WELCOME
Addiction Medicine ECHO Clinic

The session will begin promptly at **12 pm**.

Please **mute** the audio on your device.

Sessions take place **Thursday on the 2cd and 4th week of the month**.

Please connect your **camera**.

Need technical assistance? Call 907.729.2622 or text your phone number into the chat.

Project ECHO®

ALASKA NATIVE MEDICAL CENTER

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

Foundation *for* Opioid Response Efforts

Recording

We will record the **didactic portion** of every session. After the session, the didactic portion of this clinic will be available on the ANTHC Addiction Medicine ECHO page.

By participating in this clinic you are consenting to be recorded.

If you do not wish to be recorded, please email behavioralhealth@anthc.org at least one week prior to the ECHO Clinic you plan to attend.

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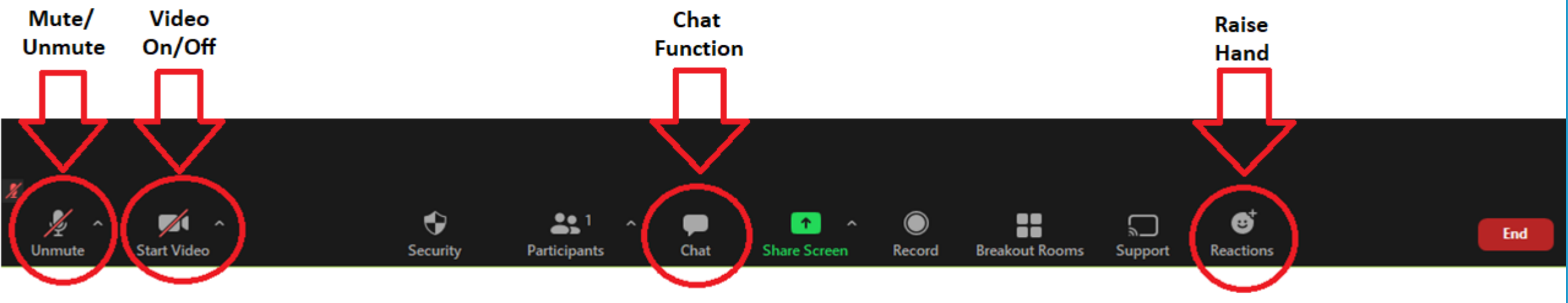
- Please mute microphone when not speaking
- Use chat function
- Position webcam effectively
- Test both audio & video

Need technical assistance? Use the chat function or call 907.729.2622



ANTHC Clinical ECHO Series

Approved Provider Statements:

In support of improving patient care, Alaska Native Medical Center (ANMC) is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Contact Hours:

ANMC designates this activity for a maximum of 25 contact hours, including 12 total pharmacotherapeutics contact hours, commensurate with participation.

Financial Disclosures:

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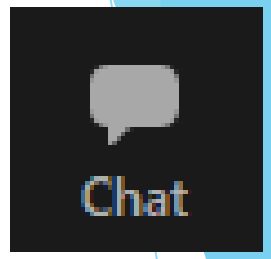
Requirements for Successful Completion:

To receive CE credit be sure you are included in attendance record as directed by the facilitator/session moderator, and complete the course evaluation or post session survey via this link: https://forms.gle/QhwCeGTf4zLNwpBX7

For more information contact Jennifer Fielder at jlfielder@anthc.org or (907) 729-1387

Introductions

Addiction Medicine ECHO



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  - Name
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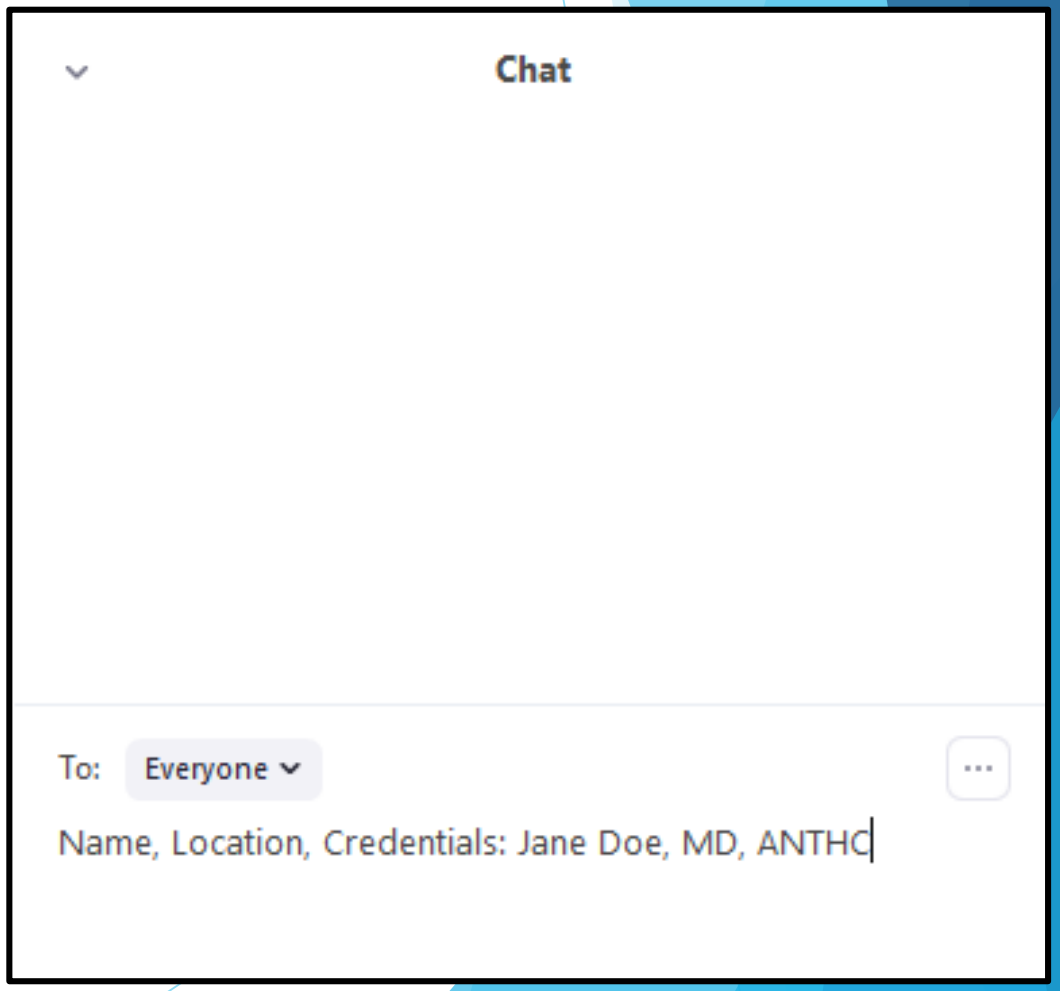
  - *Note*: The chat will be saved as our attendance record for continuing education credits.



