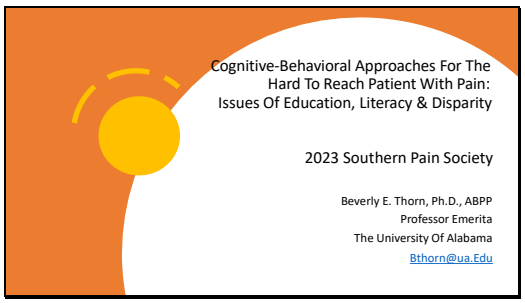
Dr. Green’s presentation is not available

Slide 1



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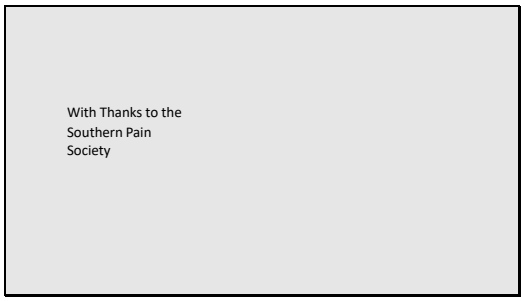


Slide 3

Slide 4

Historical & Current Treatment
Of Chronic Pain

Biomedical

Biopsychosocial

• A CULTURE SHIFT?

Slide 5

Biomedical Model Of Pain (Pain Specificity Theory)

• Specificity Theory: Tissue damage = pain; Nociception = pain

Slide 6

Biomedical Model Of Pain

Slide 7

Tissue Damage & Pain Perception *Are* Related

Slide 8

But….Tissue Damage Is Less Predictive Than Expected (Especially Chronic Pain)

Many People *Without* Any Back Pain Show Significant Disc Abnormalities

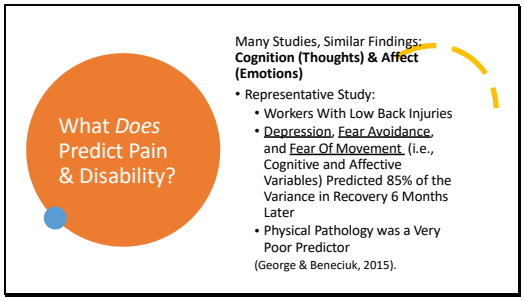
True For Back, Hip, And Knee

- Blankenbaker Et Al., 2008; Borenstein Et Al., 2001; Brinjiki W Et Al, 2015; Carragee, Alamin, Miller, & Carragee, 2005; Jarvik Et Al., 2005; Jensen Et Al., 1994; Link Et Al., 2003.

Slide 9

What *does* Predict Pain & Disability?

Slide 10



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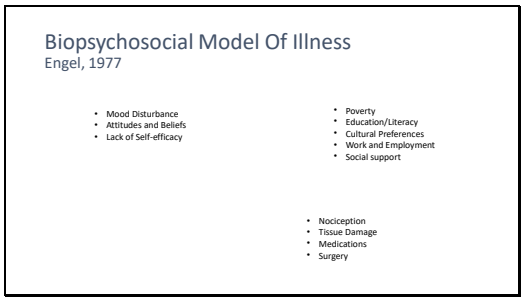

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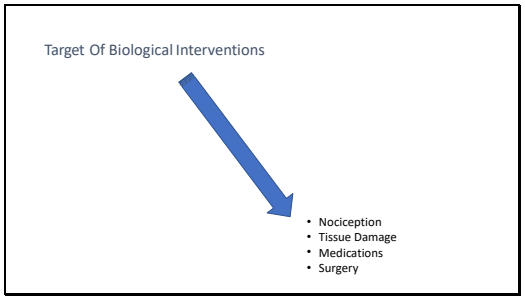


Slide 13

The Cognitive-Behavioral Model

Slide 14

Target Of Cognitive-Behavioral Interventions

- Mood Disturbance
- Attitudes and Beliefs
- Lack of Self-efficacy

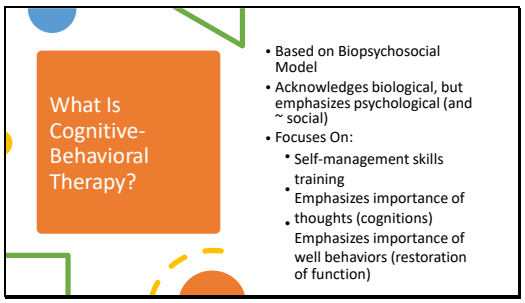
Slide 15

Treatments for Chronic Pain

Missing Target

- Education/Literacy
- Poverty
- Cultural Preferences
- Social support
- Work and Employment

Slide 16



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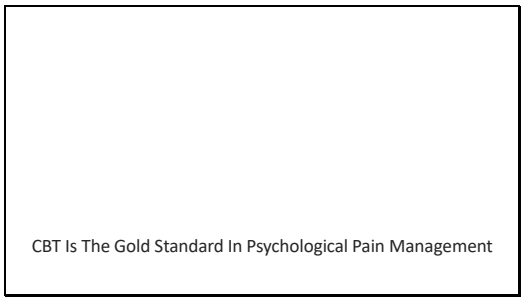

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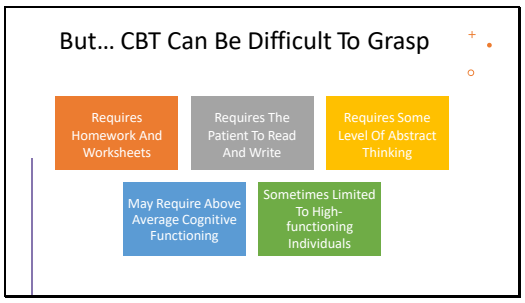

