ECHO IDAHO:
Behavioral Health in Primary Care

MDMA & PTSD

12/18/2024

Chris Stauffer, MD

Associate Professor of Psychiatry, Oregon Health & Science University

Chris Stauffer, speaker for this educational event, reported a financial relationship as an independent contractor with Lykos Therapeutics. All of the relevant financial relationships listed for these individuals have been mitigated.

MDMA-ASSISTED THERAPY FOR PTSD

CHRIS STAUFFER, MD

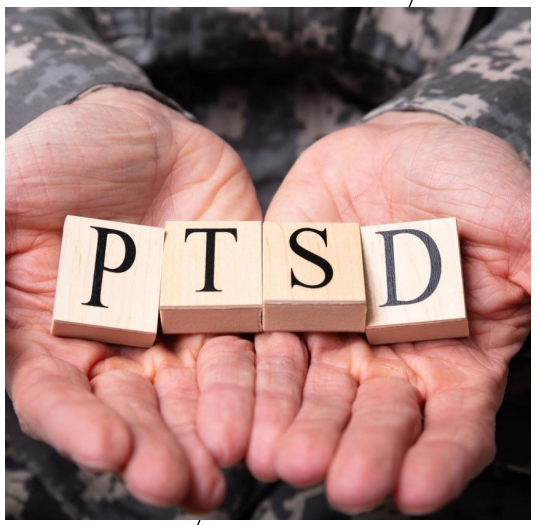
DISCLOSURE: Dr. Stauffer contracted to conduct MDMA-AT psychotherapy training for MAPS Public Benefit Corporation (now Lykos Therapeutics LLC) 5/2021-10/2023.

DISCLAIMERS:

- MDMA is currently a Schedule I substance and has not been approved by the FDA for any clinical use.
- Legal administration of MDMA is restricted to regulated research settings in the U.S.

PTSD

- Most people experience a traumatic event in their lifetime.
- Most people will *not* develop PTSD.
- About 6% of the U.S. population will have PTSD at some point in their lives.
- About 29% of U.S. Military Veterans serving in Iraq or Afghanistan will have PTSD at some point in their lives.



National Center for PTSD. www.ptsd.va.gov. Accessed 11-DEC-2024

WHAT IS PTSD?

Posttraumatic stress disorder, or PTSD, is a mental health concern that some people develop after they see or experience a traumatic event.

What it's like to have PTSD may be different for everyone. There are four types of PTSD symptoms.

Reliving or re-experiencing the event

- Nightmares
- Flashbacks
- Triggers

Avoidance

- Avoiding Crowds
- Avoiding certain smells, sights, or sounds
- Avoiding talking or thinking about the event

Hyperarousal or being on guard

- Being jittery or overly alert
- Difficulty sleeping or concentrating
- Feeling angry or irritable

Negative changes in beliefs and feelings

- Losing interest in things you used to enjoy
- Feeling guilty or ashamed
- Unable to trust others

TREATMENT OF PTSD: PSYCHOTHERAPY

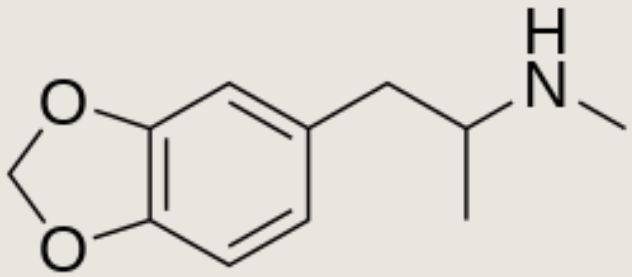
We recommend the following individual, manualized trauma-focused psychotherapies for the treatment of PTSD: Cognitive Processing Therapy (CPT), Prolonged Exposure (PE), or Eye Movement Desensitization and Reprocessing (EMDR).

- Cognitive Processing Therapy (CPT): CPT teaches you how to change the upsetting thoughts and feelings you have had since your trauma.
- Prolonged Exposure (PE): PE teaches you to gradually approach trauma-related memories, feelings, and situations you have been avoiding since your trauma.
- Eye Movement Desensitization and Reprocessing (EMDR): EMDR helps you process and make sense of your trauma while paying attention to a back-and-forth movement or sound (such as a light or tone).

TREATMENT OF PTSD: MEDICATIONS

We recommend **paroxetine**, **sertraline**, and **venlafaxine** for the treatment of PTSD.

