

# Methodological issues in psychedelic trials

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# Disclosures

- Full time employee and shareholder of Cybin, a biopharmaceutical company developing psychedelics as therapeutics
- Own shares in GSK and AstraZeneca

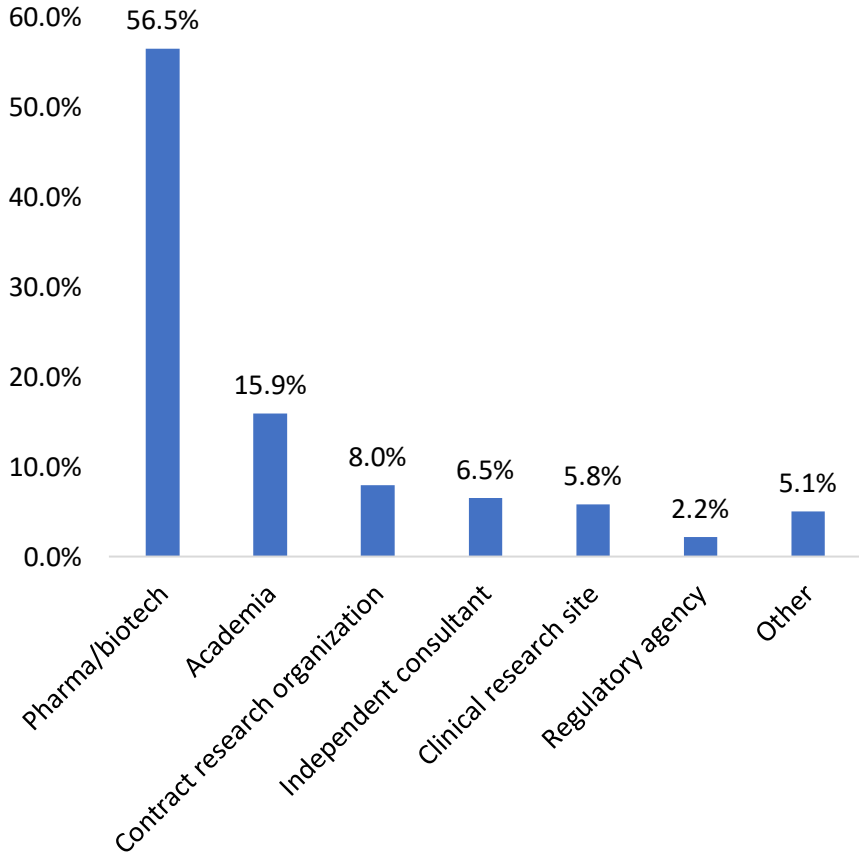
# Outline of the session

11.25 am - 11.40 am	Introduction to psychedelics and overview of key methodological issues	Amir Inamdar & Joyce Tsai
11.40 am – 12.10 pm	Choice of comparator and placebo controls in psychedelic trials	David Hellerstein
12.10 pm – 12.40 pm	Assessing blinding and minimising expectancy bias	Christine Moore
12.40 pm – 1.00 pm	Discussion	All