Psychedelics in the Treatment of SUDs

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Pharmacy Resident

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Conflict of Interest Disclosure

No conflicts of interests to report.

Objectives

- Review efficacy of psychedelics in the treatment of substance use disorders (SUD)
- Review risks and benefits of the use of psychedelics in the treatment of SUD
- Review best practices of the use of psychedelics in the treatment of SUD

What are psychedelics?

- Activate the serotonin-2A (5-hydroxytryptamine-2A; 5-HT2A) receptor which results in unique hallucinogenic and mystical-type experiences.
- There are classic psychedelics and dissociative hallucinogenic that share many of the same properties.
- How do they work?
  - Substances like alcohol or heroin 'hijack' the brain's reward system, causing the user to eventually only gain positive emotion from being under the influence. Psychedelics are theorized to restore the brain's reward system by creating a psychological landscape that enables a person to practice self-acceptance and enlightenment.

DiVito, AJ, et al. Mol Biol Rep (2020).

Classic Psychedelics

LSD (d-lysergic acid diethylamide)

Psilocybin (4-phosphoryloxy-N,N-dimethyltryptamine) “Magic Mushrooms”

Peyote (Mescaline)

DMT (Dimethyltryptamine)/ Ayahuasca

NIDA. Common Hallucinogens and Dissociative Drugs. 2022.

Dissociative Hallucinogens

Very similar and has many of the same properties at classic psychedelics but can cause a person to separate from reality or disassociate. Usually does not activate serotonin receptors like classic psychedelics do.

Ketamine

Phencyclidine (PCP)

NIDA. Common Hallucinogens and Dissociative Drugs. (2022)

Most psychedelics are schedule I. What does that mean?

- Most are classified as **schedule I controlled substances** by the Comprehensive Drug Abuse Prevention and Control Act of 1970
  - **Schedule I** - drug or other substance that has a high chance of being abused or causing addiction and has no FDA-approved medical use
  - LSD, heroin, ecstasy, marijuana, peyote
- **Schedule II** - Drug has a high potential for abuse. The drug has a currently accepted medical use. Abuse of the drug may lead to severe psychological or physical dependence.
  - **Painkillers**: methadone, meperidine, oxycodone, fentanyl, morphine, opium, codeine, and hydrocodone
  - **Stimulants**: amphetamine, and methylphenidate
- **Schedule III** - substances with a moderate to low potential for physical and psychological dependence.
  - Formulations containing buprenorphine.
  - **Ketamine –** is often used in clinical settings and has indications in veterinary medicine.

LSD: An Overview

- Schedule I
- Lysergic acid diethylamide
- Can produce important alterations of consciousness at doses as low as 20 μg
- LSD also became popular as a recreational drug during the 1960s as part of the counter-culture era, despite the negative impact on its reputation
- Has mostly been studied in treatment of alcohol use disorder.

Fúlvio RM, et al, Addiction Neuroscience (2022).

LSD: Meta-Analysis

- Analyzed available trials on treatment of AUD with LSD – all from the 60s.
- Included a total of 6 trials with **536 participants** total. All had considerable limitations.
- **Single** oral doses of LSD ranged from approximately 210 mcg (3 mcg/kg) to 800 mcg, with a median dose of 500 mcg
- 185 of 315 (**59%**) **LSD patients** and 73 of the 191 (**38%**) **control patients** were improved at the first reported follow-up, and the pooled benefit difference was 16% (95% CI, 8%–25%; p = 0.0003), or, equivalently, the **number needed to treat is six**.

Krebs TS, et al. J Psychopharmacol. 2012.

Adverse Events Reported in the LSD: Meta-Analysis

- “Acted bizarrely’ (N=2)
- Agitation (N=1)
- Grand mal seizure (N=1 – alcohol withdrawal induced)
- Unspecified ‘adverse reactions’ (N=3)
- Transient ‘moderate confusion’ (N=1)
- Nausea, vomiting and ‘moderate agitation’ that was relieved by social support, relaxation, or changing the lights and music. (small number of participants)

Table 1. Included randomized controlled trials of LSD for alcoholism.