- Paroxetine
- Sertraline
- Venlafaxine

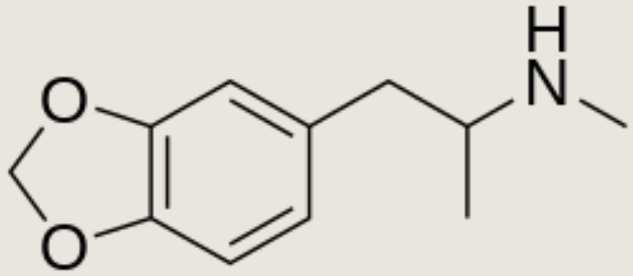


MDMA

- Ring-substituted phenethylamine
- Empathogen-Entactogen
- Monoamine-releasing agent: 5HT>>>>>>NE>>DA
- Downstream release: oxytocin, cortisol
- Duration of Acute Effects: 3-6 hours
- 80% liver metabolism: CYP2D6, CYP3A4, COMT

PHARMACOLOGY

MDMA



1912 — Merck first synthesizes and MDMA

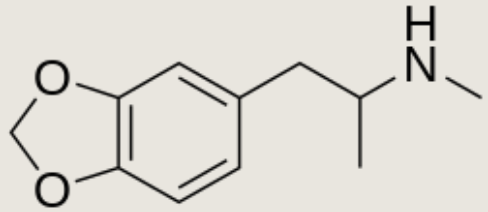
1970's — First legal use as an adjunct to psychotherapy (and first used recreationally)

1985 — MDMA becomes a Schedule I substance

1986 — Multidisciplinary Association for Psychedelic Studies (MAPS) is founded

HISTORY

MDMA-ASSISTED THERAPY FOR PTSD



1986 — Multidisciplinary Association for Psychedelic Studies (MAPS) is founded

2004 — First Phase 2 clinical trial of MDMA-AT for PTSD

2017 — FDA grants ‘Breakthrough Therapy’ status & Special Protocol Assessment based on 6 Phase 2 studies

2022 — Completion of two Phase 3 clinical trials

HISTORY

MAPS
MULTIDISCIPLINARY ASSOCIATION FOR PSYCHEDELIC STUDIES

A Manual for MDMA-Assisted Psychotherapy in the Treatment of Posttraumatic Stress Disorder

Michael C. Mithoefer, M.D.

PREVIOUS VERSIONS	Version 1: 30 May 2005 Version 2: 24 November 2008 Version 3: 23 October 2010 Version 4: 16 January 2011 Version 5: 30 November 2011 Version 6: 04 January 2013 Version 7: 31 March 2015
CURRENT VERSION	**Version 8.1: 22 August 2017**
SPONSOR	Multidisciplinary Association for Psychedelic Studies 1115 Mission Street Santa Cruz, CA 95060
SPONSOR DESIGNEE	Amy Emerson Executive Director MAPS Public Benefit Corporation
USE OF MANUAL	In accordance with an approved MAPS-sponsored Stu Interested parties wishing to copy any portion of this are encouraged to do so but are kindly requested to c and include our address: MAPS 1115 Mission Street Santa Cruz, CA 95060 Phone: 831-429-6362 Web: www.maps.org
CONTRIBUTORS	Annie Mithoefer, B.S.N., Lisa Jerome, Ph.D., June Ruse, Psy.D., Rick Doblin, Ph.D., Elizabeth Gibson, M.S., Marcela Ot'alora G., L.P.C., Evan Sola, Psy.D. candidate

https://maps.org/mdma/mdma-resources/treatment-manual-mdma-assisted-psychotherapy-for-ptsd/

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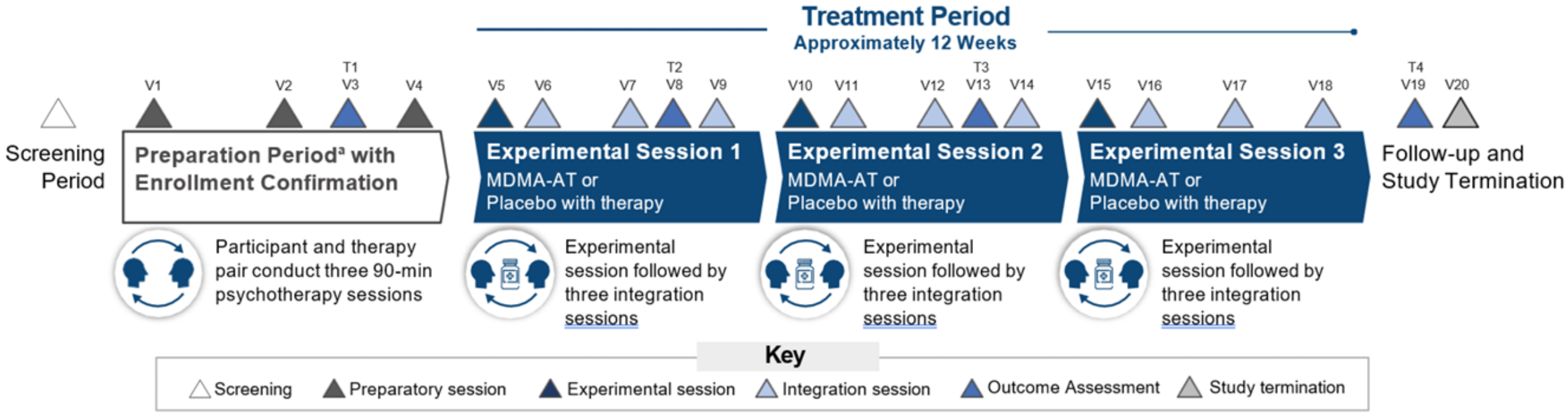
MDMA-ASSISTED THERAPY FOR PTSD