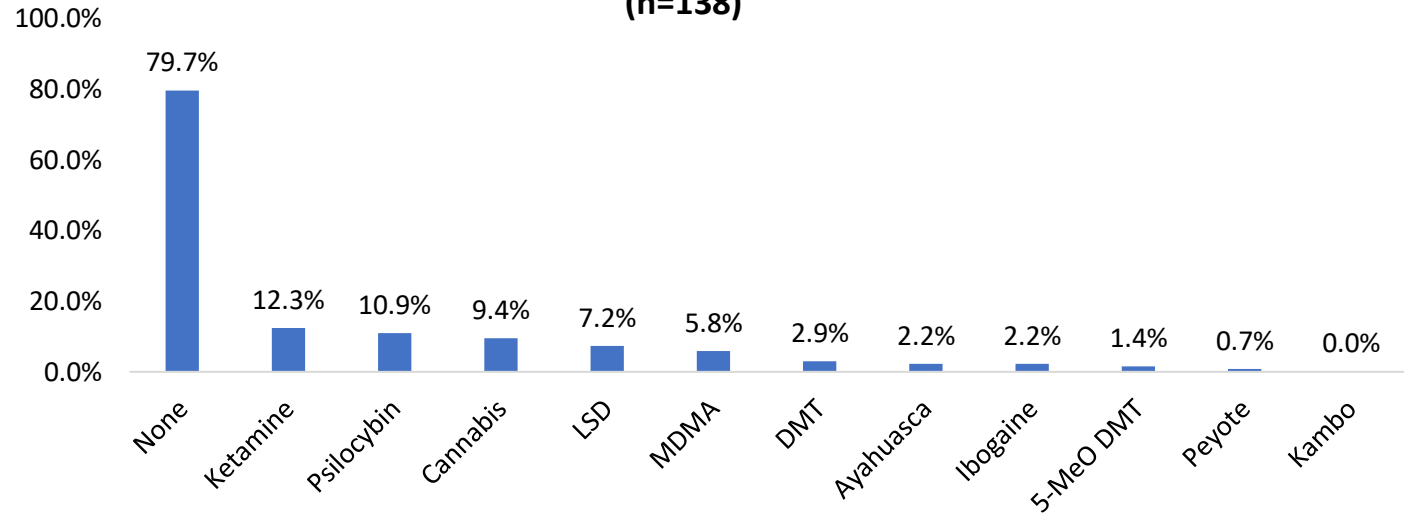
# Psychedelic Awareness Survey

(N=153)

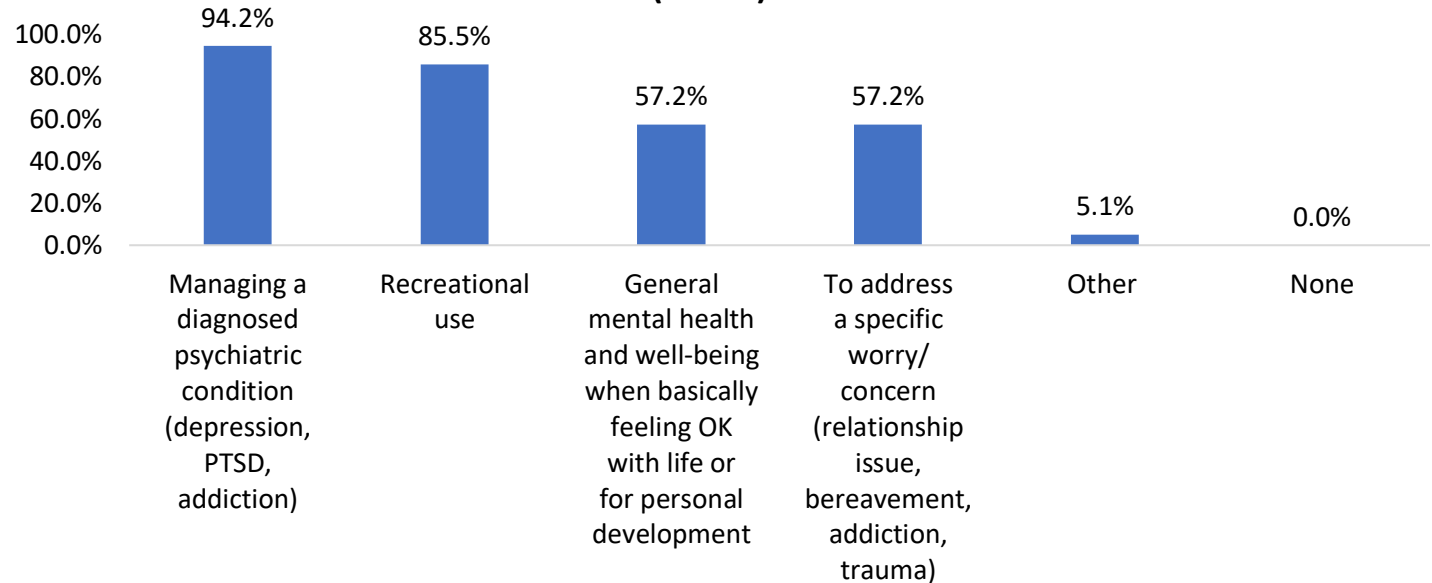
**In which setting are you employed?**  
(n=138)



