadia) - 60% Sativa:40% Indica - 58	15%	6 () 10gm	1500	0		170	0.11	l .	0.11
Flower (THC)	T18 Flower (Uplift Lemnos)- 60% Sativa:40% Indica - S8	18%	6 0) 10gm	1800	0		170	0.09)	0.09
Flower (THC)	T19 Flower (Beersheba) - 70% Sativa:30% Indica - S8	19%	6 () 10gm	1700	0		150	0.09)	0.09
Flower (THC)	T17 Flower (Jerusalem) - 50% Sativa:50% Indica - S8	17%	6 () 10gm	1700	0		150	0.09)	0.09
Flower (THC)	T18 Flower (Jasmine) - 5% Sativa: 95% Indica - 58	18%	6 () 10gm	1800	0		150	0.09)	0.09
Flower (THC)	T20 Flower (Relax Daylesford)- 30%Sativa:70%Indica-S8	20%	6 () 10gm	1 2000	0		170	0.08	3	0.08
Medical Vapouriser devices	3 approved TGA devices (150+\$, 500\$, 800\$)										
Dry Herb Vaporisers											
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CBD vs THC



CBD	ТНС
Non-intoxicating	Intoxicating
Anti-inflammatory and reduces pain	Anti-inflammatory and reduces pain
May reduce anxiety	May improve appetite
Anticonvulsant	May reduce nausea
Regulate THC effects	May help with insomnia

https://www.xativahub.com/cannabis



Izzo AA, Borrelli F, Capasso R, Di Marzo V, Mechoulam R. Non-psychotropic plant cannabinoids: netherapeutic opportunities from an ancient herb. Trends Pharmacol Sci. 2009 Oct;30(10):515-27. doi: 10.1016/j.tips.2009.07.006. Epub 2009 Sep 2. Erratum in: Trends Pharmacol Sci. 2009 Dec;30(12):609. PMID: 19729208.

https://www.cell.com/trends/pharmacological-sciences/pdf/S0165-6147(09)00182-5.pdf

CBD only	THC only	THC + CBD			
Anxiety	Anxiety	Anxiety			
ASD		ASD			
Cancer pain & Sx Mx	Cancer pain & Sx Mx	Cancer pain & Sx Mx			
Chronic pain	Chronic pain	Chronic pain			
Epilepsy					
Migraine	Migraine				
Movement disorder		Movement disorder			
Multiple Sclerosis					
		Nausea			
Neuropathic pain	Neuropathic pain	Neuropathic pain			
Palliative care	Palliative care	Palliative care			
Sarcoidosis					
Sleep disorder	Sleep disorder				
Tinnitus					
Tourette Syndrome					



TGAapproved indications [formulationdependent]

Use in Psychiatry



TGA-approved

- Anxiety
- ADHD
- ASD
- PTSD
- Sleep disorder

TGA Non-Approved

- Cannabis Use Disorder
- Depression
- Psychosis
- Bipolar Disorder

Contraindications, Adverse effects and Drug interactions

Contraindications

- Young people <25yo (potential adverse effects on developing brain) [NB: use in severe, treatment-resistant epilepsy in children]
- Pregnancy/lactation
- Cardiac history severe and unstable heart disease (angina, peripheral vascular disease, cerebrovascular disease and arrhythmias) or risk factors for heart disease

Adverse / Undesirable Effects

Increased heart rate, dizziness, impaired coordination and reaction times, drowsiness, impaired short-term memory, dry mouth, nausea, anxiety, respiratory irritation (if inhaled), increased appetite, euphoria

Drug interactions

- 1. Medicinal cannabis can interact with other medicines, particularly **other CNS depressants**, causing drowsiness and potentiating any side effects; this also applies to **alcohol**.
- 2. Pharmacokinetics:
- Metabolism: THC (2C9, 3A4), CBD (2C19, 3A4), CBN (2C9, 3A4)
- THC (& tobacco smoking): induces 1A2 (clozapine, olanzapine), inhibits 2C9, 3A4
- CBD: inhibits 1A2 (CLZ, OLZ), 2D6 (antidepressants, antipsychotics), 3A4 (AED), UDP-glucuronosyltransferases UGT1A9 and 2B7, (?) glycoprotein P (P-gp)