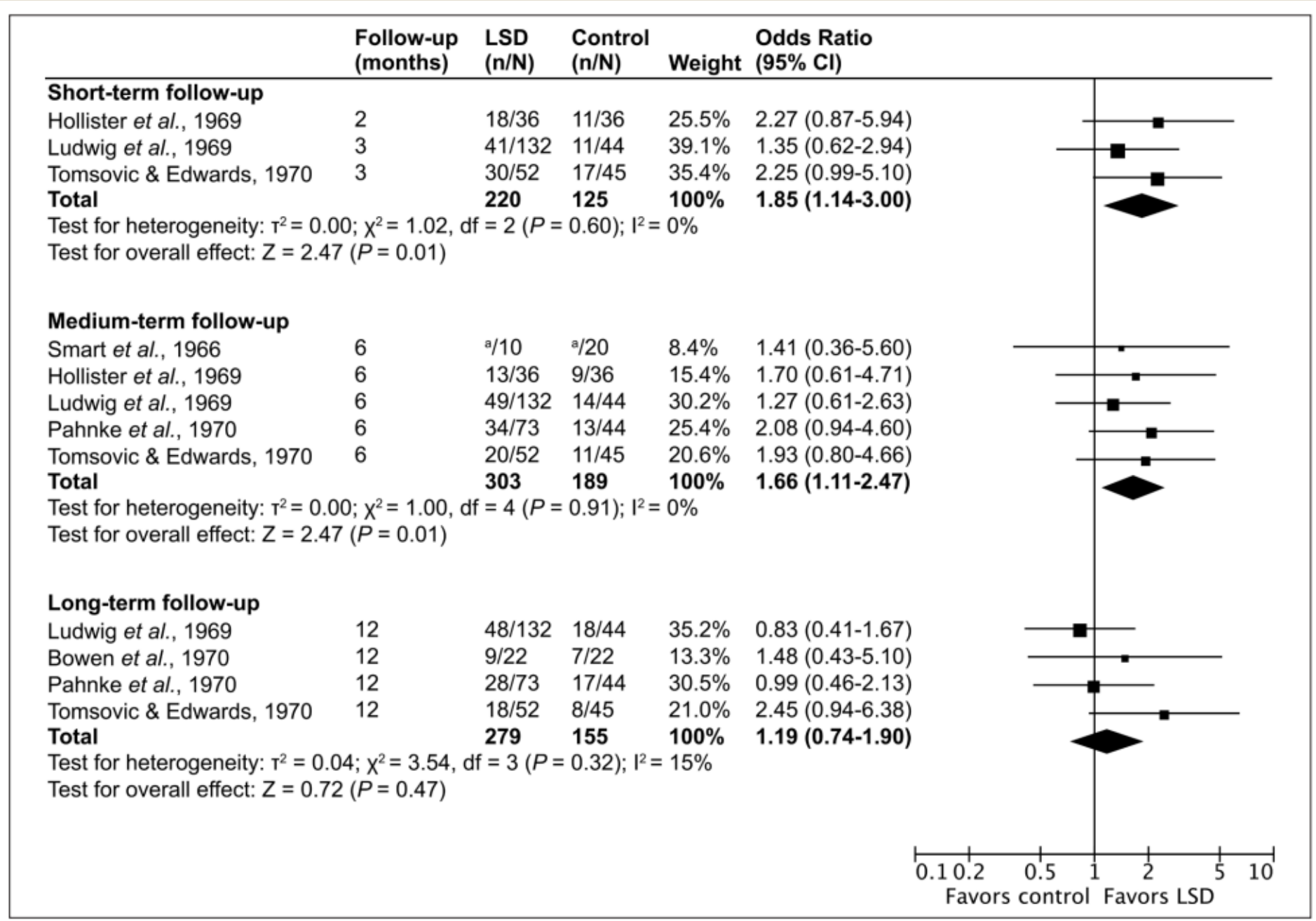
	LSD (*n*)	Control (*n*)	Blinding of patients, staff, outcome assessors	Participant characteristics[a]	Age (years)	Alcohol misuse outcome, criteria for improvement (months follow-up)	Retention at first follow-up	Location (Funding)
Smart et al., 1966	800 mcg (10)	60 mg ephedrine sulfate (10) or no drug (10)	Double-blind, independent assessors	Male and female alcoholics, 'all had a long history of excessive and uncontrolled drinking'	Median 38.5, range 26–59	Drinking History Questionnaire, % change in time abstinent, continuous (6 mo)	100%	ARF, Toronto, Canada (NR)
Hollister et al., 1969	600 mcg (36)	60 mg d-amphetamine (36)	Double-blind, independent assessors	Male veterans, 'acute alcoholic episode' within 2 weeks of admission, 'all were problem drinkers'	Median 45, range 31–51	Drinking Behaviour Interview, score ≤ 10, 'Abstinent' or 'Social' drinking (2, 6 mo)[b]	81% LSD; 64% control	VA Hospital, Palo Alto, CA, USA (NIMH)
Ludwig et al., 1969	3 mcg/kg, ~210 mcg (132)	No drug, sit alone and write for 3 hr (44)	Double-blind until LSD session, independent assessors	Male alcoholics, up to four previous admissions for treatment of alcoholism	Range 21–55	Abstinence (1, 3 mo); Behavior Rating Scale, change score ≥ 5, 'Much improved' (6, 12 mo)[b]	100%	MSH, Madison, WI, USA (NIMH)
Bowen et al., 1970	500 mcg (22)	25 mcg LSD (22)	Double-blind, not stated if assessors independent[c]	Male veterans, voluntarily applied for treatment of alcoholism	Median 44.5	Adjustment Scale, score ≥ 6, 'Good adjustment' (12 mo)	100%	VA Hospital, Topeka, KS, USA (NR)
Pahnke et al., 1970	450 mcg (73)	50 mcg LSD (44)	Double-blind, independent assessors	Male alcoholics, voluntarily applied for treatment of alcoholism	NR	Drinking Behaviour Scale, score ≥ 8, 'Minimal departure from total abstinence' (6, 12 mo)	88% LSD; 91% control	MPRC, Baltimore, MD, USA (NIMH)
Tomsovic & Edwards, 1970	500 mcg (52)	Treatment as usual (45)	Double-blind until LSD session, self-report assessment[c]	Male alcoholics, average 12 years of problem drinking	Mean 43	Drinking Adjustment Scale, no more than 1 drinking episode in follow-up period, 'Much improved' (3, 6, 12 mo)[b]	92% LSD; 73% control	VA Hospital, Sheridan, WY, USA (VA)

ARF: Alcoholism and Drug Addiction Research Foundation; MPRC: Maryland Psychiatric Research Center; MSH: Mendota State Hospital; NIMH: National Institute of Mental Health; NR: not reported; VA: Veterans Administration.

[a]All participants were recruited after admission to alcoholism treatment programs.

[b]Provided data on abstinence from alcohol.

Krebs TS, et al. J Psychopharmacol. 2012.



Krebs TS, et al. J Psychopharmacol. 2012.

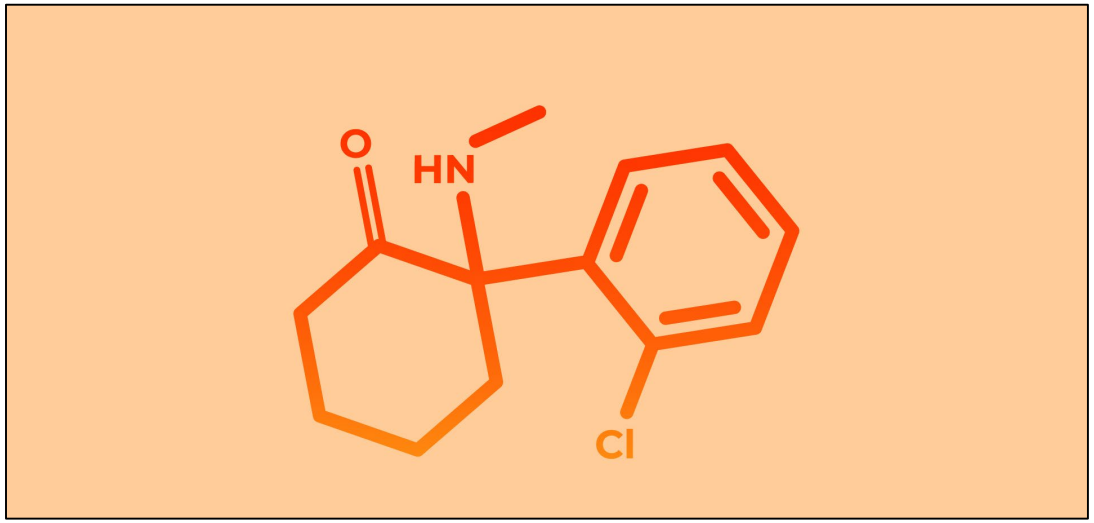
So, what does it mean? Is LSD useful?