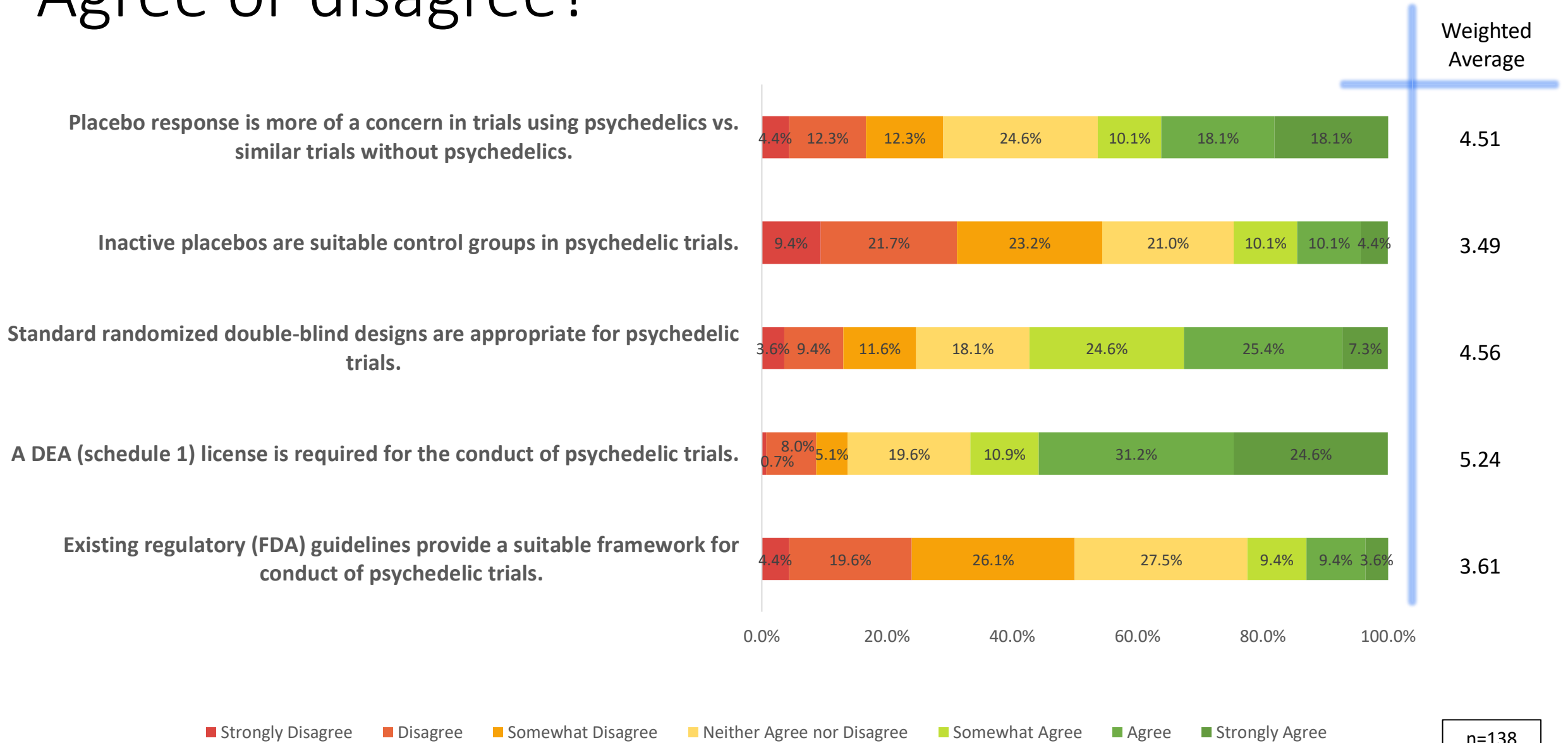
**In the last 12 months, have you used any of the following in a therapeutic setting?**  
(n=138)