- ↓amygdala & ↑prefrontal
- ↑therapeutic “window of tolerance”
- ↑ fear extinction & memory reconsolidation
- Enhanced therapeutic alliance
- Increased openness
- We don’t exactly know the whole picture

THERAPEUTIC MECHANISMS

PHASE 3: MDMA(vs placebo)-Assisted Therapy for PTSD



MDMA-AT has not been approved by any regulatory agency. The safety and efficacy of MDMA-AT have not been established for the treatment of PTSD.

Mitchell, J. M., Ot'alora G, M., van der Kolk, B., Shannon, S., Bogenschutz, M., Gelfand, Y., ... & Yazar-Klosinski, B. (2023). MDMA-assisted therapy for moderate to severe PTSD: a randomized, placebo-controlled phase 3 trial. *Nature Medicine*, *29*(10), 2473-2480.

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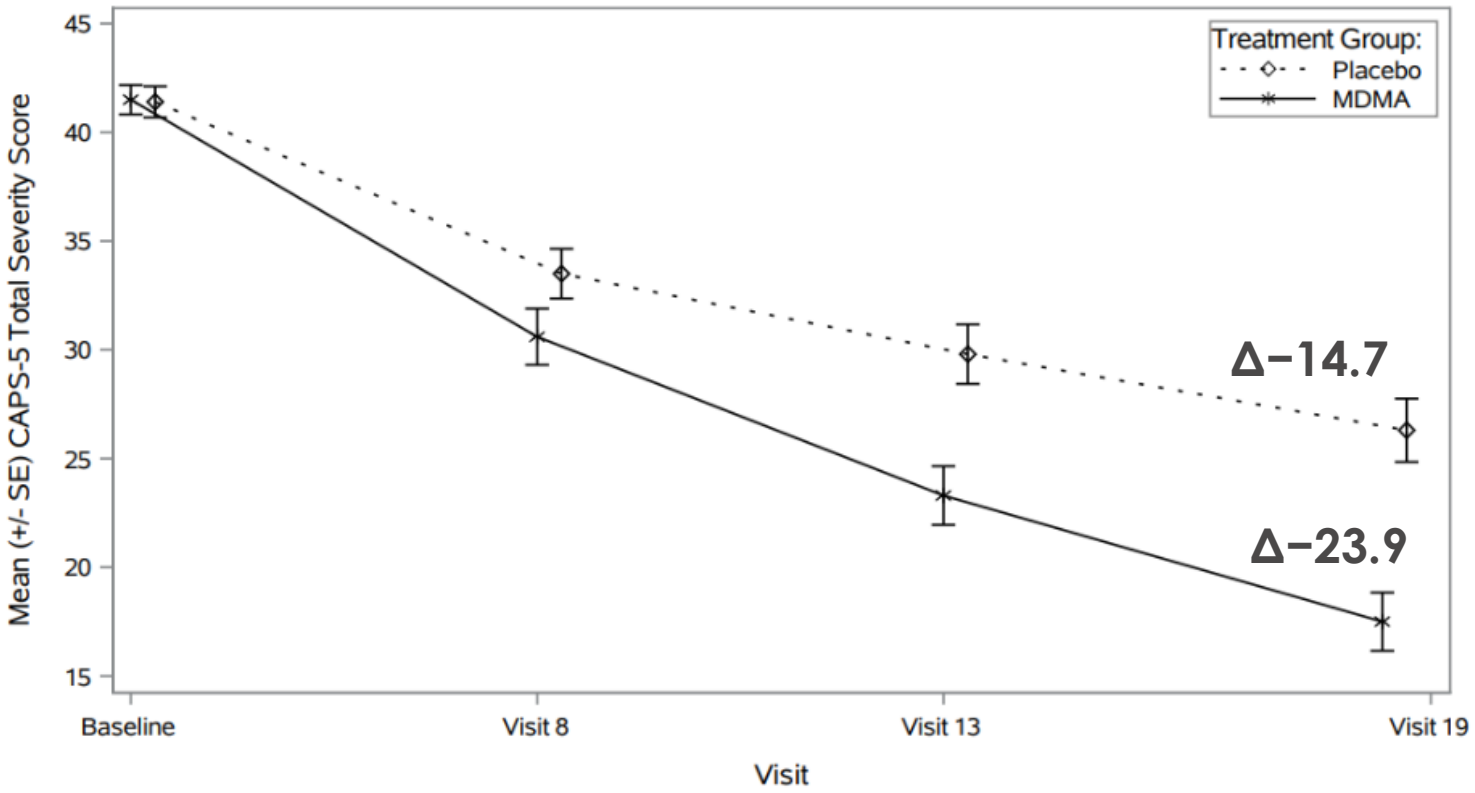
POOLED PHASE 3 MDMA-AT FOR PTSD