- **There is a lack of recent controlled trials.**
- **No consensus has been reached in the scientific community regarding its therapeutic use in SUD.**
- **Studies conflict with each other as some showed positive results and others failed to show statistical significance between LSD and the control group.**
- **Unclear if LSD is an effective treatment by itself or if it offers benefit as an adjunct to existing treatments.**

Krebs TS, et al. J Psychopharmacol (2012).; Fúlvio RM, et al, Addiction Neuroscience (2022).

Ketamine: An Overview

- Schedule III (it's used in clinical practice)
- Potent, non-competitive NMDA receptor antagonist
- Administered as an injectable solution either by intravenous or intramuscular route
- CNS effects onset is within 5 min after injection.
- Doses from 0.5 to 2. mg/kg of IV racemic ketamine are usually employed for induction of anesthesia with lower doses for maintenance.
  - Subanesthetic doses are used for psychedelic experience.
  - Very low doses used in treatment of depression - generally do not produce strong psychedelic effects.



Ketamine Indication	Dose
Anesthesia	0.5-2 mg/kg IV
Psychedelic Experience/Analgesia	0.25-0.5 mg/kg IV bolus
Depression	0.5 mg/kg IV over 40 min

Fúlvio RM, et al, Addiction Neuroscience (2022).; Lexicomp – Ketamine.

Ketamine's Limited Evidence of Effectiveness

Cocaine (N=8)

- Ketamine increased motivation to quit cocaine over lorazepam
- There was a significant reduction in frequency (22 days of use/28 days at baseline vs. 5/28 days at 4 week follow-up, $p = 0.012$) and amount of cocaine use in the follow-up period ($149.30/use day at baseline vs. $10.50/use day at 4 week follow-up, $p < 0.001$).

Opioids (N=70)

- High Dose vs. Low Dose:
  - Abstinence rates at 1 month: 85% in 2 mg/kg group (55% in the 0.2 mg/kg group, $p < 0.01$)
  - Abstinence rates at 1 year: 24% in 2 mg/kg group (compared to 6% in the 0.2 mg/kg group, $p < 0.05$).
- Multiple Treatments vs. Single Treatment:
  - Abstinence at 1 year: 50% of subjects receiving multiple ketamine treatments (compared to 22% of single-session treatments ($p < 0.05$)) They also noted significantly greater reductions in heroin craving in the repeated treatment group as compared to the single treatment group.

Fúlvio RM, et al, Addiction Neuroscience (2022).; Jones JL, et al. Front Psychiatry (2018).

Lack of placebo makes it **difficult** to gage ketamine's efficacy in comparison to conventional therapies such as buprenorphine.

DMT: An Overview

- Schedule I
- N, N-dimethyltryptamine is an indole alkaloid found in plants and endogenously in some animals
- Potent 5-HT2A (serotonin) agonist
- Used in the ritual drink, **ayahuasca**. This mixture contains carbolines, which inhibit enzymes that usually metabolize DMT in the brain. Thus, DMT can elicit a stronger psychedelic experience.
- An observational report (N=15) recorded that individuals diagnosed with AUD were not replacing alcohol with ayahuasca but were able to "expand their conscience and change their attitudes."
- Other qualitative reports indicate that ayahuasca may be useful to 'improve **neurobiological and psychological processes** that support the recovery from SUD and the **prevention of relapses**.'

Clinical trials are currently not available to further assess the use of this drug.

Fúlvio RM, et al, Addiction Neuroscience (2022).

DMT / Ayahuasca

Substance	Type of study and sample	Intervention / survey methodology	Results	Reference
Crack-Cocaine	Cross-sectional observational study, $N = 40$ crack-cocaine users and former users.	Qualitative semi-structured interviews using the DSM-IV criteria for dependence. Ayahuasca doses were not clearly reported.	80% of participants ceased drug consumption after starting using ayahuasca. The others 20% reported having fallen back into crack/cocaine use after having attained abstinence with the help of ayahuasca. Among the reasons for relapse, detachment from the ayahuasca community stood out.	Cruz & Nappo 2018 [90]
Multiple substances	Cross-sectional observational study, $N = 84$.	Interviews with adolescents regarding the use of a variety of psychoactive substances, comparing ayahuasca users and non-users (controls). Ayahuasca doses were not clearly reported.	Ayahuasca users were mostly comparable to control except for a considerably smaller consumption of alcohol in the past and at the time of the study. Religious affiliation may have played a central role as a possible protective factor for alcohol use.	Doering-Silveira et al., 2005 [84]
Multiple substances	Longitudinal observational study, $N = 242$, 12-month follow-up.	Addiction severity was assessed using the Addiction Severity Index (ASI), and records of history of the alcohol and illicit drug use. Two subsamples: - Study 1: jungle-based sample; - Study 2: urban-based sample. Ayahuasca doses were not clearly reported.	Ayahuasca users showed lower scores on the ASI - Alcohol Use and Psychiatric Status subscales. Jungle-based ayahuasca users showed a higher frequency of previous illicit drug use but ceased at the time of examination, except for cannabis. 12-month follow-up showed abstinence from illicit drug use was maintained in both groups except for cannabis in the jungle-based sample. Differences on ASI scores were still significant in the jungle-based group but not in the urban group.	Fábregas et al., 2010 [83]
Multiple substances	Longitudinal observational study, $N = 12$, inpatient, 6-month follow-up.	Four days of group counselling combined with two expert-led ayahuasca ceremonies. Data was collected by several psychological and behavioral factors related to problematic substance use and qualitative information from their experience. Ayahuasca doses were not clearly reported.	The treatment provided significant improvements in scales assessing hopefulness, empowerment, mindfulness and quality of life meaning and outlook subscales. Self-reported alcohol, tobacco and cocaine use declined, although cannabis and opiate use did not. Reported reductions in problematic cocaine use were significant. All study participants reported positive and lasting changes from participating in the retreats.	Thomas et al., 2013 [85]
Multiple substances	Longitudinal observational study, $N = 53$, inpatient.	Integrative program with sessions of detoxification, diet and ayahuasca ritualistic sessions, together with sessions of psychotherapy. Data was collected by several scales, like, ASI and Craving Experience Questionnaire (CEQ). Ayahuasca doses were not clearly reported.	A significant decrease in addiction severity outcomes, drug use, alcohol use, psychiatric status, emotional distress and substance craving was observed. Quality of life increased significantly from beginning to treatment completion. First indications for significantly improved SUD symptoms after the Amazonian medicine-based treatment.	Berlowitz, 2019 [92]

Fúlvio RM, et al, Addiction Neuroscience (2022).