**Have you heard of LSD, psilocybin (active compound in Magic Mushrooms), Ketamine, MDMA, Peyote, Kambo, DMT, 5-MeO DMT (active compound in toad venom), Ayahuasca, or Ibogaine for any of the following? (select all that apply)**  
(n=138)



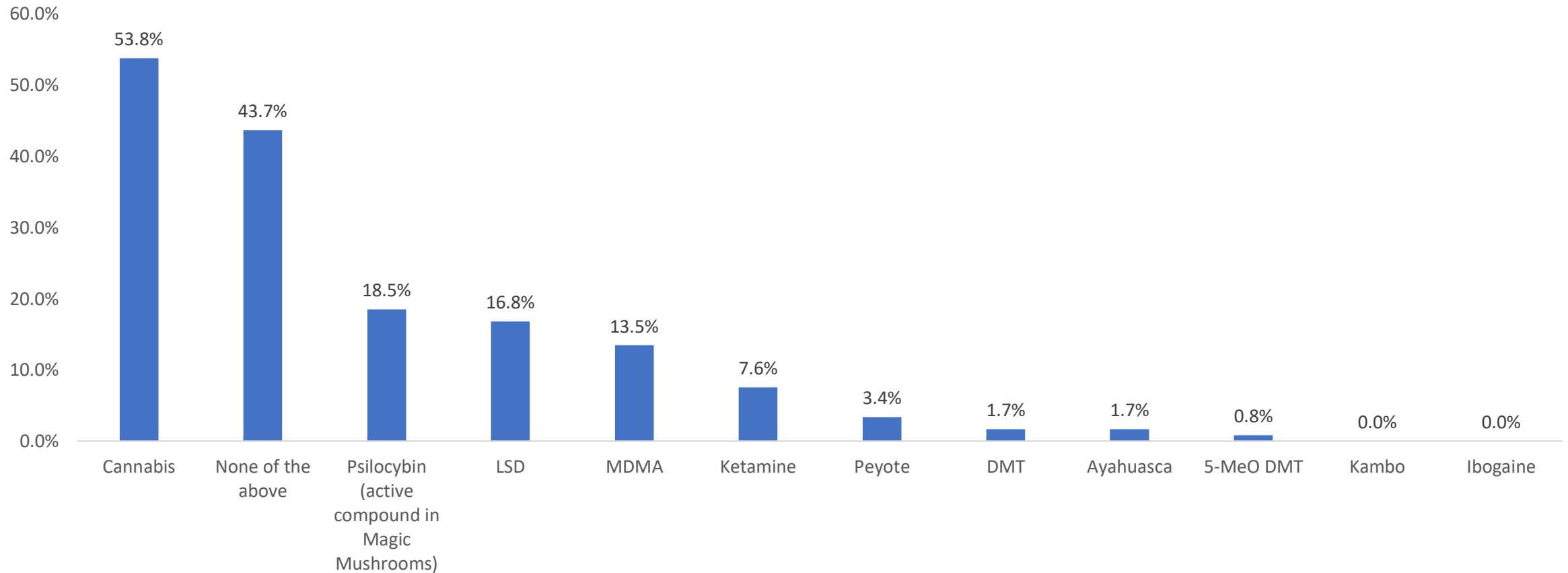
# Agree or disagree?



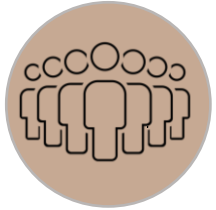
n=138

# Personal experience

**At ANY TIME, have you had personal experience with any of the following? Select all that apply.  
Please remember this is an anonymous survey and this is an optional question.  
(n=119)**



# Unmet needs in mental health disorders



**350 million**

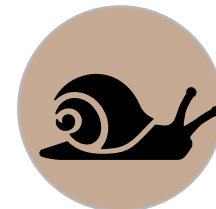
People live with depression globally



**40% fatal traffic accidents due to alcohol**



**Anxiety disorders are 6<sup>th</sup> leading cause of disability globally**



**Slow treatments**

Several weeks/ months to meaningful improvements



**2000 die due to suicide everyday**

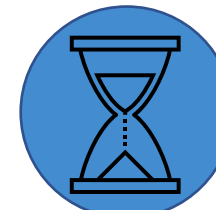


**\$210 billion- MDD  
\$249 billion- AUD**



**Comorbidities**

- 70% anxiety patients have depression
- High risk of substance use
- Increased risk of suicide



