AUSTRALIA'S WORLD-FIRST PSILOCYBIN STUDIES:

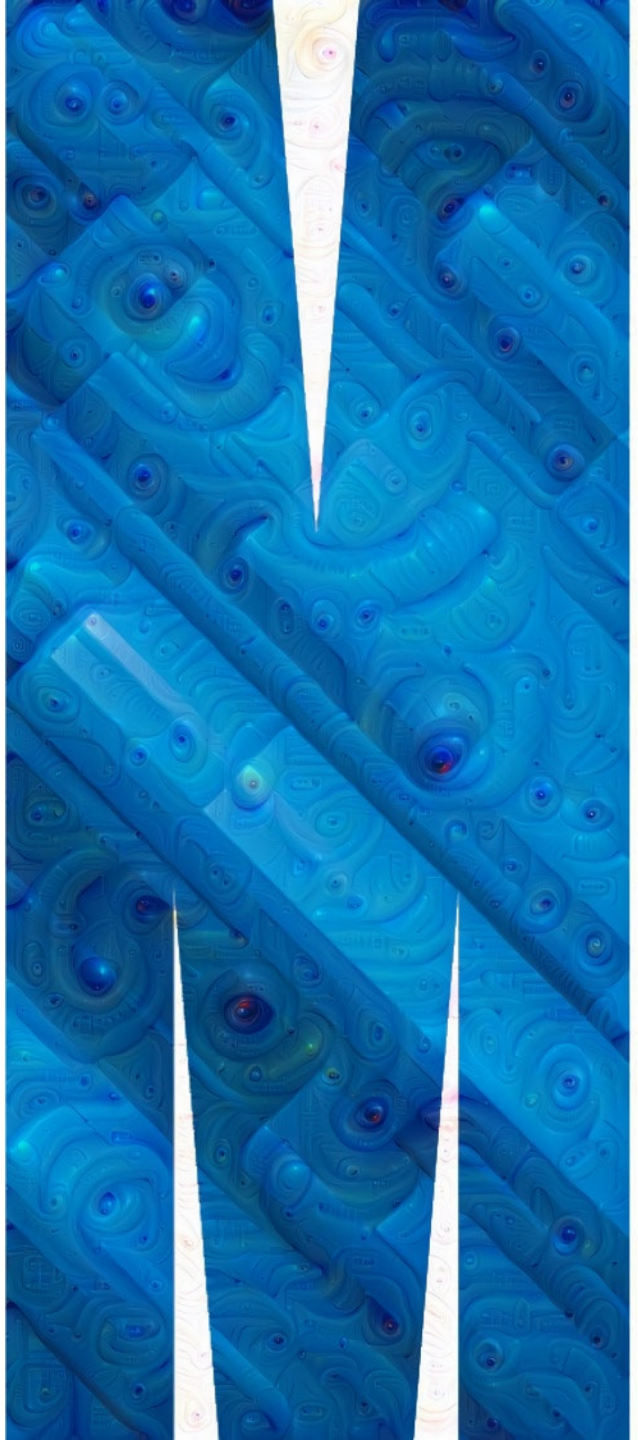
CLINICAL INSIGHTS, THERAPIST TRAINING APPLICATIONS, AND FUTURE INNOVATIONS

1 Nov 2024 - APSAD

PAUL LIKNAITZKY, PhD
Head, The Clinical Psychedelic Lab
Dept of Psychiatry
Monash University

Paul.L@monash.edu
@pliknaitzky
www.monash.edu/psychedelics

MONASH University



AFFILIATIONS AND FUNDING

Founder, Head – Clinical Psychedelic Lab, Dept Psychiatry, Monash University (Aus)

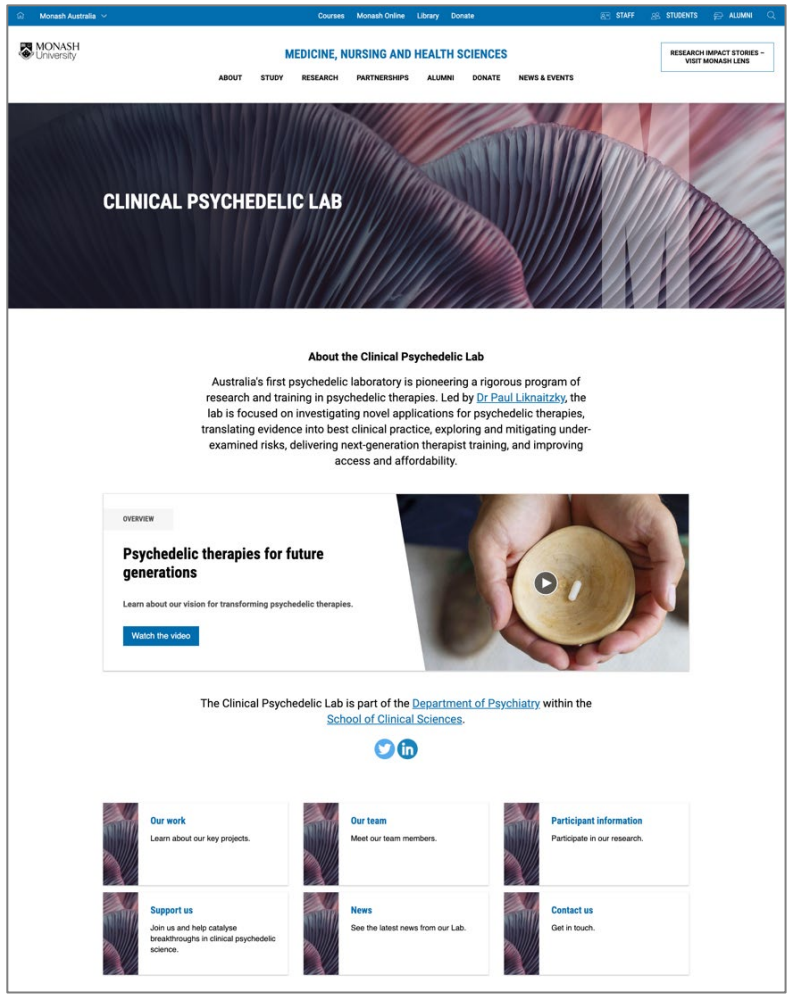
Co-founder, CSO – Clarion Clinics (Aus)

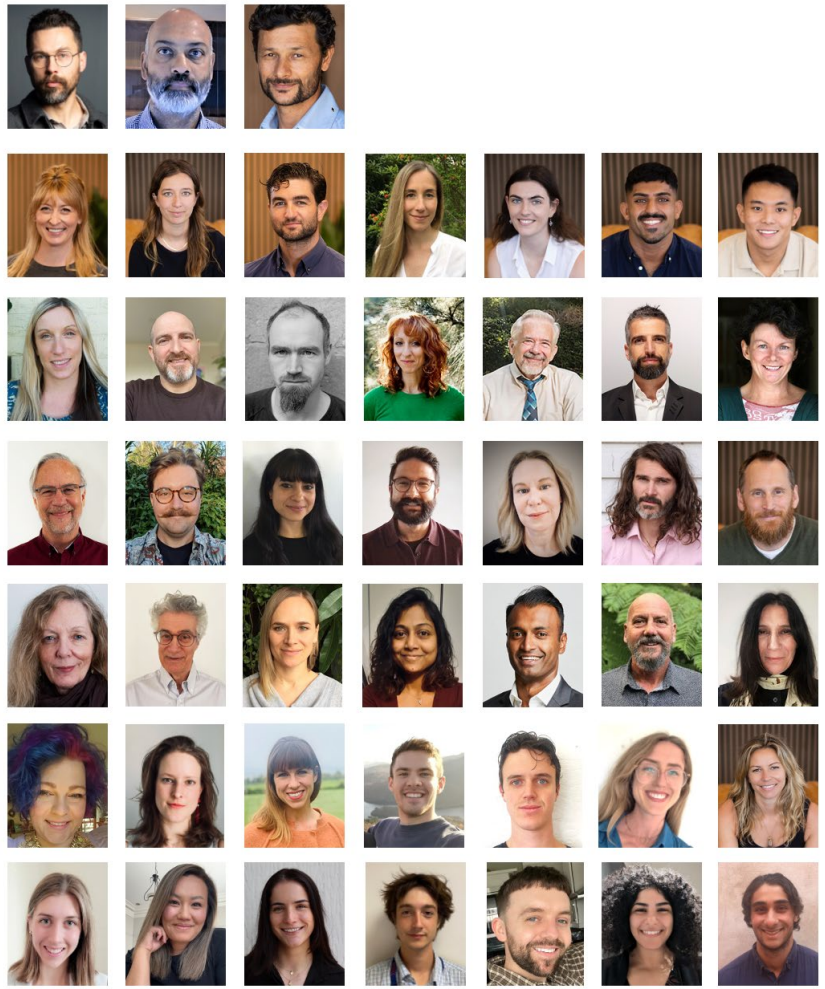
Scientific Advisory – MIND Foundation (Germany); Incannex Healthcare (Aus /USA); Enosis Therapeutics (Aus)

Grants, funding – Incannex Healthcare (Aus /USA); Multidisciplinary Association for Psychedelic Studies (USA)

Consulting – Cybin Inc (Canada); Otsuka Pharmaceuticals (USA)