References:

Medicinal Cannabis—Potential Drug Interactions

Specific examples: [not an exhaustive list]

- Anti-depressants (fluoxetine, fluvoxamine)
- Anti-coagulants (warfarin, apixaban, rivaroxaban)
- Antiretroviral drugs used in the treatment of HIV/AIDS
- Stomach acid inhibitors (omeprazole)
- Certain antibiotic and antifungal medications (ketoconazole, itraconazole, ritonavir, clarithromycin; rifampicin)
- Some heart medications (amiodarone, diltiazem, verapamil)
- Some anti-epileptic medications (carbamazepine, phenytoin, clobazam)
- St John's Wort
- Cannabinoid Metabolites as Inhibitors of Major Hepatic CYP450 Enzymes, with Implications for Cannabis-Drug Interactions
- Sativex Product Information (PI); Spectrum Cannabis Softgels Consumer Medicine Information (CMI)



For nurse and medical practitioners seeking to prescribe a medicinal cannabis product not included in the Australian Register of Therapeutic Goods (ARTG), Therapeutic Goods Administration (TGA) approval is required.

- TGA's Special Access Scheme
- Authorised Prescriber ('established history of use'; must report the number of patients treated every 6 months; "Treatment of refractory anxiety [and/or chronic pain] in adult patients")

New SAS submission		Look	skup records	×
Prescriber details	The TGA regulates therapeutic goods as either Medicines, Biologicals or Medical Devices. These definitions may differ from those used in the clinical setting. For example, the TGA regulates blood products as medicines and not biologicals. It is recommended that you search all three therapeutic good types before utilising the free text function. If you use the free text function and categorise your product incorrectly, you will be asked to withdraw the application/notification and create a new submission.		category	۲.
	Therapeutic Good Type *	~	Name 🛧	
selection	Medicine Biological		Category 1-CBD medicinal cannabis product (CBD≥98%)	-
	O Medical Device		Category 2-CBD dominant medicinal cannabis product (CBD≥60% and less than 98%)	
Product details	Medicine Please use the search below to make your product selection (including active ingredient, dosage form		Category 3-Balanced medicinal cannabis product (CBD less than 60% and ≥40%)	
	and indication).		Category 4-THC dominant medicinal cannabis product (THC 60-98%)	
Patient details	Active ingredient(s) *		Category 5-THC medicinal cannabis product (THC greater than 98%)	
E	found through the search tool			
E Summary	Patient has chronic generalised anxiety which has not respective treatment including prescription medications and psychology	onded jical th	d well to conventional medical Select Cancel Remove value	e
	4-weekly monitoring; 2-year permit		Page 21	

Victorian Department of Health – Medicines and Poisons Regulation (MPR)



- Any doctor or nurse practitioner in Victoria can prescribe medicinal cannabis for any patient with any condition, if they believe it is clinically appropriate to do so.
- **Commonwealth** and/or state approvals may be required
- From 28 February 2022, prescribers no longer require a Schedule 8 treatment permit from the Victorian Department of Health when prescribing a Schedule 8 medicinal cannabis product to non-drug dependent patients
- For drug-dependent patients, an application for a treatment permit can be made Application for a permit to treat a patient with Schedule 8 drugs form [specify pt is drug-dependent]
- Prescribers are still required to check SafeScript each time before prescribing any Schedule 8 medicinal cannabis products to any patient."