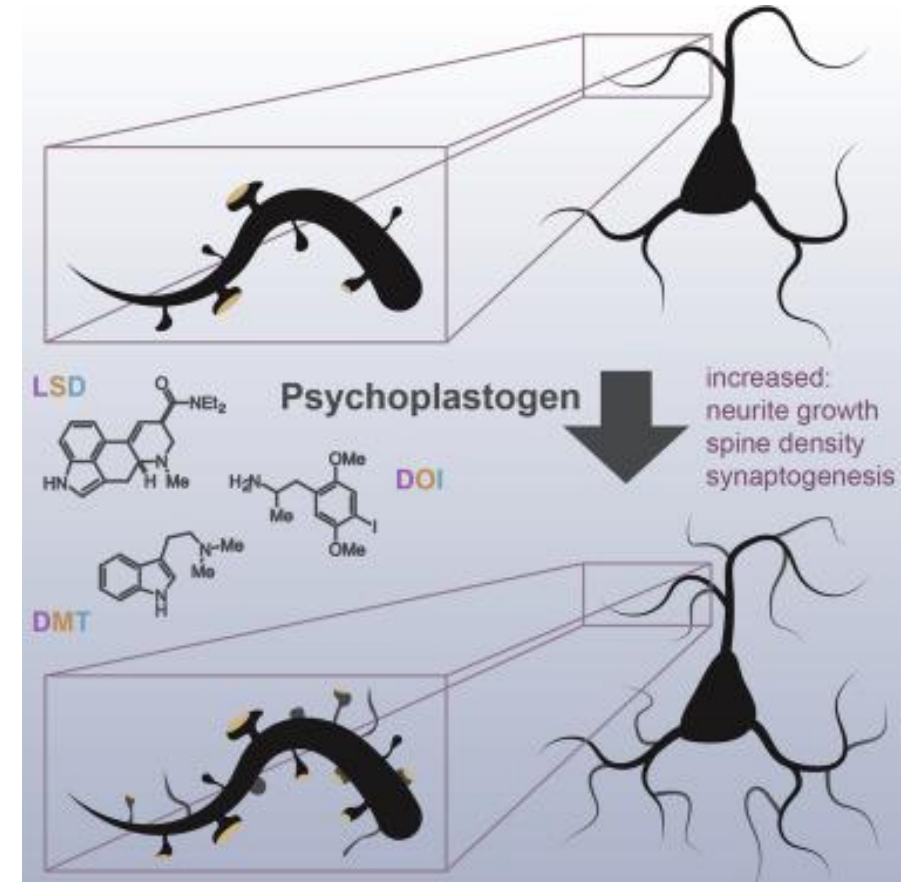
**Inadequate treatments**

- 1/3<sup>rd</sup> MDD patients treatment resistant
- Remission in anxiety 25%-35% but 20% relapse in 5 years

# Definitions

- Psychedelics<sup>1</sup> / entheogens – mind-revealing, 5-HT<sub>2a</sub> receptor agonists, profound changes in perception (psilocybin, LSD, mescaline)
- Empathogens/ entactogens – increase empathy (MDMA, 2C-X)
- Psychoplastogens - increase neuritogenesis, spinogenesis, and synaptogenesis