AUSTRALIA'S FIRST PSYCHEDELIC LAB





AUSTRALIA'S FIRST PSYCHEDELIC LAB

TREATING GAD

TRAINING THERAPISTS

REDUCING POLARISATION

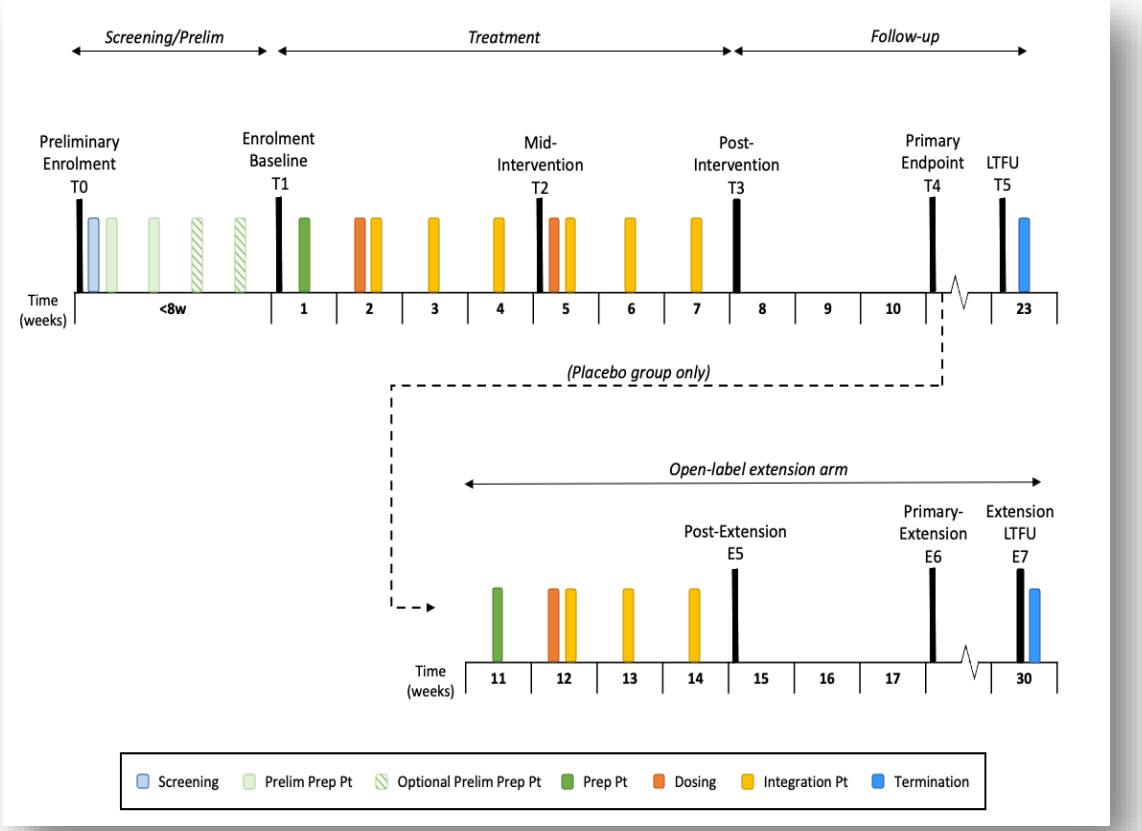
PsiGAD1

Safety and efficacy of psilocybin-assisted psychotherapy for Generalised Anxiety Disorder: a randomised quadruple-blind active-placebo-controlled trial

PsiGAD1 TRIAL BASICS

- World-first psilocybin-AT trial for a primary anxiety condition
- Sponsor: Monash University (IIT)
- Funder: Incannex Healthcare Ltd
- ANZCTR number: 12621001358831; pre-registered Statistical Analysis Plan: osf.io/m24ag
- FPFV: May 2022; LPLV: Dec 2023 (Main); Feb 2024 (OLE)
- Participants: Severe GAD, n=73
- Design: quadruple-blind, randomized active-placebo-controlled trial with open-label extension [psilocybin vs diphenhydramine]

INTERVENTION



- 9x 1.5hr therapy sessions
- 2x psilocybin sessions (25mg and 30mg)
- 2x highly qualified and experienced psychedelic-trained therapists
- Therapist consistency through course of treatment (with rare exceptions)
- ‘Set-setting’ psychotherapy (including ‘limited best care’ approach)

KEY OBJECTIVES

Determine whether a brief psilocybin-assisted psychotherapy program:

- is superior to active placebo-assisted psychotherapy in decreasing symptoms of GAD [efficacy]
- is safe, in terms of serious adverse events, adverse events and suicidality [safety]
- is tolerable, in terms of retention [tolerability]

PARTICIPANTS

Characteristic	Psilocybin (N=35)	Diphenhydramine (N=38)	Total (N=73)
Age			
Mean (SD)	39.5 (11.30)	38.1 (9.84)	38.8 (10.52)
Sex assigned at birth			
Female	23 (65.7%)	23 (60.5%)	46 (63.0%)
Male	12 (34.3%)	15 (39.5%)	27 (37.0%)
HAM-A Baseline (severity)			
Mean (SD)	29.5 (6.81)	29.8 (7.96)	29.6 (7.38)
Duration of GAD (years)			
Mean (SD)	20.8 (13.58)	19.3 (11.74)	20.0 (12.59)
Antidepressants at pre-screening			
Yes	5 (14.3%)	13 (34.2%)	18 (24.7%)
Prior psychedelic use			
No	18 (51.4%)	22 (57.9%)	40 (54.8%)
Country of birth			
Australia	25 (71.4%)	31 (81.6%)	56 (76.7%)
BMI (kg/m2)			
Mean (SD)	24.4 (3.53)	23.7 (4.01)	24.0 (3.77)
Highest completed education			
High school	4 (11.4%)	7 (18.4%)	11 (15.1%)
Undergraduate degree	13 (37.1%)	16 (42.1%)	29 (39.7%)
Postgraduate degree	17 (48.6%)	15 (39.5%)	32 (43.8%)
Relationship status			
Currently in a long-term relationship	24 (68.6%)	26 (68.4%)	50 (68.5%)

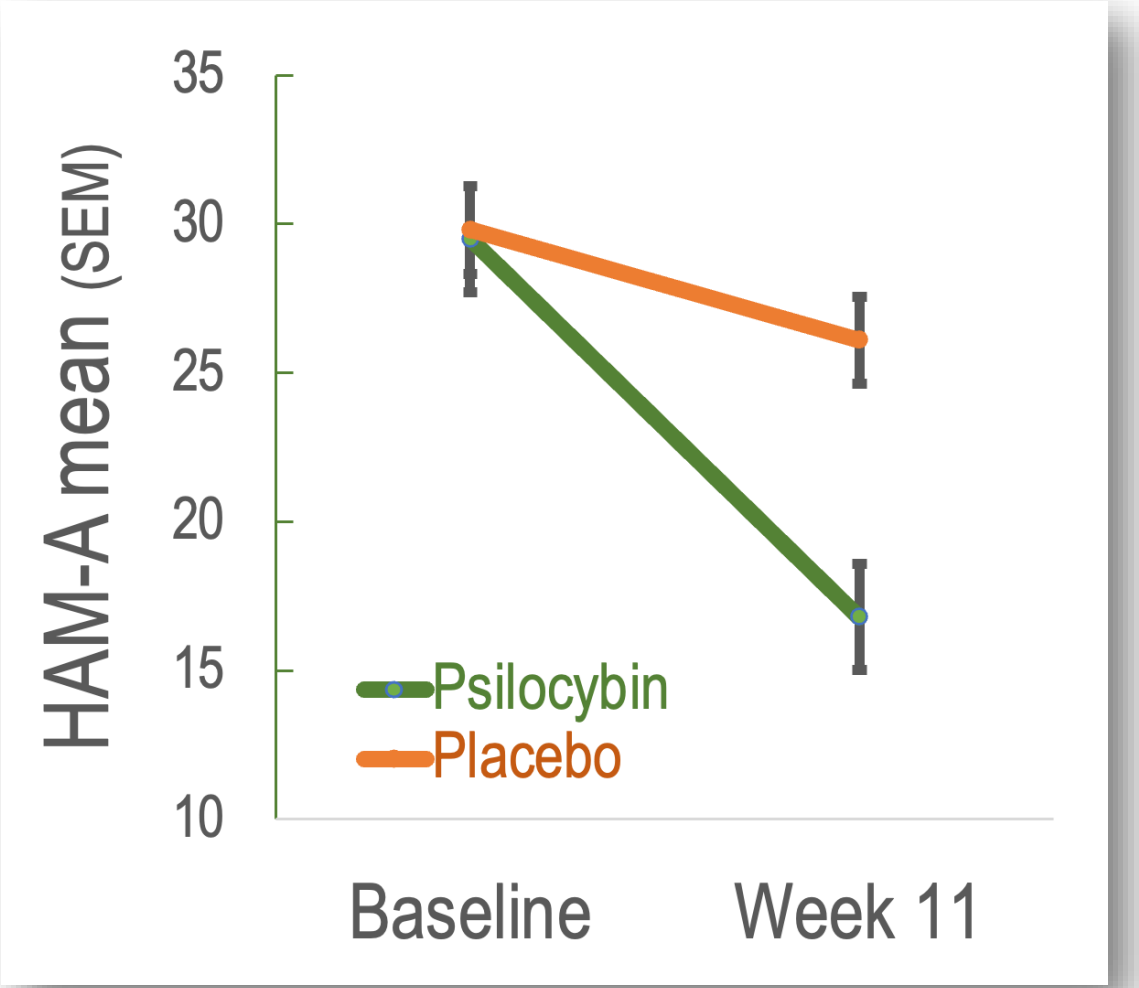
HAM-A scoring thresholds

- Mild Anxiety: 0-17
- Mild to Moderate Anxiety: 18-24
- Moderate to Severe Anxiety: 25-30