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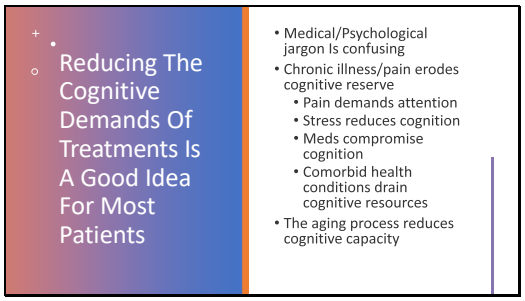
Slide 20



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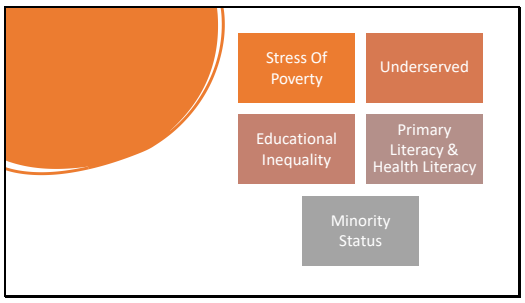

Slide 22

How Did We Simplify CBT Materials?

Simplified Patient Materials:

- Reduced reading level (to 5th grade)
- Reduced text Added
- illustrations Increased
- font size Increased
- white space

Slide 23

Illustrations Enhanced the Meaning of the Text….

Slide 24

How Did We Simplify The CBT Process?

Reduced Cognitive Demand Of Treatment (Cognitive Load Theory):

- Simplified oral presentation of concepts
- Collaborative learning via Flip Chart
- Homework Worksheets In Session
- Example Worksheets

Slide 25

Feasibility & Acceptability Study

Cognitive-Behavioral Chronic Pain Trial Among Rural Minorities and non-Minorities

- Rural Location Captured A Quadruple Disparity: Participants Were Mostly Female African Americans With Low Literacy And Low SES.
- Funding: National Institute On Nursing Research And Nimh (Nr010112)

Slide 26

PAIN® 152 (2011) 2710–2720

Randomized trial of group cognitive behavioral therapy compared with a pain education control for low-literacy rural people with chronic pain

Beverly E. Thorn [a,*], Melissa A. Day [a], John Burns [b], Melissa C. Kuhajda [c], Susan W. Gaskins [d], Kelly Sweeney [a], Regina McConley [a], L. Charles Ward [f], Chalanda Cabbil [a]

- Non-initiation of tx predicted by education, literacy, catastrophizing
- **Treatment drop-out higher in CBT (w/less accurate homework completion & lower retention of material)**

Slide 27

- Limited # concepts per session
- Behavioral techniques followed by cognitive skills
- Increased # of relaxation activities per session
- Added more illustrations
- **No Required Written Homework**
- Catch Phrases :
  - Pain Facts
  - Pain Toolbox
  - "Gate Closers"

Audio Session summaries
- "Session Tips" & relaxation audios
- (Thank You Melissa Day!)

Slide 28

Does Simplified CBT Work??

Slide 29

Reducing Disparities with Literacy-Adapted Psychosocial Treatments for Chronic Pain: A Comparative Trial

Whatley Health Services

Patient-centered Comparative Effectiveness Trial

PCORI Contract #941
- 5/15/13-7/31/17

Slide 30

Comparative Effectiveness Trial

3 Conditions:
- Cognitive-Behavioral Therapy - CBT (N=95)
- Biopsychosocial Pain Education - EDU (N=97)
- Medical Treatment As Usual - UC (N=98)

83% Retained at Primary Endpoint (Post-tx)
- CBT (87%)
- EDU (84%)
- UC (80%)

75% Retained At 6 Mo. Follow-up

Slide 31

Does Simplified CBT Work??

Yes

- CBT & EDU, Pre-post, And At 6 Mos. (Not UC)
- Moderate Effect Sizes
- CBT Slightly Better
  - Larger Effects
  - More CMI's (Post & Fu)
- But EDU Is A Viable Alternative

Slide 32

Annals of Internal Medicine ORIGINAL RESEARCH

Literacy-Adapted Cognitive Behavioral Therapy Versus Education for Chronic Pain at Low-Income Clinics

A Randomized Controlled Trial

Beverly E. Thorn, PhD; Joshua C. Eyer, PhD; Benjamin P. Van Dyke, MA; Calia A. Torres, MA; John W. Burns, PhD; Minjung Kim, PhD; Andrea K. Newman, MA; Lisa C. Campbell, PhD; Brian Anderson, PsyD; Phoebe R. Block, MA; Bentley J. Bobrow, MD; Regina Brooks; Teya T. Burton, DC, MPH; Jennifer S. Cheavens, PhD; Colette M. DeMonte, PsyD; William D. DeMonte, PsyD; Crystal S. Edwards; Minjeong Jeong, PhD; Mazharuddin M. Mulla, MA, MPH; Terence Penn, BS; Laura J. Smith, BA; and Deborah H. Tucker, MBA*

Ann Intern Med. doi:10.7326/M17-0972

http://annals.org/aim/fullarticle/2673506/literacy-adapted-cognitive-behavioral-therapy-versus-education-chronic-pain-low

http://annals.org/aim/fullarticle/2673752/shining-lamp-efforts-transform-pain-care-america