Risks of Individual Psychedelics

LSD

- Acute psychiatric adverse events such as **anxiety and confusion** should be anticipated, and LSD administration should occur in a comfortable environment with informed participants

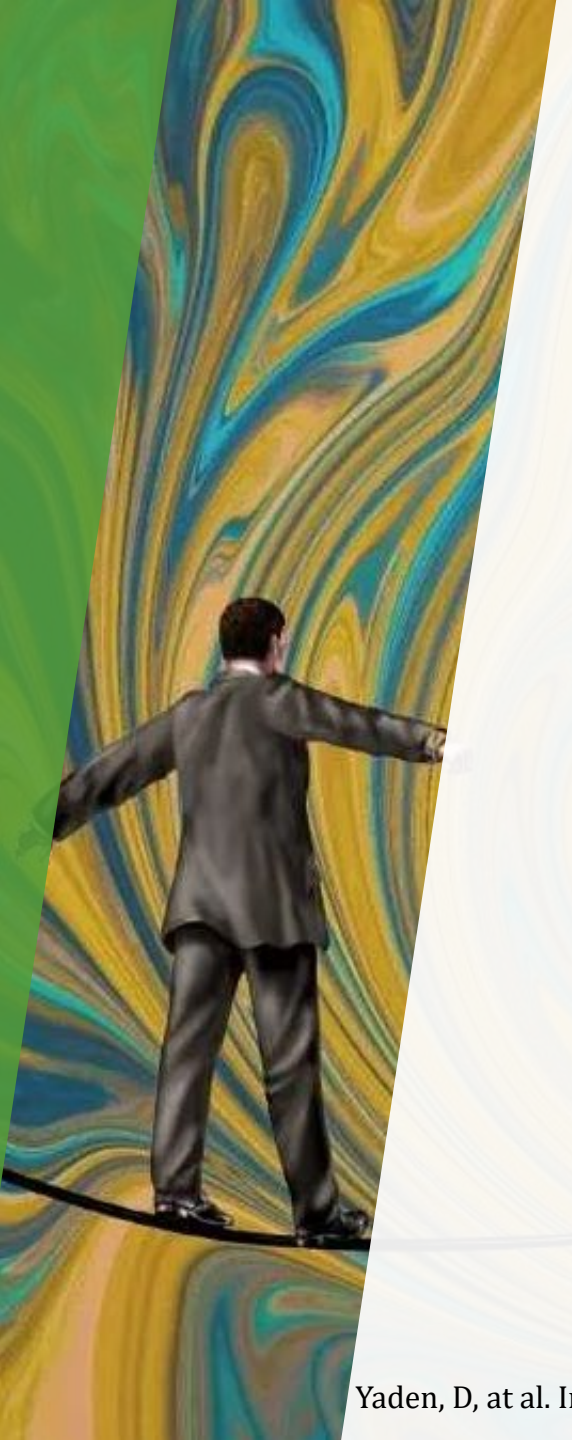
Ketamine

- Airway complications, cardiovascular effects, reports of abuse, emergence reactions, genitourinary effects, and respiratory depression have been rarely reported when used at anesthetic doses.
- Contraindicated in patients with underlying conditions in which increased blood pressure would pose a risk of complications.

DMT

- Appears to have limited neurotoxicity and other adverse effects except for **intense cardiovascular effects when administered IV in large doses**.
- Several early studies demonstrated that DMT does not produce tolerance except in cardiovascular and endocrine effects.
- Animal pregnancy models show increased incidences of cleft palates and skeletal deformities.

Fúlvio RM, et al, Addiction Neuroscience (2022).; Lexicomp – Ketamine.; Krebs TS, et al. J Psychopharmacol. 2012; Carbonaro TM, et al. Brain Res Bull (2016).; Rosenbaum SB, et al. Ketamine. StatPearls Publishing; 2022.



Risks Continued

- Cardiac events may happen in those at high cardiovascular risk, destabilization of those with psychotic disorders or predisposition, and high levels of anxiety or dangerous behavior while under the influence.
  - **Risks may be mitigated in a clinical setting through screening, preparation, monitoring, and follow-up care.**