MONASH University

PsiGAD1 Trial

PRIMARY EFFICACY RESULTS



Between-group effect size: Cohen's *d* = 0.95, *p* < 0.0001

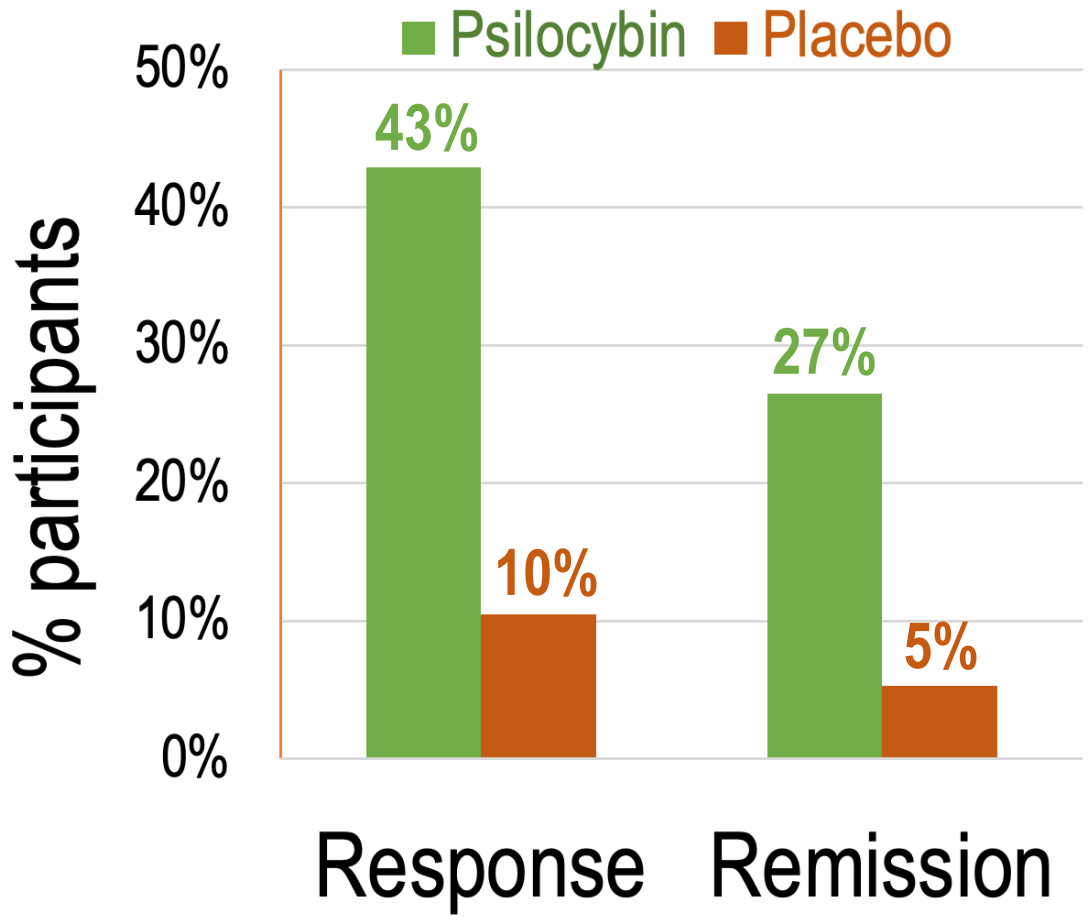
Within-group – pre-post effect size: Cohen's *d* = 1.44

Translation: very large clinical effect, highly significant.

PRIMARY EFFICACY RESULTS

Statistic	Psilocybin (N=35)	Diphenhydramine (N=38)
Crude change - Mean (95% CI)	-12.8 (-16.6, -9.0)	-3.7 (-6.4, -1.0)
Adjusted for baseline		
Estimated change - Mean (95% CI)	-12.9 (-15.9, -9.8)	-3.6 (-6.5, -0.7)
Estimated difference in change - Mean (95% CI)	-9.2 (-13.4, -5.0)	
P-value	<.0001	
Adjusted for baseline, sex, age and duration of GAD		
Estimated change - Mean (95% CI)	-13.4 (-16.5, -10.4)	-4.4 (-7.3, -1.5)
Estimated difference in change - Mean (95% CI)	-9.0 (-13.2, -4.9)	
P-value	<.0001	

EFFICACY RESULTS



Response = clinically substantial reduction (HAM-A ≥50% of baseline)

Remission = anxiety-free, or normal levels (HAM-A ≤7)

SAFETY RESULTS

Adverse events	Psilocybin (N=35)	Diphenhydramine (N=38)	Total (N=73)
All Adverse Events	239 34 (97.1%)	208 34 (89.5%)	447 68 (93.2%)
Mild	212 34 (97.1%)	182 33 (86.8%)	394 67 (91.8%)
Moderate	27 16 (45.7%)	26 13 (34.2%)	53 29 (39.7%)
Severe	0 0 (0.0%)	0 0 (0.0%)	0 0 (0.0%)
All Serious Adverse Events	0 0 (0.0%)	0 0 (0.0%)	0 0 (0.0%)
Treatment Emergent Adverse Events	155 32 (91.4%)	92 29 (76.3%)	247 61 (83.6%)
Mild	141 32 (91.4%)	86 27 (71.1%)	227 59 (80.8%)
Moderate	14 9 (25.7%)	6 4 (10.5%)	20 13 (17.8%)

Note: total number of events | total number participants | (% participants)

SAFETY RESULTS

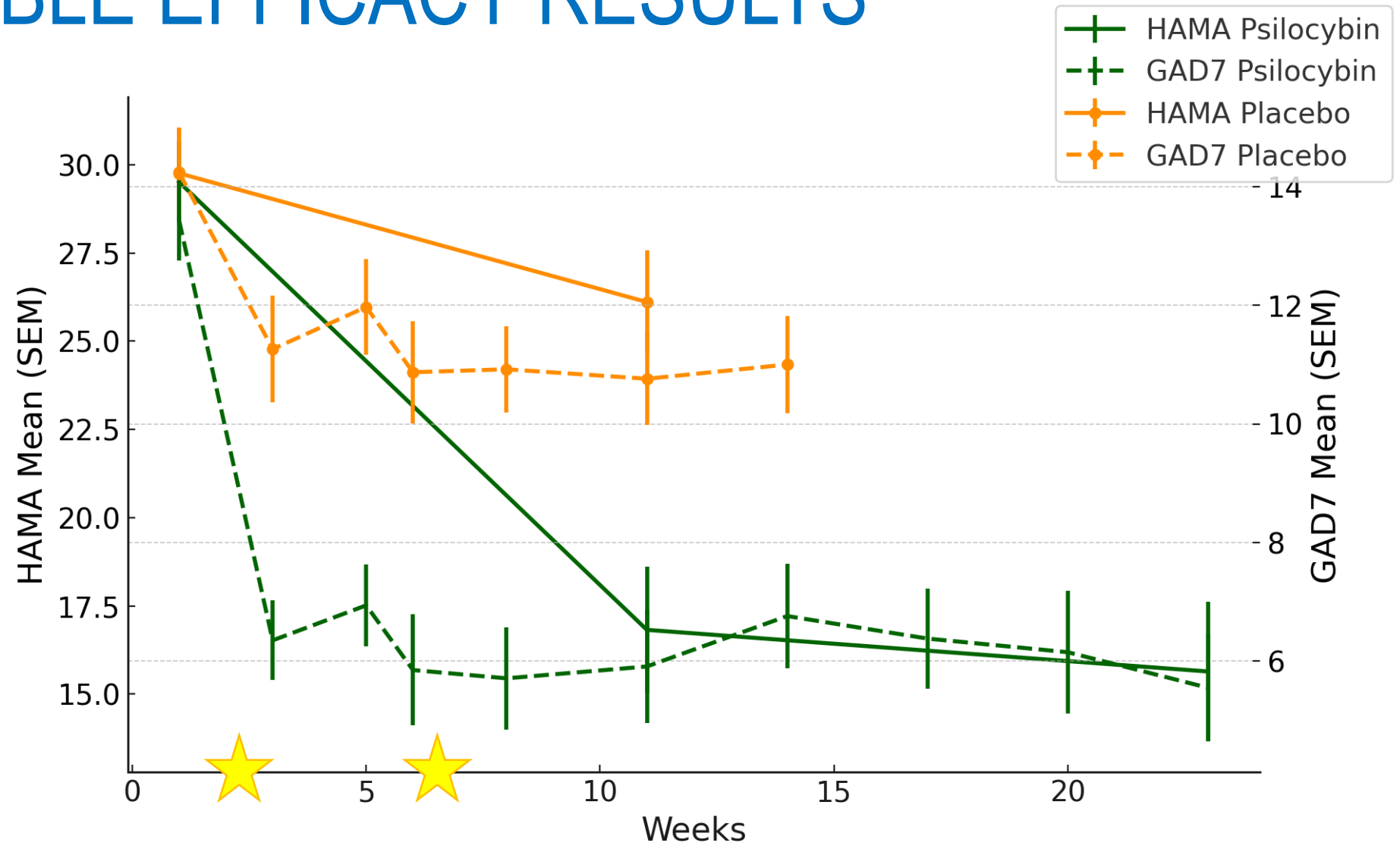
Adverse events	Psilocybin (N=35)	Diphenhydramine (N=38)	Total (N=73)
Nervous system disorders	60 28 (80.0%)	30 21 (55.3%)	90 49 (67.1%)
Headache	39 25 (71.4%)	22 15 (39.5%)	61 40 (54.8%)
Dizziness	8 8 (22.9%)	3 3 (7.9%)	11 11 (15.1%)
Paresthesia	7 5 (14.3%)	0 0 (0.0%)	7 5 (6.8%)
Psychiatric disorders	20 14 (40.0%)	27 16 (42.1%)	47 30 (41.1%)
Anxiety	8 7 (20.0%)	9 7 (18.4%)	17 14 (19.2%)
Depression	7 6 (17.1%)	10 5 (13.2%)	17 11 (15.1%)
Insomnia	1 1 (2.9%)	4 4 (10.5%)	5 5 (6.8%)
Gastrointestinal disorders	35 20 (57.1%)	6 5 (13.2%)	41 25 (34.2%)
Nausea	24 16 (45.7%)	3 3 (7.9%)	27 19 (26.0%)
Musculoskeletal and connective tissue disorde	12 9 (25.7%)	8 6 (15.8%)	20 15 (20.5%)
Muscle cramp	7 5 (14.3%)	4 4 (10.5%)	11 9 (12.3%)
Myalgia	5 5 (14.3%)	2 2 (5.3%)	7 7 (9.6%)
Cardiac disorders	10 6 (17.1%)	5 4 (10.5%)	15 10 (13.7%)
Sinus tachycardia	10 6 (17.1%)	5 4 (10.5%)	15 10 (13.7%)
Vascular disorders	7 7 (20.0%)	4 3 (7.9%)	11 10 (13.7%)
Hypertension	6 6 (17.1%)	4 3 (7.9%)	10 9 (12.3%)