Slide 33

Patient Characteristics as Treatment Moderators

The Journal of Pain

Heterogeneity of Treatment Effects in a Randomized Trial of Literacy-Adapted Group Cognitive-Behavioral Therapy, Pain Psychoeducation, and Usual Medical Care for Multiply Disadvantaged Patients With Chronic Pain

Slide 34

Slide 1

Cannabis and Psychedelics for Pain Management: the Long Strange Trip Continues

Kevin Boehnke, PhD
Research Assistant Professor
Chronic Pain and Fatigue Research Center, Anesthesiology Department, Michigan Medicine

1

Slide 2

Disclosures

- Support from NIH grants:
  - K01DA049219 (NIDA)
  - R34AR078435 (NIAMS)
  - R01AT010381 (NCCIH)
- Industry:
  - Received grant funding from Tryp Therapeutics for protocol development
  - Data safety and monitoring committee for ongoing clinical trial with Vireo Health (unpaid)
- State of Michigan:
  - Veteran's Marijuana Research Program

2

Slide 3

Learning Objectives

- 1. Provide relevant legal background and definitions of cannabis and psychedelic medicines.
- 2. Overview current trends in medical use of cannabis and psychedelics for chronic pain - clinical trials and naturalistic use.
- 3. Identify useful practices for effectively working with patients who use cannabis and psychedelic medicines.

3

Slide 4

Outline

- Cannabis and chronic pain
- Parallels between cannabis and psychedelic landscape
- Psychedelics for chronic pain

4

Slide 5

Hemp? Cannabis? Marijuana?

- All are *Cannabis sativa*
- Hemp: <0.3% THC
- Marijuana: >0.3% THC, used in cannabis prohibition campaigns
- Cannabis: scientifically accurate catch all term that I will use in this talk

5

Slide 6

Two popular cannabinoids: THC vs. CBD

- **Δ-9-Tetrahydrocannabinol (THC)**
  - Analgesic, mood-altering, appetite stimulating[1]
- **Cannabidiol** (CBD)
  - Non-intoxicating, potentially protective against psychoactive effects of THC[2]
  - Anti-convulsant[3]
  - Some anxiolytic evidence[4]
  - In non-human animal studies, anti-inflammatory[5]
- **Other cannabinoids:** CBN, CBG, CBC, etc. –**The "Entourage Effect"**[2]

1. National Academies of Sciences, engineering, and medicine. Health effects of cannabis and cannabinoids (2017). 2. Russo, Ethan B. *British journal of pharmacology* 163.7 (2011): 1344-1364 3. Devinsky, Orrin, et al. *New England Journal of Medicine* 376.21 (2017): 2011-2020. 4. Masataka, Nobuo. *Frontiers in Psychology* 10 (2019): 2468.5. Mallaet, A. M., et al. *Proceedings of the National Academy of Sciences* 97.17 (2000): 9561-9566.

6

Slide 7

Endocannabinoid system

Some known functions of the endocannabinoid system:

- Functions: "Relax, eat, sleep, forget, protect"
- Memory
- Neurogenesis
- Analgesia
- Immune function
- Stress
- Appetite

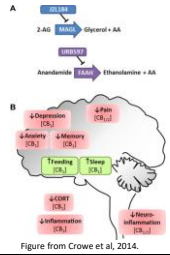

Figure from Crowe et al, 2014.

1. Rom S. Journal of Neuroimmune Pharmacology. 2013; 8(3): 608-620. 2. Hill et. al. PNAS 2010; 107(20) 9406-9411. 3. Crowe S et. al. Brain, Behavior, and Immunity, Volume 42, 2014, 1 - 5

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Slide 8

Bonini, Sara Anna, et al. "Cannabis sativa: A comprehensive ethnopharmacological review of a medicinal plant with a long history." Journal of ethnopharmacology 227 (2018): 300-315.

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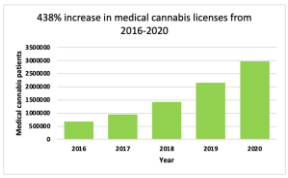
Slide 9

Slide 10

10

Slide 11



Data from Boehnke et al., 2022, *Annals of Internal Medicine*

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Slide 12

Figure 2. Most common patient-reported qualifying conditions 2016-2020

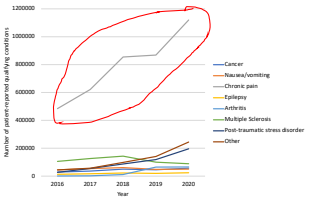


Figure 2. Chronic pain was the most common reason patient-reported qualifying condition, accounting for more licenses than all other conditions combined. Patients could report a qualifying condition or symptom. Significant contributors to the "Other" category include: vague categories such as "Chronic or debilitating disease or medical condition", "Psychiatric conditions", "multiple conditions", or "other" in state reports. The years for which each state contributed data are as follows:

From Boehnke et al., 2022, *Annals of Internal Medicine*. (In Press)

Slide 13

Cannabis clinical trials for chronic pain

Systematic Review and Meta-Analysis

PAIN

Cannabinoids, cannabis, and cannabis-based medicine for pain management: a systematic review of randomised controlled trials

Emma Fisher[a,b,*], R. Andrew Moore[c], Alexandra E. Fogarty[d], David P. Finn[e], Nanna B. Finnerup[f,g], Ian Gilron[h,i], Simon Haroutounian[h], Elliot Krane[j,m], Andrew S.C. Rice[k], Michael Rowbotham[l,n], Mark Wallace[o], Christopher Eccleston[a,b,*]