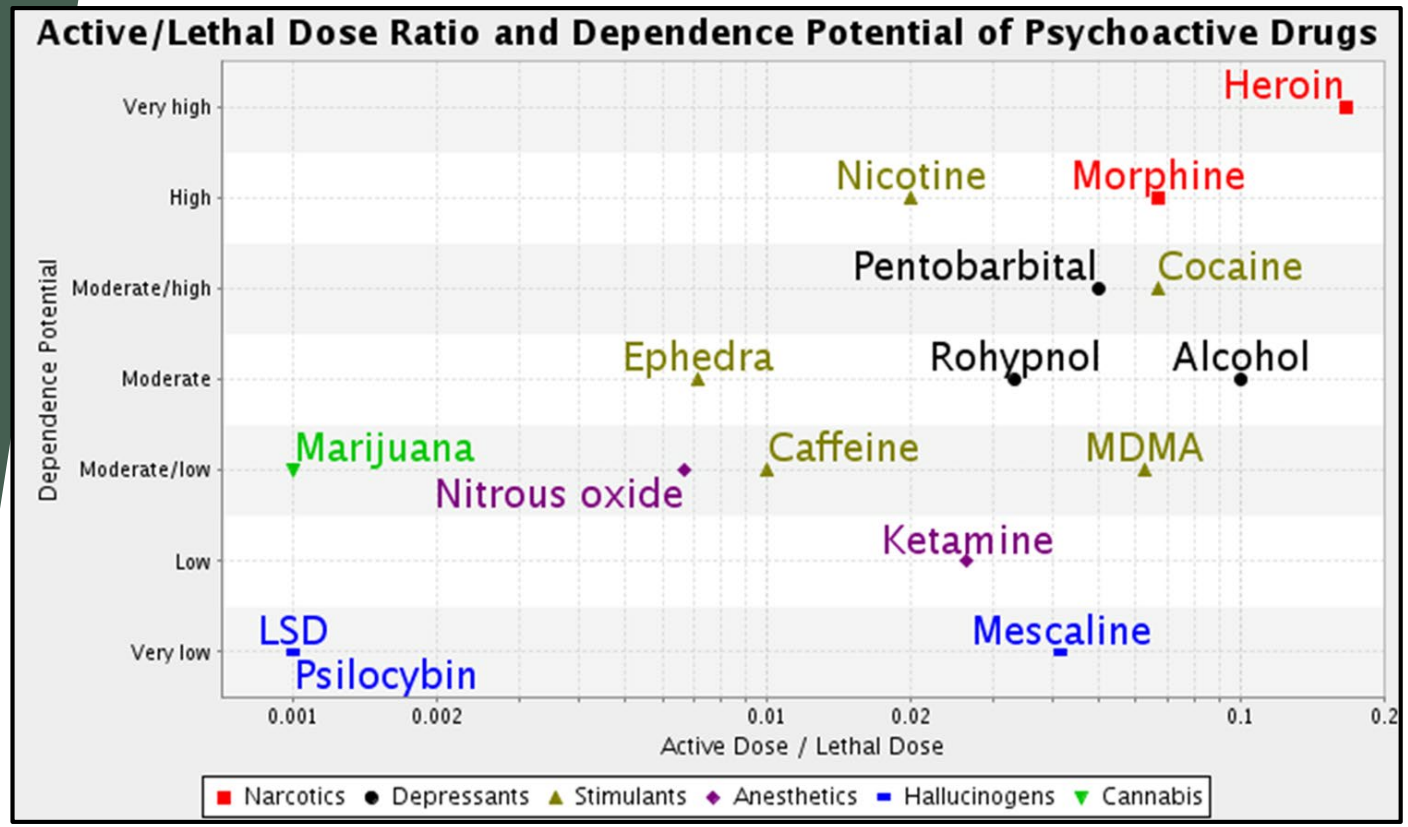
"It is also important to emphasize the risks of classic psychedelics when used recreationally and outside the context of therapist-supervised psychedelic therapy, which is a highly structured process involving ongoing follow-up and aftercare. In the recreational context, individuals are at higher risk of psychological distress and worsening of mental health issues"

Yaden, D, at al. Int. J. Drug Policy (2021).; Dos Santos RG, et al. Ther Adv Psychopharmacol (2016).

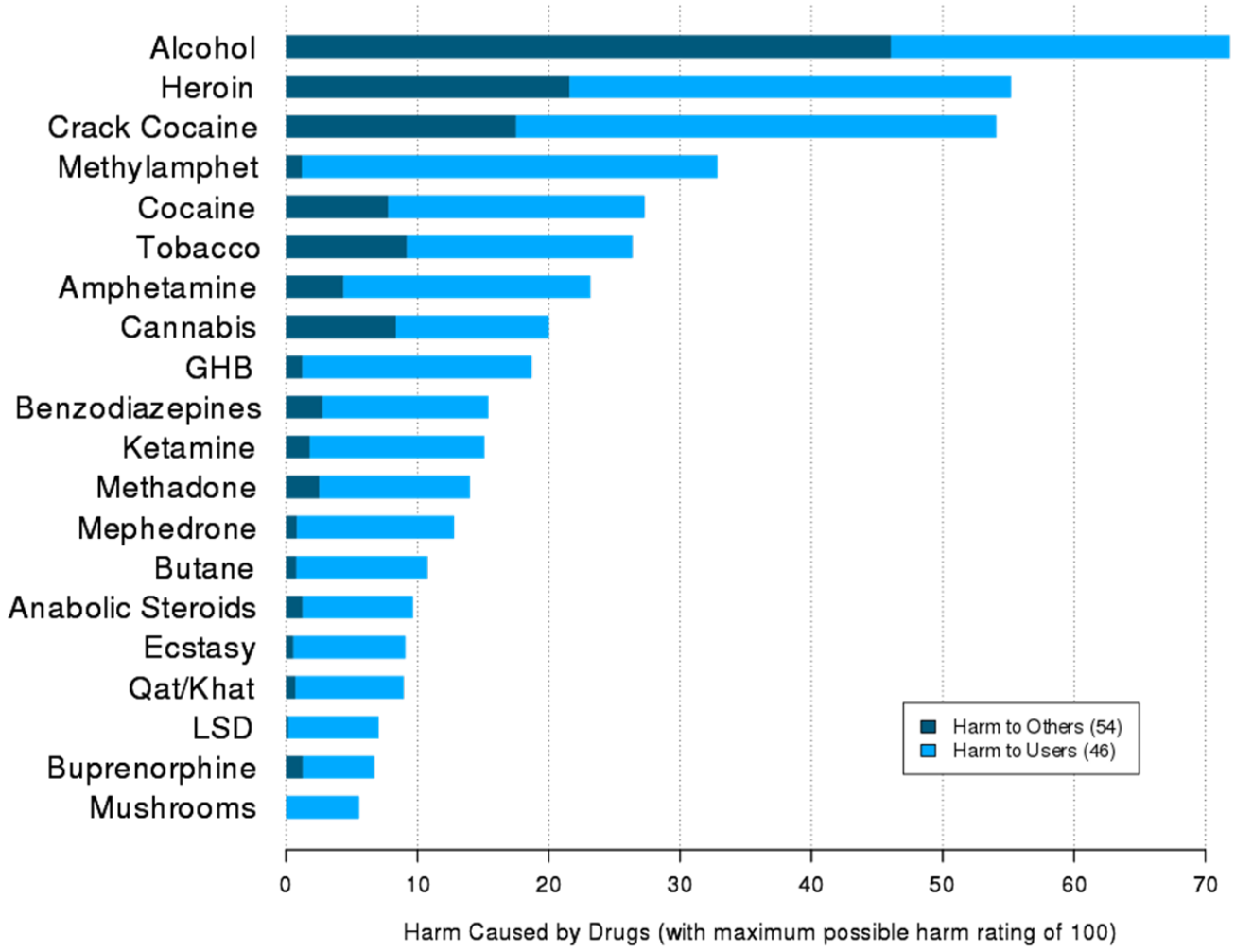
Despite the risks, why are we interested in psychedelics?