Note: total number of events | total number participants | (% participants)

SECONDARY EFFICACY RESULTS

Measure	BASELINE		WEEK 11		GROUP DIFFERENCE		
	Psilocybin Mean (SD)	Placebo Mean (SD)	Psilocybin Mean (SD)	Placebo Mean (SD)	Mean (95% CI)	Cohen's d	p-value
Sheehan Disability Scale (SDS)	15.7 (5.39)	16.6 (5.84)	9.6 (7.22)	15.3 (6.60)	-5.2 (-8.2, -2.2)	**0.70**	**0.001**
Personal Wellbeing Inventory (PWI)	40.8 (8.78)	40.1 (13.61)	51.6 (12.39)	43.2 (11.46)	7.8 (3.7, 12.0)	**0.66**	**0.0003**
Patient Health Questionnaire (PHQ-9)	9.5 (3.00)	10.6 (4.72)	5.5 (5.05)	10.3 (5.27)	-4.0 (-6.3, -1.8)	**0.79**	**0.0006**
Mini-Social Phobia Inventory (Mini-SPIN)	7.0 (2.38)	7.0 (3.04)	4.0 (2.44)	5.3 (3.28)	-1.3 (-2.2, -0.3)	**0.41**	**0.0094**
Panic Disorder Screener (PADIS)	2.9 (3.53)	2.9 (2.94)	1.4 (2.53)	1.9 (2.67)	-0.5 (-1.6, 0.6)	0.19	0.3267
Alcohol Use Disorders Identification Test (AUDIT)	3.4 (2.53)	3.1 (3.59)	2.8 (2.60)	2.6 (2.96)	0.1 (-0.9, 1.0)	0.04	0.8577
Drug Use Disorders Identification Test (DUDIT)	0.3 (0.74)	0.3 (0.94)	0.3 (0.75)	0.2 (0.63)	0.1 (-0.2, 0.3)	0.15	0.6686
Cigarette Use (CU)	3.0 (15.20)	0.4 (1.67)	2.3 (10.31)	0.4 (1.80)	-0.3 (-1.3, 0.8)	0.03	0.6106
Patient Health Questionnaire (PHQ-15) Somatization	9.9 (4.71)	10.4 (5.57)	5.2 (3.83)	9.6 (5.02)	-4.4 (-6.0, -2.7)	**0.98**	**<.0001**

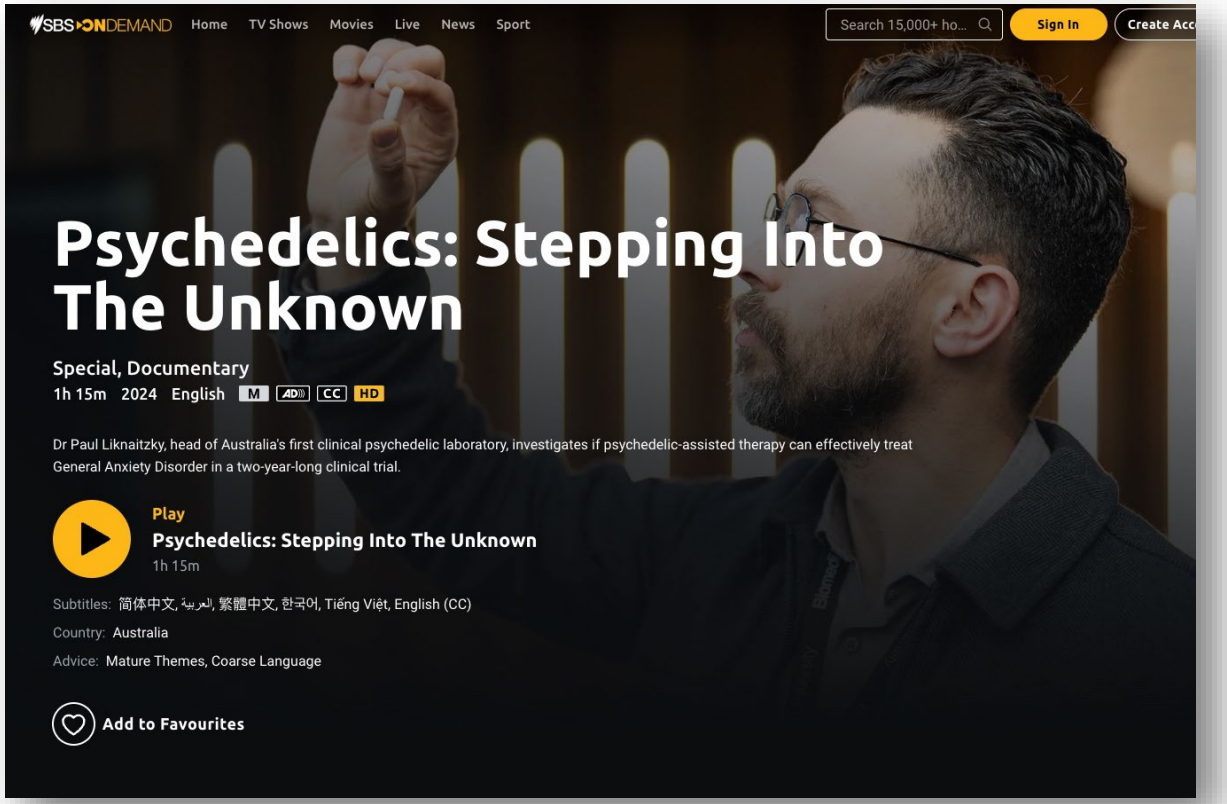
DURABLE EFFICACY RESULTS



PSIGAD1 SUMMARY

- Single site; investigator designed, initiated, and run; cohesive team.
- Well-controlled trial, highly-trained therapists (including Monash Psilocybin Therapist Study), pre-registered Statistical Analysis Plan.
- Compared to placebo, psilocybin showed large and highly significant reduction in anxiety at primary endpoint, which endured to at least 23 weeks.
- No SAEs, no severe AEs, one withdrawal.
- Compared to placebo, psilocybin showed large and significant improvements across multiple secondary clinical measures.

PSIGAD1 SUMMARY



MPTS

Monash Psilocybin Therapist Study

PSYCHEDELIC-ASSISTED TRAINING

RATIONALE – PRECEDENT, DEMAND, OPINION

1. **Therapists say it's useful:** Anecdote and early reports: Attunement? Participant trust? Adequate informed consent?
2. **Patients want it:** Mturk sample indicates preference for 'guide' to have had prior psilocybin experience[1]
3. **Its common:** eg 88% of sample of contemporary trial therapists[2]; indigenous psychedelic shamanism[3]
4. **There's precedent:** Spring Grove; MAPS; TheraPsil.

1) Earleywine, M., et al. (2023). Journal of Psychoactive Drugs, 55(1), 51-61.
2) Aday, J. S., et al. (2023). Psychedelic Medicine, 1(1), 27-37.
3) Winkleman, M. (2010).Journal for the Study of Religion, Nature and Culture, 3(4), 458–489.

PSYCHEDELIC-ASSISTED TRAINING

RATIONALE - METAPHOR

The value of first-person experience?

PSYCHEDELIC-ASSISTED TRAINING

RATIONALE – INFERENTIAL

1. **Therapist competencies:** empathise, attune, provide useful support, engender trust and safety, build alliance… with client + their situation
2. **The psychedelic situation:** ineffable, inconceivable, profoundly ‘different’, and central in PAT (i.e., important information is non-transferable)
3. **The conjecture:** For PAT, the development of (1) may benefit from exposure to (2)

MONASH PSILOCYBIN THERAPIST STUDY

- World-first study approval to test psilocybin as therapist training tool
- Two purposes: therapist exposure + initial (“practice”) therapist session with healthy participant
- Key Questions:
  - Safety, feasibility, benefits and harms (personal, professional)?
  - Methods of use?
  - Attitudes of clinical participants?