- Limited: short length, small sample size, generalizability
  - Many used THC alone or THC + CBD
- Most support in neuropathic pain (THC+CBD).
- Increased risk of short-term AEs (mostly minor) for study participants

Slide 14

Mechanistic Characterization of Pain

Variable degrees of any mechanism can contribute to any disease

	Nociceptive	Neuropathic	Nociplastic
Cause	Inflammation or damage	Nerve damage or entrapment	CNS or systemic problem
Clinical features	Pain is well localized, consistent effect of activity on pain	Follows distribution of peripheral nerves (i.e. dermatome or stocking/glove), episodic, lancinating, numbness, tingling	Pain is widespread and accompanied by fatigue, sleep, memory and/or mood difficulties as well as history of previous pain elsewhere in body
Screening tools		PainDETECT	Body map or FM Survey
Treatment	NSAIDs, injections, surgery, ? opioids	Local treatments aimed at nerve (surgery, injections, topical) or CNS-acting drugs	CNS-acting drugs, non-pharmacological therapies
Classic examples	Osteoarthritis Autoimmune disorders Cancer pain	Diabetic painful neuropathy Post-herpetic neuralgia Central Pain	Fibromyalgia Functional GI disorders Temporomandibular disorder Tension headache Interstitial cystitis, bladder pain syndrome

Mixed Pain States

Slide 15

Study drugs used in clinical trials

Slide 16

Medical cannabis and CBD products

Slide 17

Substitution of cannabis for medications

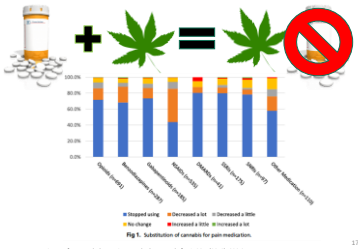


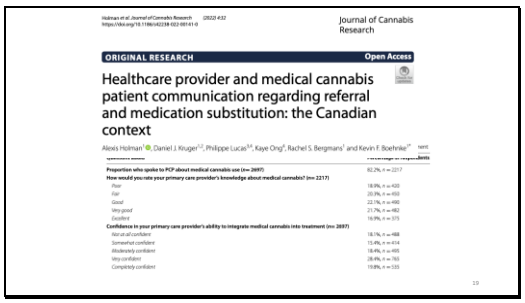
Figure 1 from: Boehnke, Kevin F., et al. *The Journal of Pain* 20.7 (2019): 830-841.

Slide 18

Communication Breakdown

- How do patients select cannabis products?
  - 2.6% via consultation with medical provider vs. 54.6% via consultation with budtender
- How do patients select CBD products?
  - 63.2% through personal research
  - 36.2% through advice from employee at place of purchase
  - 16.4% due to endorsement of medical professional

Slide 19



Holman et al. Journal of Cannabis Research (2022) 4:32
https://doi.org/10.1186/s42238-022-00141-0

Journal of Cannabis Research

ORIGINAL RESEARCH — Open Access

Healthcare provider and medical cannabis patient communication regarding referral and medication substitution: the Canadian context

Alexis Holman[1], Daniel J. Kruger[1,2], Philippe Lucas[3,4], Kaye Ong[5], Rachel S. Bergmans[1] and Kevin F. Boehnke[1,6*]

Proportion who spoke to PCP about medical cannabis use (n= 2697)	82.2%, n = 2217
How would you rate your primary care provider's knowledge about medical cannabis? (n= 2217)	
Poor	18.9%, n = 420
Fair	20.9%, n = 450
Good	22.1%, n = 490
Very good	21.7%, n = 482
Excellent	16.9%, n = 375
Confidence in your primary care provider's ability to integrate medical cannabis into treatment (n= 2697)	
Not at all confident	18.1%, n = 488
Somewhat confident	15.4%, n = 414
Moderately confident	18.4%, n = 495
Very confident	28.4%, n = 765
Completely confident	19.8%, n = 535

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Slide 20

FEATURE STORIES

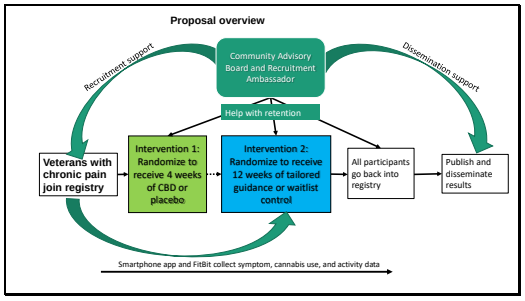
State of Michigan awards U-M researchers $7.4 million to study effect of CBD and medical cannabis therapy on Veterans' chronic pain

Share

Clarissa Piatek

September 9, 2022

Slide 21



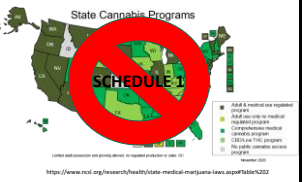
Slide 22

Why behavioral intervention?