Addictive Properties of Psychedelics

- Evidence currently suggests that few psychedelics can be considered addictive. Some current literature indicates that they may be 'anti-addictive'. Nonetheless, understanding the full risk and benefits of psychedelics will increase as studies continue.



Gable, R. S. U.S. Public Policy, pp.149-162, 2006.



UK Statistics

http://www.thelancet.com/cms/attachment/2001010052/2003786747/gr4.jpg


Our current system to treat addiction is not optimal.

68,630 total **overdose deaths** involving opioids in 2020

65.9% had at least one **potential opportunity** for intervention

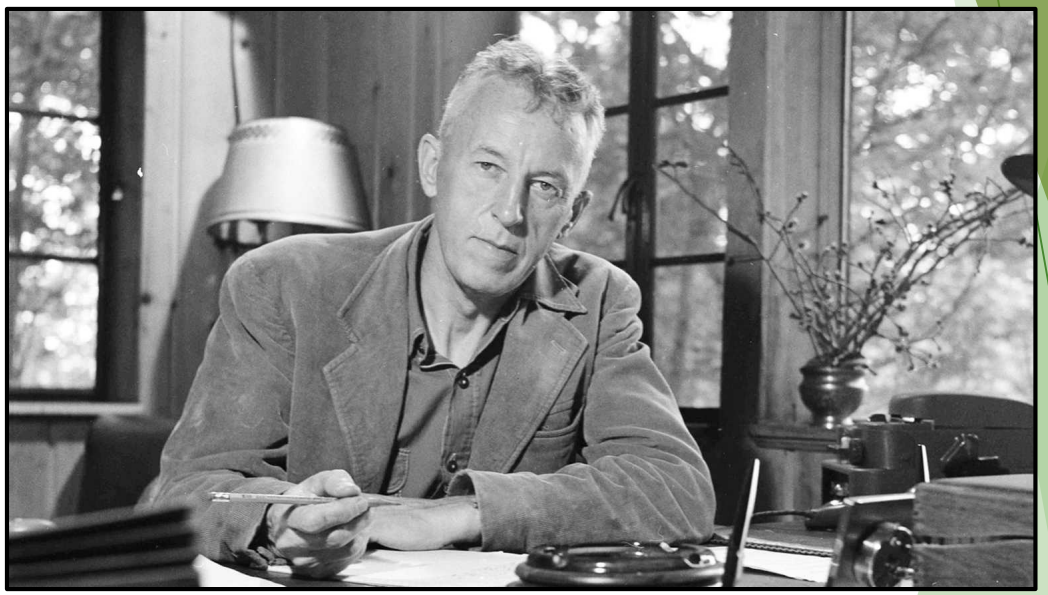
There are currently **no FDA approved** treatments for **meth, cocaine, or cannabis**.

Rate of **overdose** deaths increased by **31%** from 2019 to 2020

Number of **alcohol-induced deaths,** excluding accidents and homicides: **49,061**

Dropout rates for conventional SUD treatments are approximately **30%**.

Lappan SN, et al. *Addiction* (2020).; FastStats - Alcohol Use (cdc.gov); SUDORS Dashboard: Fatal Overdose Data (cdc.gov)



Bill Wilson

Founder of Alcoholics Anonymous.
Supported the use of psychedelics in those who are recovering.

Yaden DB, et al. Int J Drug Policy (2021).

Introducing Psychedelics Into the 12-Step Program

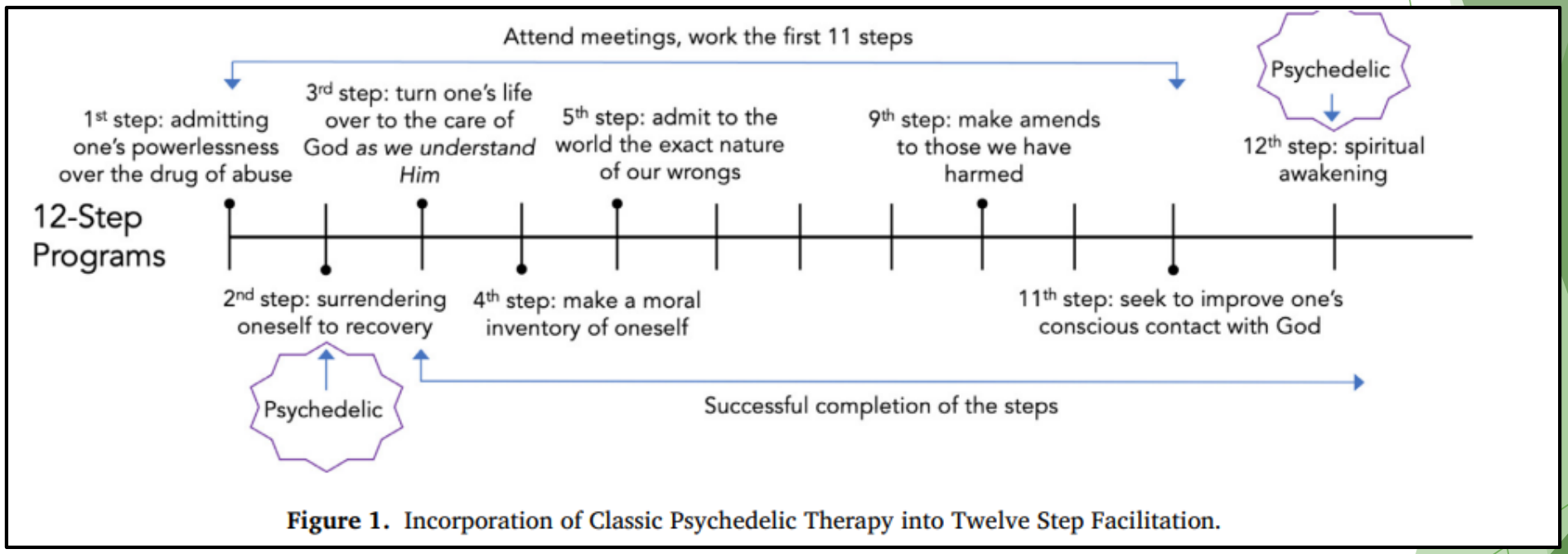


Figure 1. Incorporation of Classic Psychedelic Therapy into Twelve Step Facilitation.