THERAPIST TRAINING FOR PsiGAD1

Selection

- Qualified and experienced MH clinicians (>Masters MH; >1000 clinical hours; experience with GAD; membership in good standing with peak body; interview…)

Training and Supervision

- 3 months: online (50hrs); in-person (7 full days): no fees
- Optional participation in Psilocybin Therapist Study
- Supervision for duration of clinical trial

Supported by experts from:

MAPS
MULTIDISCIPLINARY ASSOCIATION FOR PSYCHEDELIC STUDIES

THE CENTRE FOR PSYCHEDELIC RESEARCH
Imperial College London

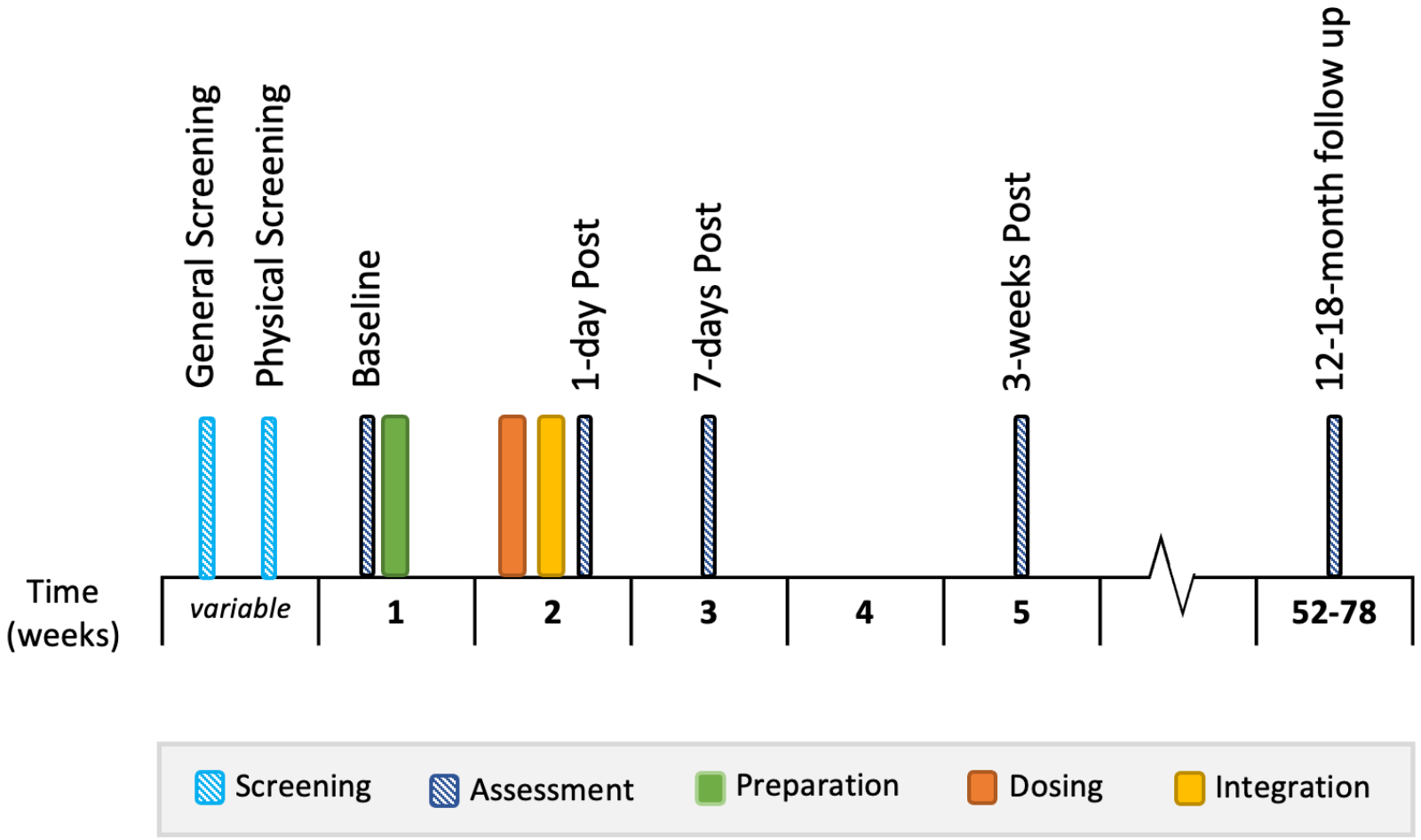
JOHNS HOPKINS
Center for Psychedelic & Consciousness Research

PRATI PSYCHEDELIC RESEARCH AND TRAINING INSTITUTE

CALIFORNIA INSTITUTE OF INTEGRAL STUDIES

Usona Institute

STUDY TIMELINE



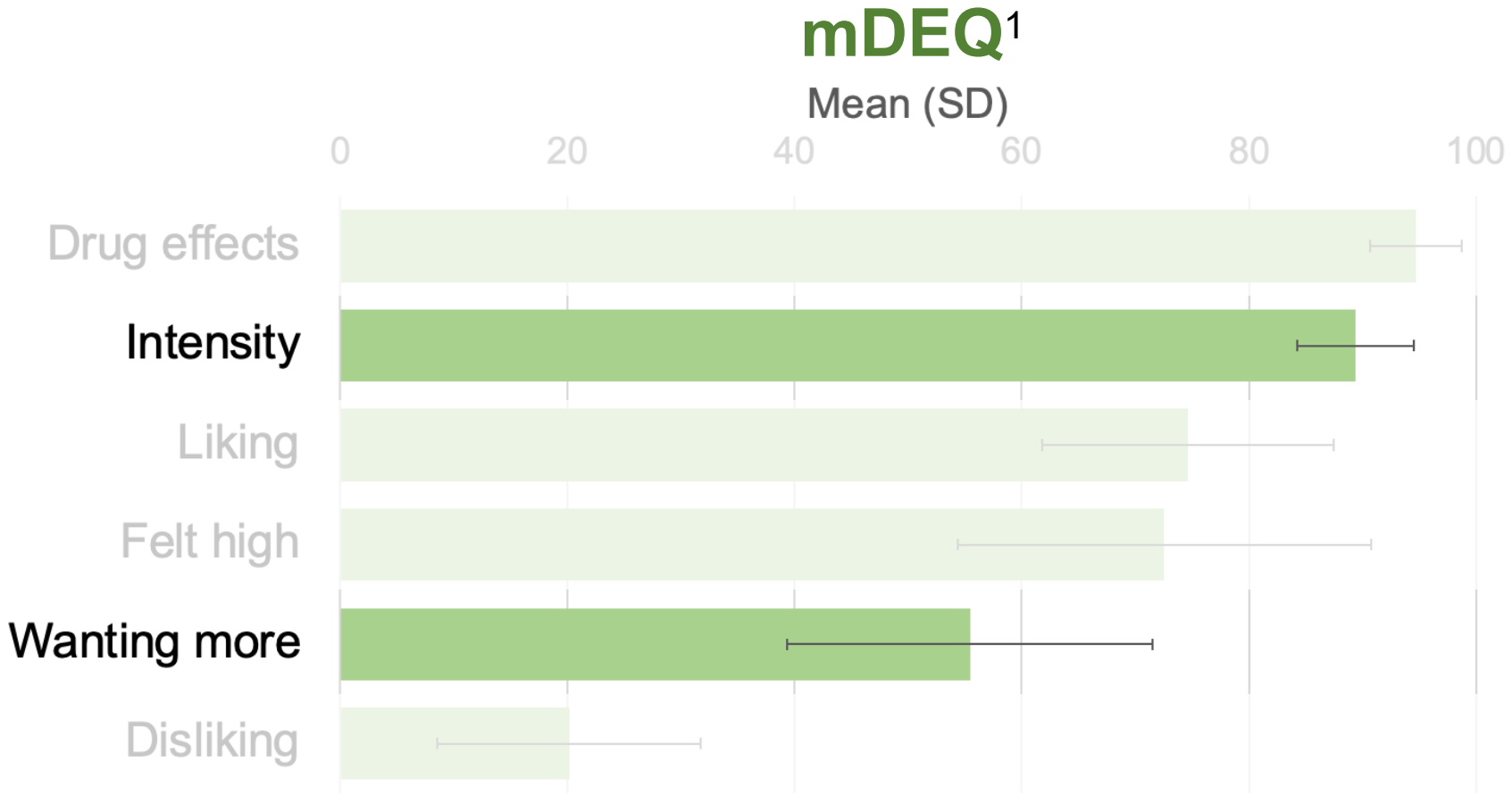
1x preparation
1x 25mg psilocybin
1x integration
2x therapists

PARTICIPANT CHARACTERISTICS

- *n*=14 (therapists working on PsiGAD1 clinical trial)
- Not all therapists participated