- We have evidence on methods of ingestion, cannabinoid effects, and dosing
- No official clinical guidance on use for pain
- Goal to optimize use: reduce harm, maximize benefit

Impact

- Create scalable program that can be used by healthcare providers and budtenders



https://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx#Table%202

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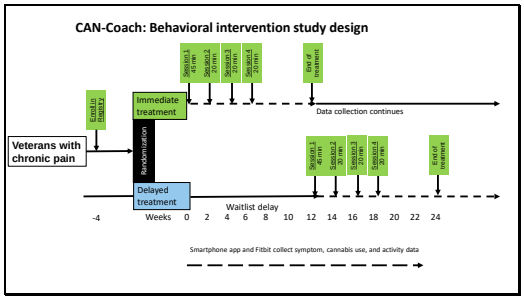

Slide 24

Summary and Practical Tips

- Medical cannabis clinical trials for pain are limited, but patients are using cannabis regardless.
- How to effectively communicate?
  - Develop a treatment plan with symptom tracking
  - "Start low, go slow"[1] – starting with CBD alone or high CBD products
  - Consider different administration routes
  - Build partnership – requiring flexible mentality
  - Share useful legal information (e.g., CBD products may cause positive drug test)
- THC?
  - Can add through Schedule III dronabinol, medical cannabis license, or adult use cannabis products

1. MacCallum, Caroline A., and Ethan B. Russo. "Practical considerations in medical cannabis administration and dosing." *European journal of internal medicine* (2018).2. Dahlgren, M. Kathryn, et al. *JAMA psychiatry* (2020).

Slide 25

Outline

- Cannabis and chronic pain
- **Parallels between cannabis and psychedelic landscape**
- Psychedelics for chronic pain

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Slide 26

Psychedelics

Mostly Schedule I drugs (Controlled Substances Act), excepting ketamine

"The potential significance of LSD and other psychedelics for psychiatry and psychology was comparable to the value the microscope has for biology or the telescope has for astronomy." – Stanislov Grof

Examples:

- Psilocybin (from magic mushrooms)
- Lysergic acid diethylamide (LSD)
- Ayahuasca (N,N-Dimethyltryptamine)
- MDMA (3,4-Methylenedioxymethamphetamine)
- Ketamine (also classified as dissociative anesthetic)

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Slide 27

JAMA Health Forum.

Viewpoint

Applying Lessons From Cannabis to the Psychedelic Highway
Buckle Up and Build Infrastructure

Parallels between cannabis and psychedelics:

- Growing availability with little or no oversight from clinical care
- Minimal physician education and training
- No systematic data collection on health outcomes
- Statutes that liberalize access do not mandate these changes

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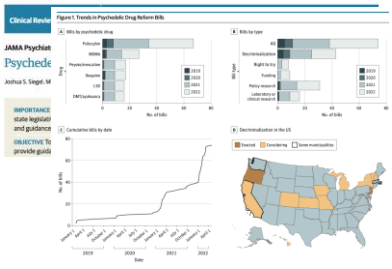

Slide 29

"An analytic model based on marijuana legalization projected that a majority of states will legalize psychedelics by 2034 to 2037."

Slide 30

- "Legislative reform for psychedelic drugs has been proceeding in a rapid, patchwork fashion in the US. Further consideration should be given to key health care issues such as establishing:
  (1) standards for drugs procured outside the medical establishment,
  (2) licensure criteria for prescribers and therapists
  (3) clinical and billing infrastructure
  (4) potential contraindications
  (5) use in special populations like youths, older adults, and pregnant individuals."

Slide 31

Table 2. Primary and Secondary Efficacy End Points (Modified Intention-to-Treat Population).*

End Point	Psilocybin, 25 mg (N = 79)	Psilocybin, 10 mg (N = 75)	Psilocybin, 1 mg (N = 79)
Primary efficacy end point			
Change from baseline to wk 3 in MADRS total score			
Least-squares mean	−12.0±1.3	−7.9±1.4	−5.4±1.4
95% CI of the least-squares mean	−14.6 to −9.3	−10.6 to −5.2	−8.1 to −2.7
Least-squares mean difference vs. 1 mg	−6.6±1.9	−2.5±1.9	—
95% CI of the least-squares mean difference	−10.2 to −2.9	−6.2 to 1.2	
P value vs. 1 mg	<0.001	0.18†	—
Secondary efficacy end points			
Response at wk 3‡			
No. of participants (%)	29 (37)	14 (19)	14 (18)
Odds ratio vs. 1 mg (95% CI)	2.9 (1.2 to 6.6)	1.2 (0.5 to 3.0)	—
Remission at wk 3§			
No. of participants (%)	23 (29)	7 (9)	6 (8)
Odds ratio vs. 1 mg (95% CI)	4.8 (1.8 to 12.8)	1.2 (0.4 to 3.9)	—
Sustained response at wk 12¶			
No. of participants (%)	16 (20)	4 (5)	8 (10)
Odds ratio vs. 1 mg (95% CI)	2.2 (0.9 to 5.4)	0.7 (0.2 to 2.0)	—

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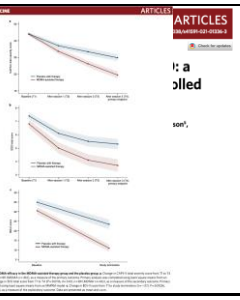
Slide 32



"At the primary study endpoint (18 weeks after baseline), 28 of 42 (67%) of the participants in the MDMA group no longer met the diagnostic criteria for PTSD, compared with 12 of 37 (32%) of those in the placebo group after three sessions. Additionally, 14 of 42 participants in the MDMA group (33%) and 2 of 37 participants in the placebo group (5%) met the criteria for remission after three sessions…"

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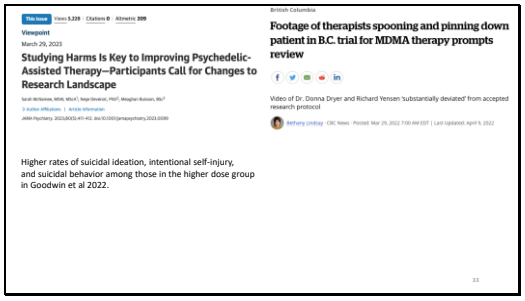
Slide 33



Viewpoint

March 29, 2023

Studying Harms Is Key to Improving Psychedelic-Assisted Therapy—Participants Call for Changes to Research Landscape

British Columbia

Footage of therapists spooning and pinning down patient in B.C. trial for MDMA therapy prompts review

Video of Dr. Donna Dryer and Richard Vensen 'substantially deviated' from accepted research protocol

Higher rates of suicidal ideation, intentional self-injury, and suicidal behavior among those in the higher dose group in Goodwin et al 2022.