<sup>1</sup> Humphrey Osmond 1957



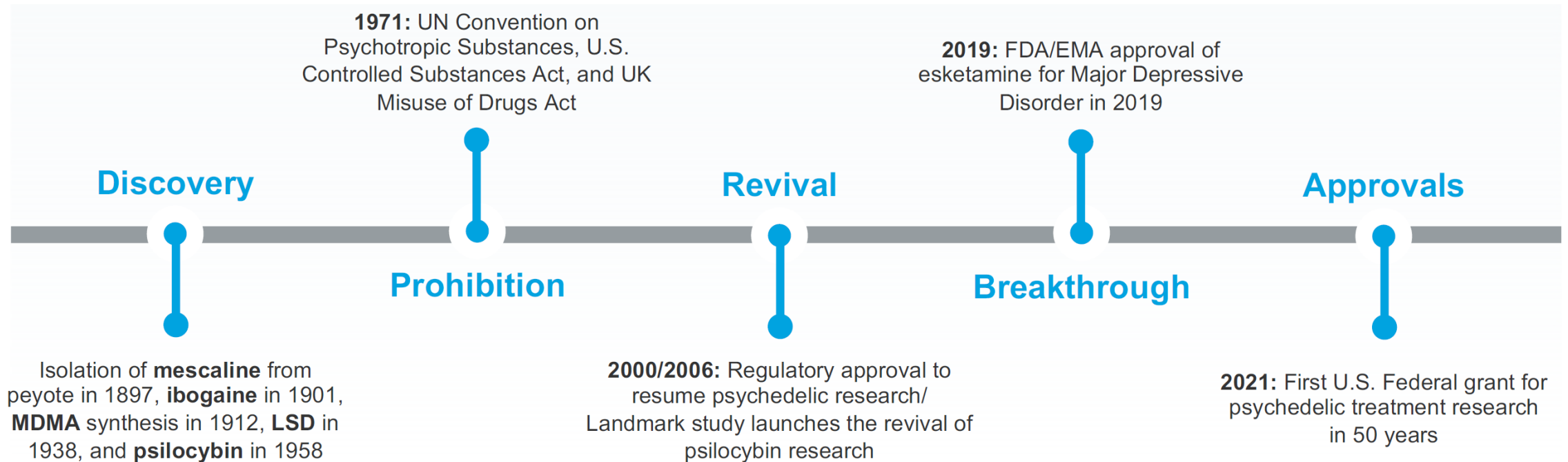
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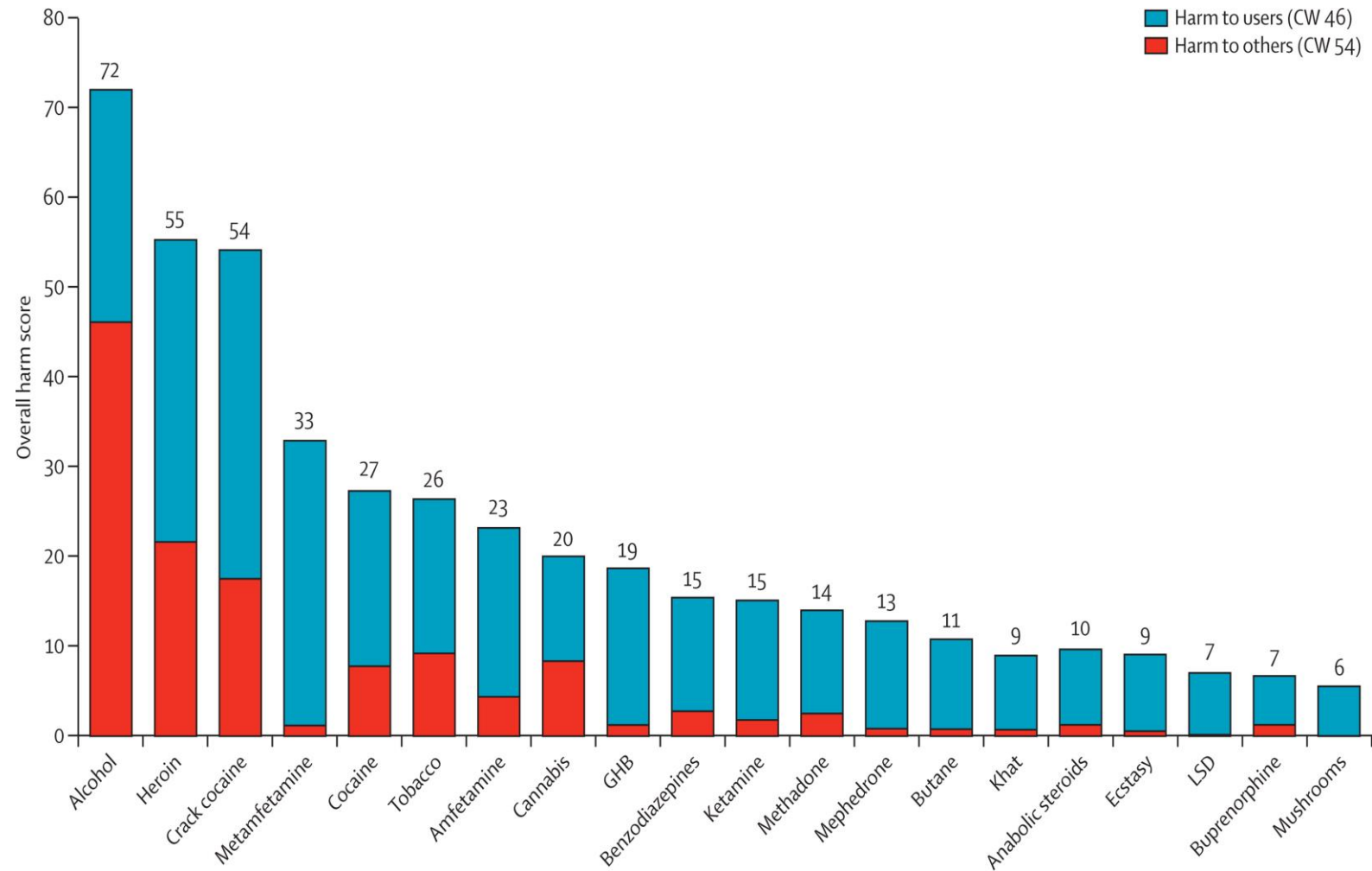
# Chemical classes of psychedelic