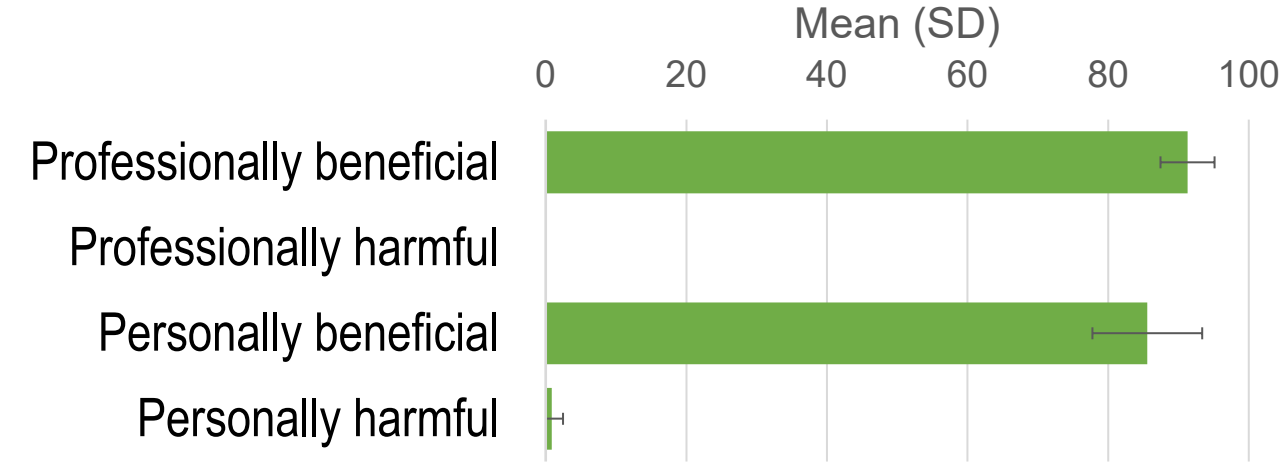
Variable	N	%	Mean	SD
Age			42.8	11.5
Gender: Woman	5	35.7		
Gender: Man	9	64.3		
Relationship: current long-term	12	85.7		
Ethnic/cultural: Non-indigenous Australian	9	64.3		
Ethnic/cultural: Non-Australian	5	35.7		
Employment: full time	7	50.0		
Highest education: postgraduate	13	92.9		
Years mental health practice			14.1	9.2
Lifetime psychedelic use - Yes	9	64.3		

ACUTE EFFECTS



1) Morean,et al. (2013). Psychopharmacology, 227, 177-192.

KEY OUTCOMES

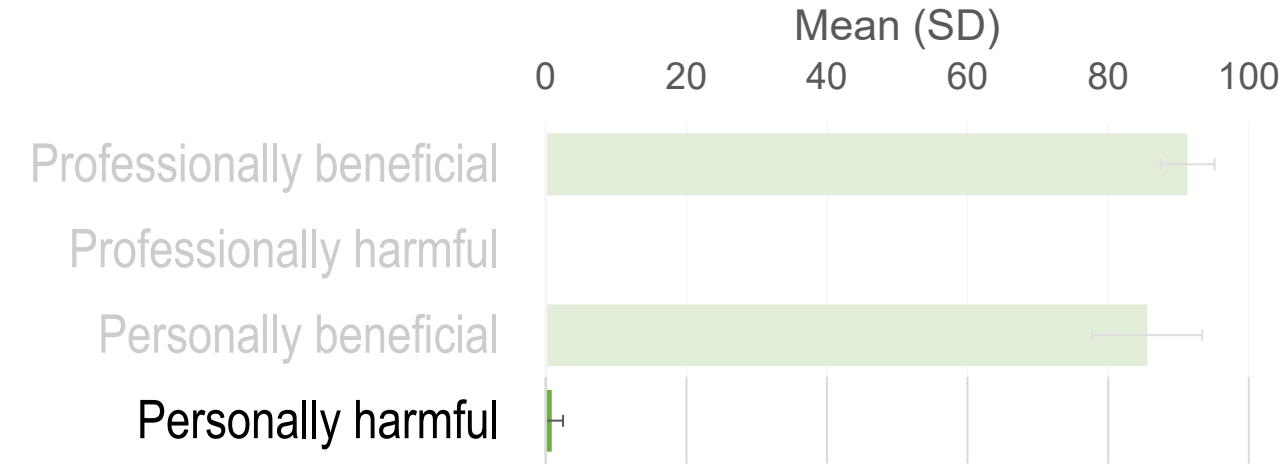


No SAEs, no severe AEs

No withdrawals

- *"It was a pivotal moment for me professionally and personally"*
- *"Profoundly improved my understanding of the work"*

KEY OUTCOMES

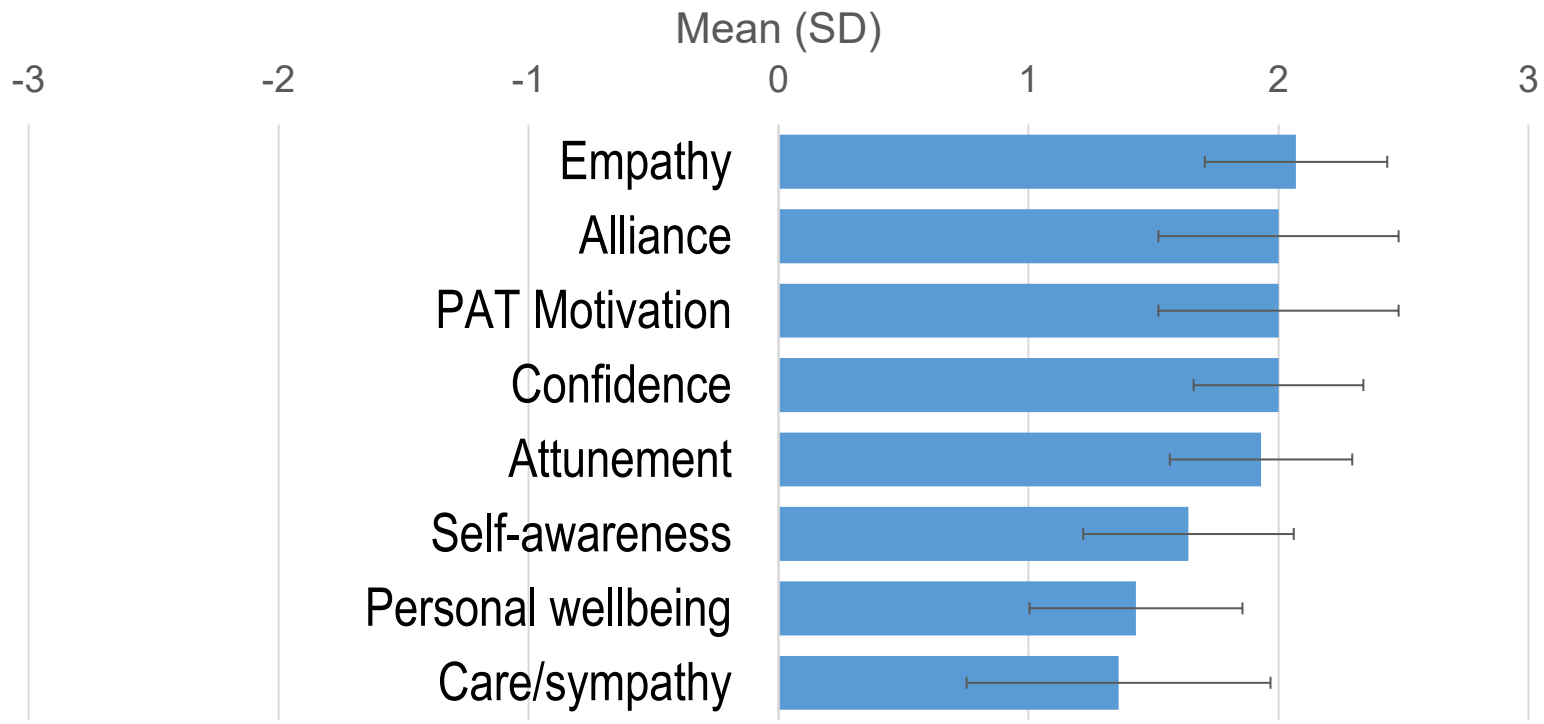


No SAEs, no severe AEs

No withdrawals

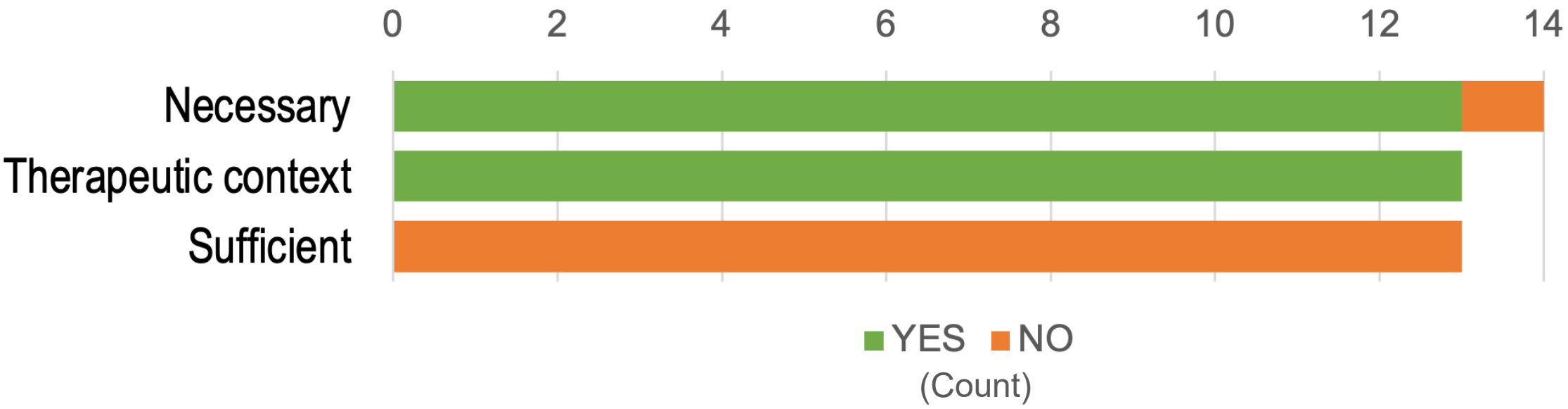
– *"…having such a radically altered state experience in the middle of a busy life knocked me out of rhythm. This is not harmful, but is challenging"*