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Entheofest survey

- Survey of naturalistic psychedelic use and knowledge conducted at Entheofest (Nick Glynos, Moss Herberholz, Chris Fields)

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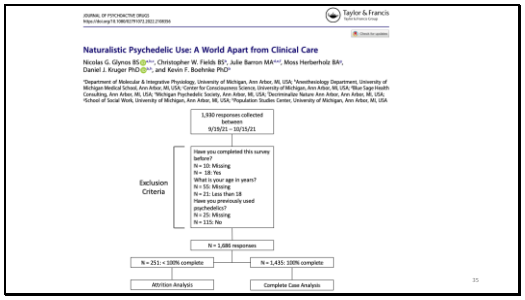

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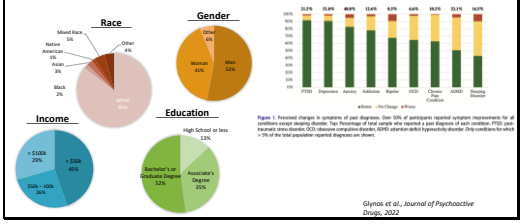
Demographics and Symptom Changes

1,435 complete responses



Glynos *et al., Journal of Psychoactive Drugs, 2022*

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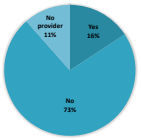
Primary Care Provider and Substance Testing

Have you ever discussed psychedelics with your primary healthcare provider?
(n = 1,435)



Why haven't you discussed psychedelics with your primary healthcare provider? (Participants could select all that apply)	N = 1040
Stigma	56.3%
I prefer to keep my psychedelic use private	40.9%
Legal concerns	37.5%
To avoid contradicting my healthcare providers advice	10.6%
I do not trust my primary healthcare provider	11.5%
My primary healthcare provider is not adequately knowledgeable about psychedelics	38.1%
I do not believe my primary healthcare provider would be able to integrate psychedelic use into my treatment	43.0%
Other	9.6%
How would you rate your primary healthcare provider's knowledge of psychedelics?	
Poor	20.5%
Fair	5.6%
Good	2.9%
Very good	2.1%
Excellent	0.5%
I Don't know	68.3%
Missing	0.2%

Glynos *et al., Journal of Psychoactive Drugs, 2022*

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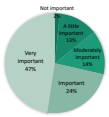
Therapeutic Support

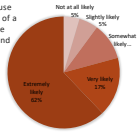
How do you most frequently use psychedelics?
(n = 1,435)

How do you most frequently use psychedelics? (Participants could select all that apply)	
Alone	41.7%
With a companion (spouse, partner, close friend, or family member) who is not using psychedelics	28.2%
With a companion who is under the influence of the same or similar substance	55.1%
With a therapist or health professional	4.4%
With a group of 2 or more companions	35.1%
With a group of strangers	4.7%
Microdosing during a normal day	26.3%
Other	4.3%
No preference	0.6%

How important was the presence of the healthcare professional to the success of your psychedelic experience?
(n = 63)



How likely is it that you would use psychedelics under the guidance of a trained therapist or healthcare professional if this were legal and available?
(n = 1,435)



Glynos *et al., Journal of Psychoactive Drugs, 2022*

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Summary

- Increasing availability
- Minimal integration into clinical care
- How to bridge this gap?

EClinicalMedicine

Research Paper

Psilocybin-assisted group therapy for demoralized older long-term AIDS survivor men: An open-label safety and feasibility pilot study

Brian T Anderson, Alicia Danforth, Prof Robert Daroff, Christopher Stauffer

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Outline

- Cannabis and chronic pain
- Parallels between cannabis and psychedelic landscape
- **Psychedelics for chronic pain**
  - **Mechanisms related to pain**
  - **Literature on psychedelics and chronic pain**
  - **Psilocybin-assisted therapy for FM**

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Mechanistic Characterization of Pain

Variable degrees of any mechanism can contribute to any disease

	Nociceptive	Neuropathic	Nociplastic
Cause	Inflammation or damage	Nerve damage or entrapment	CNS or systemic problem
Clinical features	Pain is well localized, consistent effect of activity on pain	Follows distribution of peripheral nerves (i.e. dermatome or stocking/glove), episodic, lancinating, numbness, tingling	Pain is widespread and accompanied by fatigue, sleep, memory and/or mood difficulties as well as history of previous pain elsewhere in body
Screening tools		PainDETECT	Body map or FM Survey
Treatment	NSAIDs, injections, surgery, ? opioids	Local treatments aimed at nerve (surgery, injections, topical) or CNS-acting drugs	CNS-acting drugs, non-pharmacological therapies
Classic examples	Osteoarthritis Autoimmune disorders Cancer pain	Diabetic painful neuropathy Post-herpetic neuralgia Sciatica, carpal tunnel syndrome	Fibromyalgia Functional GI disorders Temporomandibular disorder Tension headache Interstitial cystitis, bladder pain syndrome

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Psychedelic mechanisms relevant to pain

5-HT_{2a} agonism

Direct analgesic activity?