Medicinal cannabis

Prescribing medicinal cannabis

https://www.health.vic.gov.au/drugs-and-poisons/medicinal-cannabis

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Smoking cessation

https://education.quit.org.au/







View





Brief Advice training -**Hospital/Health Services** (including inpatient mental health services) - 30 min









Smoking cessation



Nicotine Replacement Therapy (NRT)



Varenicline



Bupropion

Nortriptyline

RESERVITION ONLY MEDICINE 2 Y B A Non-Statistical Release tabletis 450 mg



Price: \$69.99

***** (266)

Nicorette Quit Smoking QuickMist Mouth Spray



Price: \$69.99

***** (143)

Nicorette Quit Smoking QuickMist Mouth Spray Cool



Price: \$55.99

\$11.00 Off RRP!

***** (40)

Nicorette Quit

Smoking QuickMist

Mouth Spray

Price: \$30.99 \$9.00 Off RRP! ***** (45)

Nicorette Quit Smoking QuickMist Mouth Spray

- Approximately \$23-31 per spray pump.
- *Each* spray pump is equivalent to ~75-150 cigarettes or about 3-6 packs of 25 cigarettes

Take home messages



- Can be effective for anxiety disorders
- Can be useful for harm reduction:
 - Financial harm
 - COPD
 - Family/IPV violence
 - Reduced psychotic symptoms (CBD formulations only)
 - Risk of losing licence for drug driving (CBD-only formulations; rinse mouth if THCcontaining preparations, especially oils)

BUT ? duration of therapy, tapering/cessation process

- TGA permit process: Psychiatrist? GP with letter from psychiatrist?
- Consider addressing tobacco/nicotine

Future directions



Research

- Clinical applications and efficacy; CBD vs THC
- SVHM Department of Addiction Medicine: CBD trial for young people with CUD
- Orygen: High-dose CBD for early psychosis
- Northern Hosp ED: High-dose CBD for cannabis hyperemesis syndrome

Regulation

- **OTC CBD**: low-dose (<150 mg/d) CBD over the counter
- TGA down-scheduled CBD from a S4 (prescription medicine) to a S3 (pharmacist-only medicine) in early 2021; no product has yet been approved by the Australian Register of Therapeutic Goods (ARTG)

Tuesdays with Nexus





https://www.svhm.org.au/our-services/departments-and-services/n/nexus/tuesdays-with-nexus/resources

Resources

HOME > OUR SERVICES > DEPARTMENTS AND SERVICES > N > NEXUS > TUESDAYS WITH NEXUS > RESOURCES

2022 Resources ~ Peer Cadet Program Overview 2021 Resources ~ A Practical Guide for Working with Carers of People with a Mental Illness Bouverie Centre CCA booklet online CCISC in Victoria Presentation by Gary Croton Compassion Training Monash University Sep 2021 Contesting the term compassion fatigue Hofmeyer et al 2020 Family, carers and supporters - Royal Commission Impact on Carers - Royal Commission Intersectionality source Manal Shehab LIFT source Anshuman Chateuvedi, Banyule Community Health service Mind Australia's Lived Experience Strategy 2021-2024 Mind Australia Lived Experience strategy NEXUS Education 2021 confidentiality privacy Royal Commission - Department of Addiction Medicine Royal Commission - VAADA SSDTA Flyer Eligibility and Process source DoAM SSDTA Flyer What is SSDTA? source DoAM SSDTA Flyer What should I know? source DoAM SSDTA Presentation Nov 2021 source DoAM Youth Affairs Council Victoria Oct 2021

Panel with Nexus





HOME > OUR SERVICES > DEPART	MENTS AND SERVICES > N > NEXUS > RESOURCES > THE PANEL WITH NEXUS
The Panel with Nexus fortnightly c and integrated Interventions for pe	online sessions are an internal forum open to St Vincent's staff, exploring treatment responses tople with mental health and substance use/addiction.
Sessions will recommence in ea	arly 2022. For more information please email nexus@svha.org.au.
2021 Resources	
Alcohol and anti-craving medication	ons Dec 2021
Bernese Method (microdosing for	buprenorphine induction)
Guidelines for the treatment of alc	ohol problems
Long Acting Injectable Buprenorph	nine Nov 2021
Uniting Harm Reduction Overdose	Prevention Program - NYXOID





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