OUTCOMES – REPORTED CHANGES



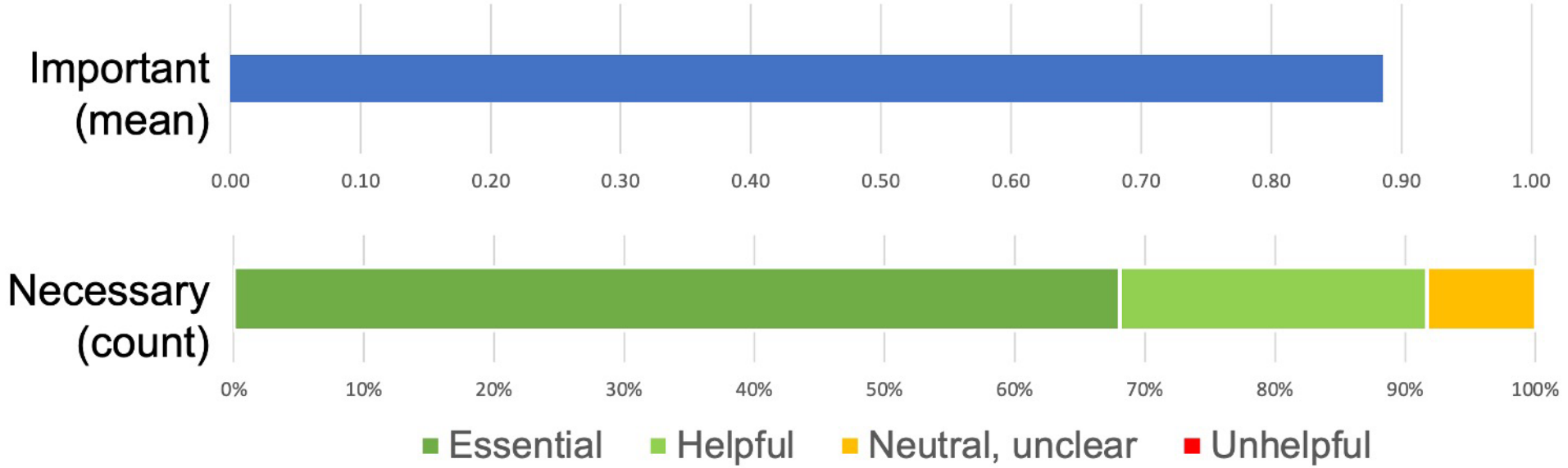
OUTCOMES – RATED VALUE

Therapist-rated necessity and sufficiency for training *already qualified* mental healthcare workers



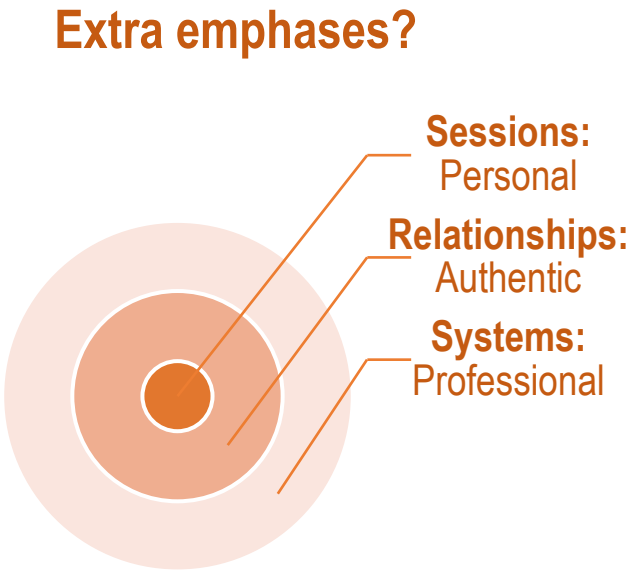
OUTCOMES – RATED VALUE

Clinical (GAD) Participants' rated importance and necessity for training therapists



KEY FINDINGS

- First case-series evidence for the use of high dose psilocybin with support as a safe and valuable therapist training tool
- Strong support from patient/client community
- Needs to be embedded within broader PAT training
- Method of use developed – added emphasis on ‘personal’ sessions; ‘authentic’ relationships; ‘professional’ systems



CONSIDERATIONS

- Cheaper, easier, more accessible alternatives? (eg, HBW)
- Risk of ‘narrowed’ therapeutic support, reduced psychological safety, evangelism? (eg, therapist projection; discounting negative reports/outcomes…).
- Inequities of access? (marginalised communities may suffer greater stigma)
- Problematic social/institutional pressure to participate?

FUTURE DIRECTIONS

- Further research to determine utility
  - Therapist self-reported benefit ✅
  - Patient demand and attributed benefit ✅
  - Validated competency assessment

- Develop best-practice guidelines, standards

- If evidence for use, aim for “on-label” psychedelic-assisted training

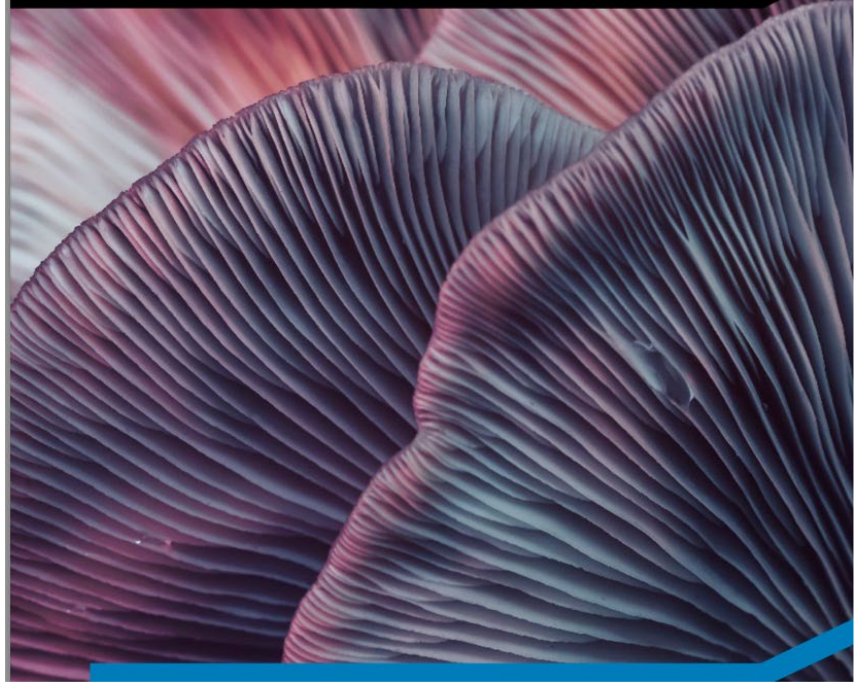
FUTURE

Psilocybin research plans within new Centre..!

MONASH University

A CENTRE OF EXCELLENCE IN PSYCHEDELIC THERAPIES

GROUNDBREAKING SCIENCE, NEXT-GENERATION TRAINING, REAL-WORLD IMPACT



1. GROUNDBREAKING SCIENCE

High-quality evidence and know-how that can inform who we treat, how we treat, and who reimburses the treatment.