Changing brain network dynamics

Subjective effects (e.g., mystical experience)

→Leading to behavior change

Figure from: Petri, Giovanni, et al. *Journal of The Royal Society Interface* 11.101 (2014): 20140873.

Castellanos, Joel P., et al. *Regional Anesthesia & Pain Medicine* 45.7 (2020): 486-494.

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Clinical trials: Chronic pain and psychedelics

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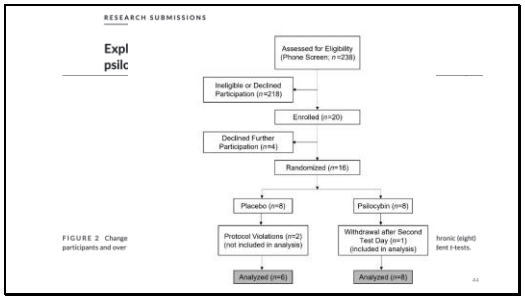

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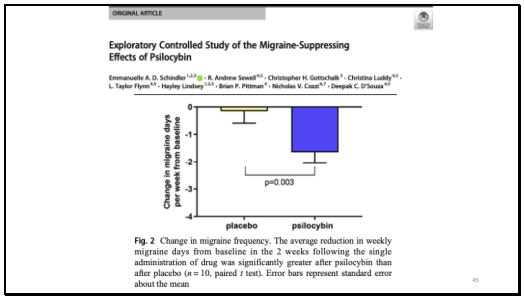

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Case reports and survey

- Cluster headache: Shortened attacks, and use during cluster period resulted in partial or complete cessation of attacks.[1,2]
- Phantom limb pain: 5/7 people with phantom limb pain who received LSD reported improved pain and decreased analgesic use[3]
- Decreased pain among people with high pain in a secondary analysis of MDMA-assisted therapy for PTSD

1. Sewell, R Andrew et al. 2006. *Neurology* 66 (12): 1920–1922.
2. Schindler, Emmanuelle A. D. et al. 2015. *Journal of Psychoactive Drugs* 47 (5): 372–381. 3. Fanciullacci, M. et al. 1977. *Headache: The Journal of Head and Face Pain* 17 (3). 4. Christie, Devon et al. 2022 Frontiers in Psychiatry. 13:939302.

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Clinical Note

PAIN®

Table 1

Summary of psilocybin use characteristics and perceived effects.

Patient	Age/Sex	Pain type	Dosing schedule	Result
DC	37 yo male	Spinal cord injury with neuropathic pain below the level of injury	Daily 250 mg ground mushroom powder for >6 mo	90%-95% relief of neuropathic pain 6-8 h and increased activation of paralyzed muscles resulting in improved mobility Additional beneficial effects on neurogenic bowel symptoms
ES	68 yo female	Complex regional pain syndrome	Daily 500 mg ground mushroom powder with occasional rest days 750 mg-1 g ground mushroom powder occasionally	80% pain relief for 3-4 h gradually returning to baseline after 12 h in absence of subjective psychotropic side effects and increased functional ability 90%-100% pain relief for 6-8 h returning to baseline after 18 h. Significant and partially debilitating side effects for first 2-4 h after ingestion, before the onset of analgesia
JP	40 yo female	Lumbar radiculopathy/neuropathic pain	1000 mg mushroom chocolate bar every 2 mo	Near complete resolution of pain without psychotropic effects, with subjective experience of improved flexibility and functional ability. Pain gradually returns to baseline over the course of 2-4 wk Repeated dosing resulted in improved pain control

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Original Manuscript

Analgesic potential of macrodoses and microdoses of classical psychedelics in chronic pai

Valerie Bonnelle
Pamela Kryskow

British Journal of Pain
2022, Vol. 0(0) 1–7
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DOI: 10.1177/20494637221114342

- 67.9% (microdoses) to 72.4% (macrodoses) reported reduction in pain
  - 5-3.14.1% reported increased pain
- Compared with microdosing, macrodosing associated with greater reductions in pain intensity and greater acceptance of pain

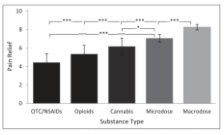

Figure 2. Comparison between perceived pain relief (0 = no pain relief, 10 = complete pain relief) achieved using microdosing and macrodosing, and the three most frequently reported conventional medications: over-the-counter (OTC)/NSAIDs, opioids and cannabis. Statistically significant differences between groups are denoted by ***(<0.001), **(<0.01) and *(<0.05). Error bars indicate standard error.