High dropout rates occur during the time of "surrendering" oneself to recovery. It is theorized that psychedelics may aid during this step.

Yaden DB, et al. Int J Drug Policy (2021).

One group exists that incorporates psychedelics into their 12-step treatment regimen…

"We do not consider the use of psychedelics to be destructive. We do not use them for numbing, escapism or avoidance. We practice openness and honesty when integrating psychedelics into our 12-Step program because they help us become more aligned with our primary goal of recovery."

https://www.psychedelicsinrecovery.org/articles/

Psychedelics in Recovery

- Some activities for engaging in this work may include routine journaling, meditation, diet, exercise, and social connections (such as therapists, guides, friends, family, etc..)
- Acknowledges that psychedelics may result in abuse and encourages its members to practice humility, respect, and caution in the conscious and moderate use of psychedelics.
- Also acknowledges that most psychedelics are illegal and users are at risk of being prosecuted.

The Future Legality of Psychedelics

- Although there has been limited push to incorporate psychedelics into clinical practice, there are many legal barriers to navigate this idea.
- MDMA, another psychedelic, has FDA approval for treatment-resistant PTSD.
- Psilocybin, or magic mushrooms, has been given FDA approval for treatment-resistant depression.

BREAKING NEWS

8/24/22

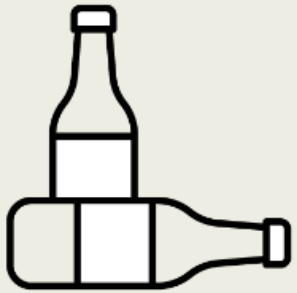
A 32-week randomized, clinical trial (N=93) compared psilocybin to a control, Benadryl, in participants who drank, on average, 7 drinks at a time. Twelve weeks of psychotherapy was given to both groups with the drugs administered at weeks 4 and 8. The doses of psilocybin were 25 mg/70 kg for week 4 and 25-40 mg/70 kg for week 8.

JAMA Psychiatry

RCT: Psilocybin-Assisted Treatment of Alcohol Use Disorder

POPULATION

53 Men, 42 Women



Adults with alcohol dependence

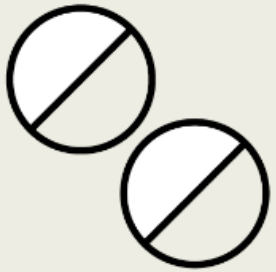
Mean age, 45.8 y

SETTINGS / LOCATIONS

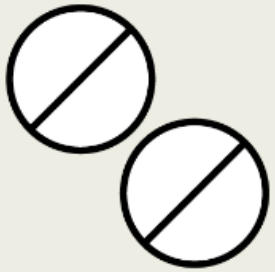
2 Academic centers in New York and New Mexico

INTERVENTION

95 Individuals randomized



49 Psilocybin
Administered orally in 2 all-day sessions (dose range, 25-40 mg/70 kg)



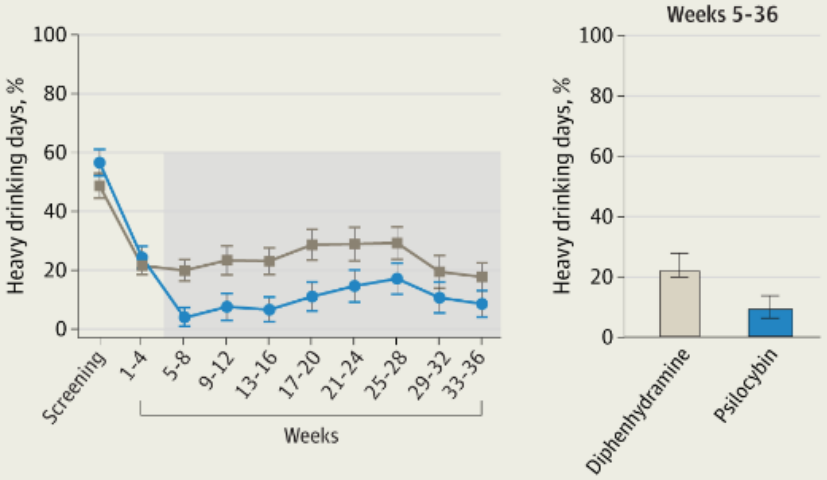
46 Diphenhydramine control
Administered orally in 2 all-day sessions (dose range, 50-100 mg)

PRIMARY OUTCOME

Percent heavy drinking days (scale, 0-100), assessed using the timeline followback interview, contrasted between groups over the 32-wk period following the first administration of study medication.

FINDINGS

Percent heavy drinking days during the 32-wk double-blind period was lower in the psilocybin group compared with the diphenhydramine group



Percent heavy drinking days
Psilocybin=9.7%
Diphenhyramine=23.6%

Mean difference, 13.9 (95% CI, 3.0-24.7; *P* = .01)

Bogenschutz MP, Ross S, Bhatt S, et al. Percentage of heavy drinking days following psilocybin-assisted psychotherapy vs placebo in the treatment of adult patients with alcohol use disorder: a randomized clinical trial. *JAMA Psychiatry.* Published online August 24, 2022. doi:10.1001/jamapsychiatry.2022.2096

	Follow-up period	No. (%)[a]		NNT	OR (95% CI)[b]	*P* value[b,c]
		Diphenhydramine (n = 45)	Psilocybin (n = 48)			
Abstinence	Weeks 5-36	4 (8.9)	11 (22.9)	7.1	3.05 (0.89-10.40)	.06
	Weeks 33-36	11 (24.4)	23 (47.9)	4.3	2.84 (1.17-6.89)	.02
No heavy drinking	Weeks 5-36	5 (11.1)	16 (33.3)	4.5	4 (1.32-12.10)	.01
	Weeks 33-36	18 (40.0)	30 (62.5)	4.4	2.5 (1.08-5.76)	.03

Citations

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Case Presentation

Project ECHO's goal is to protect patient privacy

- To help Project ECHO accomplish that goal, please only display or say information that doesn't identify a patient or that cannot be linked to a patient.
- **References: For a complete list of protected information under HIPAA, please visit www.hipaa.com**

Thank you for joining us today.
We appreciate your participation and hope to see you at the **NEXT ECHO Session:**

September 8, 2022 from 12pm -1 PM

You will be receiving a follow up survey that we hope you will complete to help us improve. If you are requesting continuing education credits, you will be required to complete the survey to receive your CMEs.


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