2. NEXT-GENERATION TRAINING

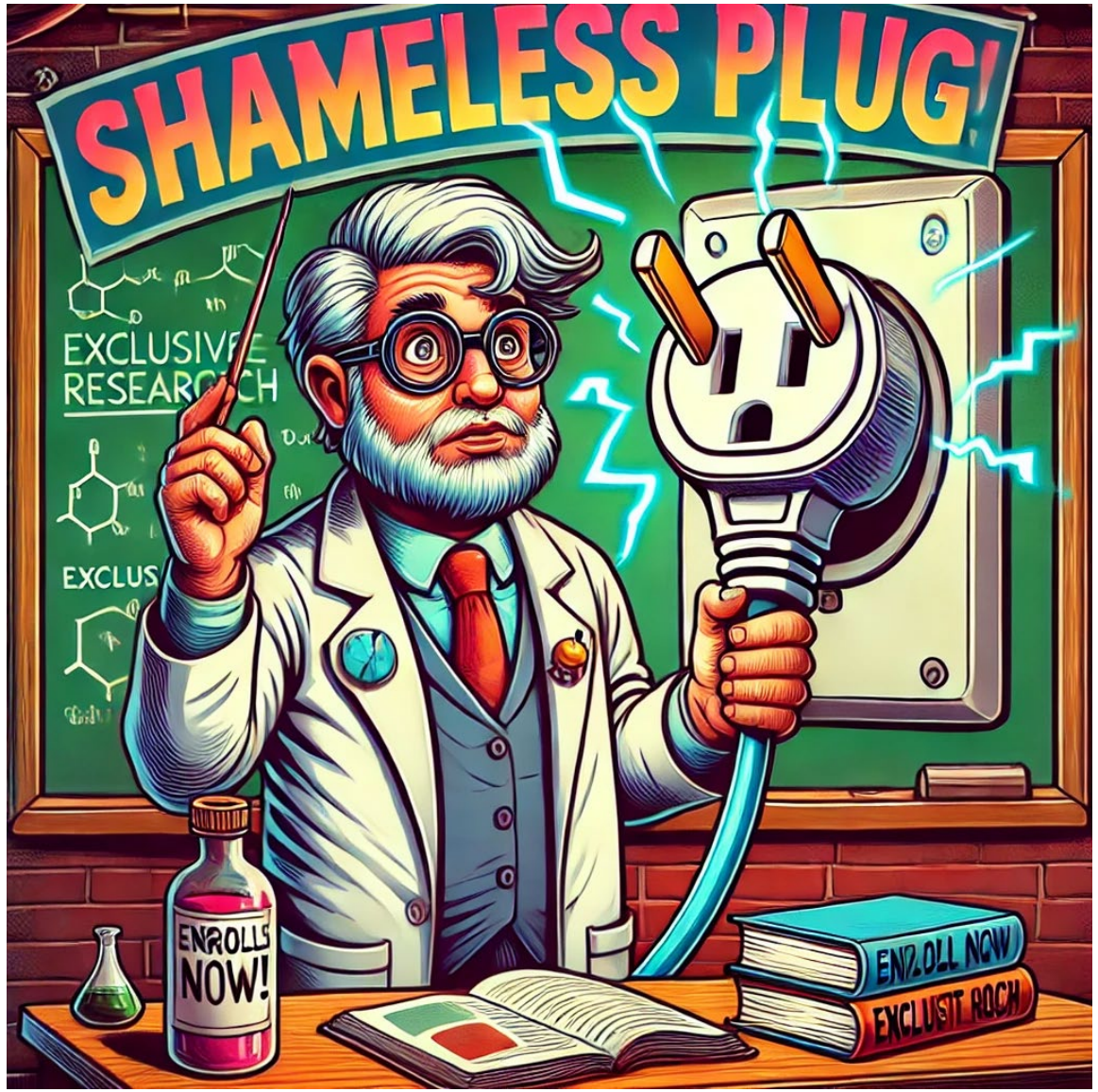
Programs that provide comprehensive skills, ongoing professional development, and mentorship for psychedelic clinicians and researchers, serving the community and equipping future leaders in the field.

3. REAL-WORLD IMPACT

Evidence-informed standards, thought leadership, and public education; informing policy and reimbursement; supporting institutional partnerships.

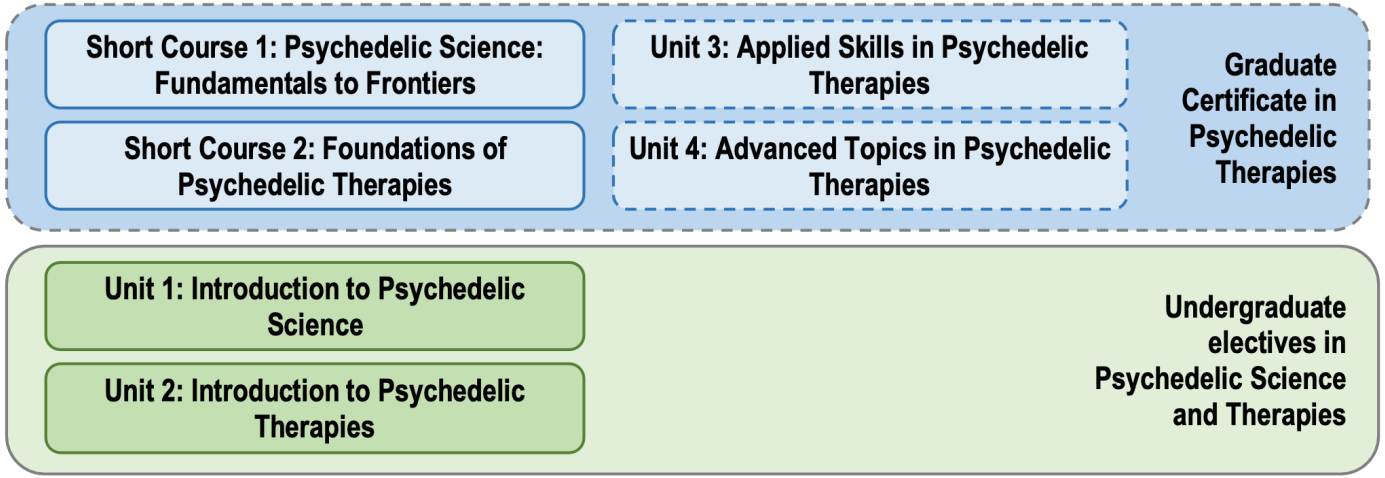
PSILOCYBIN PEACE PROJECT

- **Problem**: Rising polarisation — political, religious, ethnic… — threat to social cohesion, linked to hostility and violence.
- **Participants**: Leaders of polarised groups.
- **Therapeutic Intervention:** Group coaching and individual psilocybin with support.
- **Key Rationale**: Psilocybin enhances connectedness, empathy, cognitive flexibility…
- **Leader- and Community-Level Outcomes:** outgroup attitudes (empathy, tolerance, respect, connectedness…) and interactional dynamics (civility, active listening, perspective taking…)
- **Goal**: Increase capacity in leaders/groups to disagree and interact with the 'other', in the absence of hostility, while humanising and connecting to the 'other'.

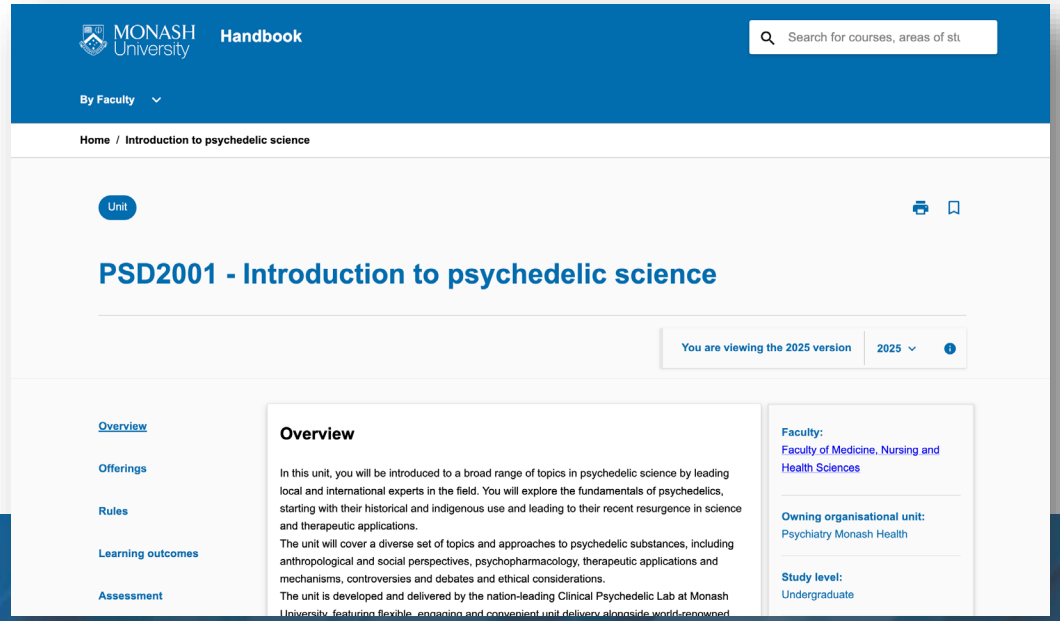

SHAMELESS PLUG!
EXCLUSIVE RESEARCH
ENROLL NOW!
ENROLL NOW
EXCLUSIVE RESEARCH

THE MONASH PSYCHEDELIC EDUCATION PROGRAM

Launches in 2025! – short courses (externally available), postgrad and undergrad units!



For notifications, subscribe at: monash.edu/psychedelics



ACKOWLEDGEMENTS

- PsiGAD1 trial participants
- Funding: Incannex Healthcare
- Study Drug: Usona

RESEARCHERS, CLINICIANS, SUPERVISORS

- Paul Liknaitzky
- Suresh Sundram
- Murat Yücel
- Hannah Bushell
- Rachel Ham
- Georgia Ioakimidis-Macdougall
- Sarah Falkenhaug
- Sean O'Carroll
- Marg Ryan
- Simon Amar
- Sarah Pant
- David Spektor
- Esme Dark
- Surabhi Hiwale
- Sabrina Adams
- Christopher Walsh
- Phil Jaksa
- James Tranter
- Campbell Townsend
- Shanti Monteiro
- Bill Richards

COLLABORATORS, TRAINERS

- John Gardner
- Adrian Carter
- Vince Polito
- Chris Letheby
- Sonali Gnanenthiran
- Kris Rotaru
- Chris Gianacas
- Bill Richards
- Ido Siemion
- Keren Tzarfaty
- Mary Cosimano
- Peter Gasser
- Roberta Murphy
- Scott Shannon
- Michael De Veer
- Karyn Richardson

INTERNS, VOLUNTEERS

- Leonie Tepe
- Eloise Head
- Emma Moon
- Ben Atkinson
- Junyan Zhang
- Breanna Urquhart
- Gretel Devendorf
- Saskia Mosford
- Emilie Kilvington
- Emily Friedel
- Lauren Pearson

MONASH.EDU/PSYCHEDELICS