Psychedelic class	Examples	Predominant action	Natural equivalent
Tryptamine	Psilocybin	5-HT <sub>2a/2b/2c</sub>	Psilocybe mushrooms
Tryptamine	DMT	5-HT <sub>2a/2b/2c</sub>	Ayahuasca
Tryptamine	5-MeO-DMT (bufotenine)	5-HT <sub>2a/2b/2c</sub>	Toad venom
Phenethylamine	MDMA	5-HT <sub>2b</sub>	--
Ergoline	LSD	5-HT <sub>2a/2b/2c</sub>	--
Other	Mescaline	5-HT <sub>2b</sub>	Peyote
Iboga alkaloid	Ibogaine	kappa - opioid	Iboga
Other	Salvinorin A	kappa - opioid	Salvia divinorum
Dissociative	Ketamine	NMDA, 5-HT <sub>2a</sub>	--

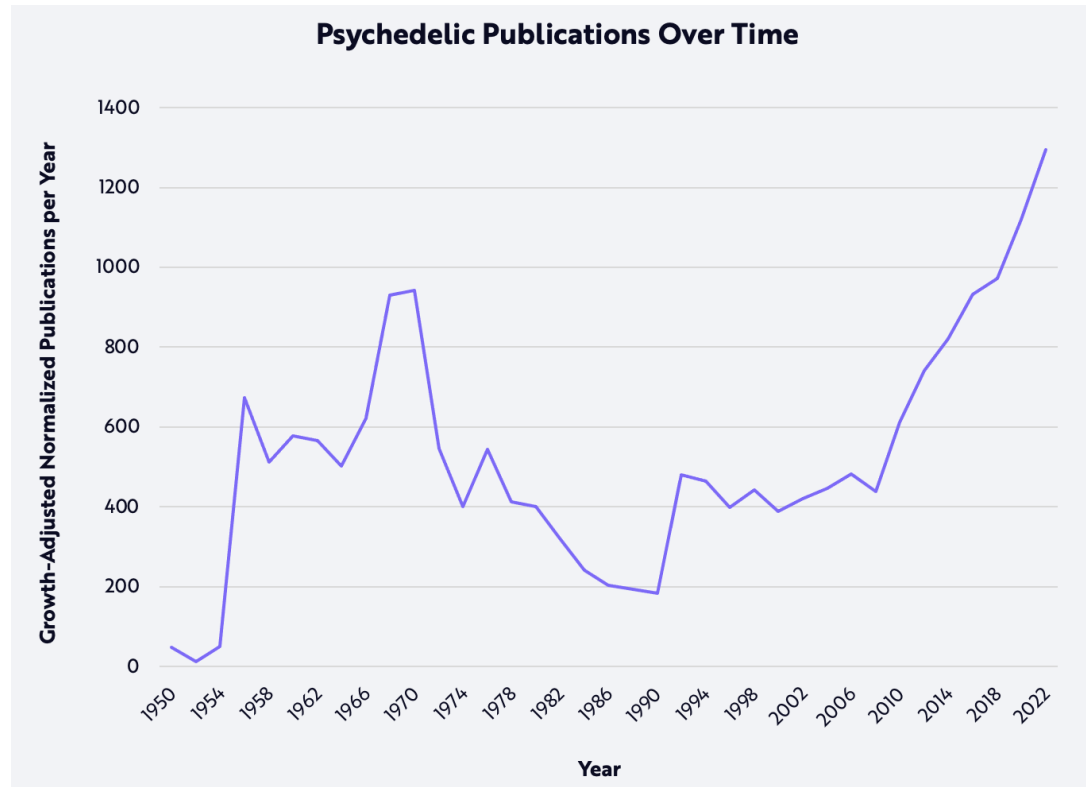
# Modern history



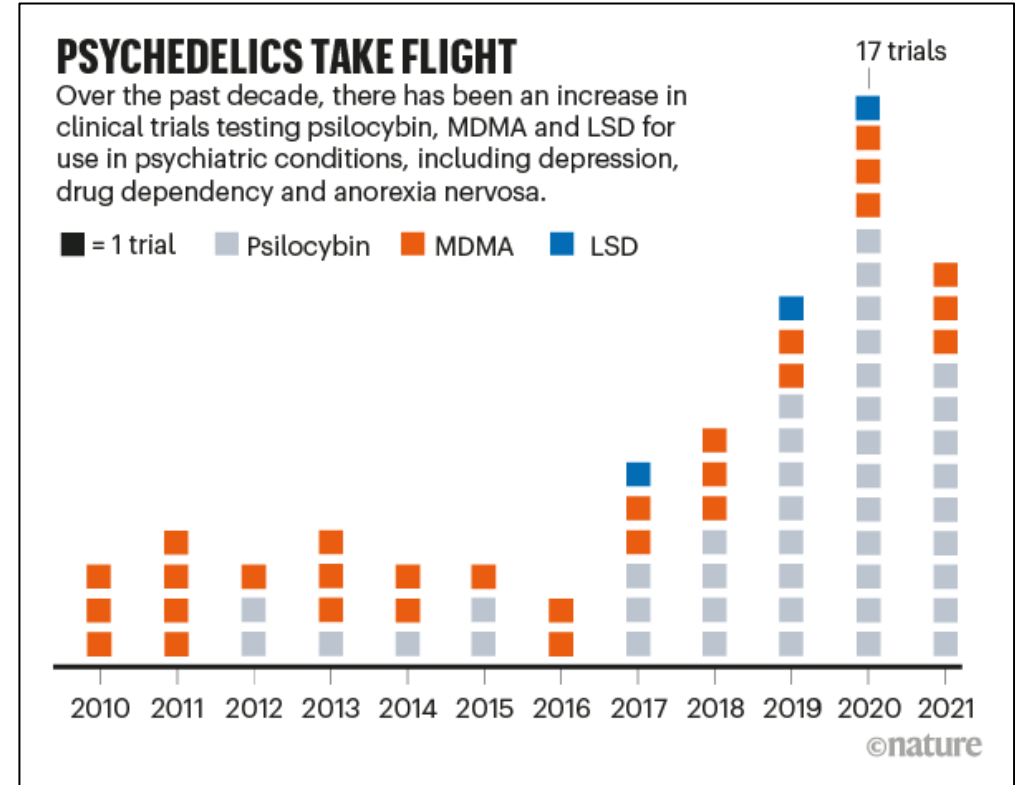
# Safety of psychedelics



# A renaissance?



Source: ARK Investment Management LLC, 2022; Data derived from Web of Science



Tullis 2021