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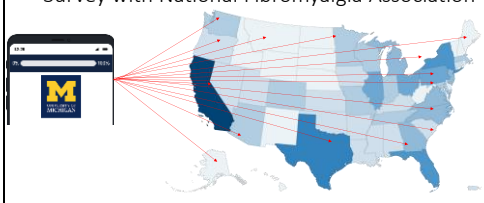
Survey with National Fibromyalgia Association



Glynos N. et al, 2022, Journal of Psychoactive Drugs

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610 started the survey

481 completed the survey

Exclusions:
- Did not have pain for ≥ 6 months or rate pain ≥4 (n = 27)
- Under 18 years old (n=1)
- Did not speak or read English (n=2)
- Geographical location not specified (n=18)
- Did not report previous FM diagnosis (n = 79)

N = 354 responses used for final analyses

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	Never Used (n = 248)	Have Used (n = 106)	t or X^2	p
Sex (Female)	94.8%	89.6%	3.1	0.08
Age: Mean (S.D.)	54.5 (12.9)	53.7 (12.2)	0.5	0.59
Income			5.7	0.06
Under $50,000	41.5%	53.8%		
$50,001 - 99,999	32.3%	27.4%		
$100,000 +	25.0%	16.0%		
Missing	1.2%	2.8%		
Education			1.0	0.81
High School Diploma, GED, or less	10.9%	14.2%		
Associate's Degree or some college	44.0%	42.5%		
Bachelor's Degree (BA, BS, AB, BBA)	26.6%	27.4%		
Master's, Professional or Doctoral degree	18.5%	16.0%		
Relationship Status			9.5	0.05
Married and living with spouse	59.7%	44.3%		
Living with partner	8.1%	15.1%		
Divorced or separated	16.1%	22.6%		
Widowed	5.6%	8.5%		
Single, never married	10.5%	9.4%		
FM Score: Mean (SD)	19.85 (5.75)	19.65 (5.62)	0.3	0.76
BPI Severity: Mean (SD)	6.14 (1.36)	5.98 (1.40)	1.1	0.29
BPI Interference: Mean (SD)	7.02 (1.83)	7.25 (1.63)	-1.1	0.27

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Self-reported changes in pain associated with psychedelic use

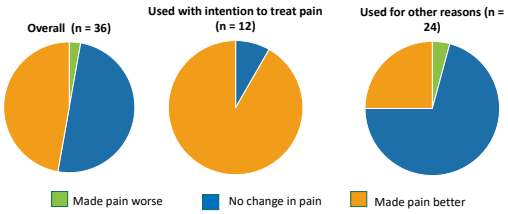

Figure 1. Only 34% (n=36) of the study population reported having chronic pain when they took psychedelics.

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Sex, Age	Duration of pain (years)	Substance Used	Please provide any additional information about why you believe the use of psychedelics improved or did not improve your chronic pain condition(s).
Participants who reported chronic pain symptom improvement following psychedelic use			
F, 53	10-20	LSD	"I was physically able to move around more and without pain"
F, 55	>30	LSD	"I experienced a profound feeling of being pain free and as if the 'weight' of my illness had been literally lifted. Did not realize the physical heavy feeling my body exists in every day. Felt actually lighter on my feet."
F, 22	1-3	LSD	"At half of a tab, I felt absolutely no pain for about 8 hours, and was no longer mentally weighed down by my pain … I have previously been prescribed NSAIDS and muscle relaxers which either helped slightly or made my pain worse in certain areas and better in others. LSD has been the only thing I have found that has covered everything from my entire body to my mental state."
F, 55	20-30	Ayahuasca	"It decreased my pain level significantly for about a year and allowed me to stop taking medication for pain. My pain has increased in the past few months, but it is still less than before the experience."
Participants who did not report chronic pain symptom improvement following psychedelic use			
F, 23	3-5	LSD	"I took a walk and all the pain still was in my body, I still had IBS cramps, I still needed to rest mid-trip in pain like I do everyday. I don't know, it helps me enjoy and have thoughts but it doesn't touch the pain"
M, 63	>30	Ketamine	"Although I found great insight, and it is a break from the pain, I feel my body is in bad shape. I believe that psychedelics can be helpful for moderate pain, I don't think that it is helpful for severe pain."
F, 47	>30	LSD	"Likely not a strong enough dosage taken"
F, 56	>30	LSD	"I did not have a good experience. I had a bad trip."

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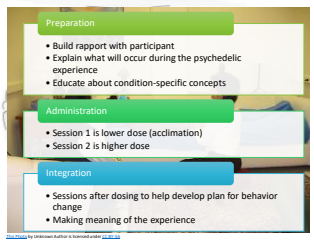
Clinical trial of psilocybin assisted-therapy for fibromyalgia



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Primary and secondary outcomes

Primary: Safety

- AEs
- Blood pressure and heart rate

Secondary: Preliminary efficacy

- Aggregate average worst pain from baseline (7 days prior to initiation of preparation therapy) to end of therapy
- Pain Interference
- Pain Acceptance
- Sleep disturbance
- Patient Global Impression of Change

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Practical tips for working with people using psychedelics for pain

- If possible, test substance for contaminants and purity
  - Vendors sell reagent test kits (e.g., DanceSafe) for synthetic psychedelics and fentanyl
- Be cognizant of mindset and setting going into the experience
- Have a trusted contact person or person to be with during and after the experience
- Special considerations:
  - Pregnancy, psychotic disorders, heart arrythmias
  - Current use of psychiatric medications (e.g., antidepressants, monoamine oxidase inhibitors), which may blunt effects

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Closing thoughts

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Final words

- "…every time a medicine is prescribed an n=1 experiment is being conducted. In some patients the experiment works and in others it fails..."
- Cannabis and psychedelics are no different!

Nutt D, Bazire S, Phillips LD, *et al* So near yet so far: why won't the UK prescribe medical cannabis? *BMJ Open* 2020;**10**:e038687. doi: 10.1136/bmjopen-2020-038687

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- Julie Barron
- Moss Herberholz

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Thank you for your kind attention

Questions?

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