Change in PTSD Severity (CAPS-5) After Each Experimental Dosing Session



- **Clinically significant improvement** (↓ ≥10 points)
  - MDMA: 82/94 (87%)
  - Placebo: 52/79 (66%)
- **Loss of PTSD diagnosis** (based on CAPS-5)
  - MDMA: 65/94 (69%)
  - Placebo: 32/79 (41%)
- **Remission** (Loss of PTSD diagnosis and CAPS-5 score ≤11)
  - MDMA: 38/94 (40%)
  - Placebo: 11/79 (14%)

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FEDERAL INVOLVEMENT IN MDMA-AT DEVELOPMENT

- **2021** – First philanthropically-funded pilot studies within VA
- **SEP 2023** – VA State of the Art (SOTA) Psychedelic Workgroup
- **DEC 2023** – **New Drug Application (NDA) submitted to the FDA**
- **JAN 2024** – VA funding announcement for MDMA-AT clinical trials
  – Approval of VA psychedelic Integrated Project Team
- **AUG 2024** – **FDA rejects MDMA-AT application; requires another Phase 3 study**
- **SEPT 2024** – DoD funding announcement for MDMA-AT clinical trials
- **OCT 2024** – National Center for PTSD starts MDMA-PE for PTSD RCT
- **DEC 2024** – VA funds first MDMA-AT trial (for PTSD/AUD)

PHASE 3: MDMA(vs placebo)-Assisted Therapy for PTSD

	MDMA-AT (*n*=53)	Placebo with therapy (*n*=51)
Summary of TEAEs and TEAESIs, *n* (%)		
Participants with ≥1 TEAE	53 (100)	49 (96.1)
Participants with ≥1 severe TEAE	5 (9.4)	2 (3.9)
Participants with ≥1 serious TEAE	0	0
Participants with ≥1 TEAE leading to study discontinuation	0	2 (3.9)
Participants with ≥1 TEAESI	6 (11.3)	3 (5.9)
Most common[a] TEAEs, *n* (%)		
Muscle tightness	31 (58.5)	13 (25.5)
Nausea	24 (45.3)	11 (21.6)
Decreased appetite	19 (35.8)	5 (9.8)
Hyperhidrosis	18 (34.0)	3 (5.9)
Feeling hot	14 (26.4)	6 (11.8)
Feeling cold	11 (20.8)	3 (5.9)
Paresthesia	10 (18.9)	1 (2.0)
Chest discomfort	9 (17.0)	2 (3.9)
Dry mouth	9 (17.0)	4 (7.8)
Chills	8 (15.1)	1 (2.0)
Feeling jittery	8 (15.1)	0
Restlessness	8 (15.1)	2 (3.9)
Vision blurred	8 (15.1)	0
Bruxism	7 (13.2)	1 (2.0)
Nystagmus	7 (13.2)	1 (2.0)
Mydriasis	6 (11.3)	0
Tremor	6 (11.3)	0

[a]The most common TEAEs occurring with incidence >10% and at least twice the prevalence in the MDMA-AT group versus the placebo with therapy group.

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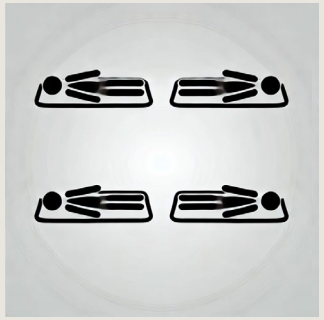
EARLY MDMA-ASSISTED GROUP THERAPY

(1970s – 1985)

GROUP MDMA SESSIONS

1. PARALLEL INDIVIDUAL

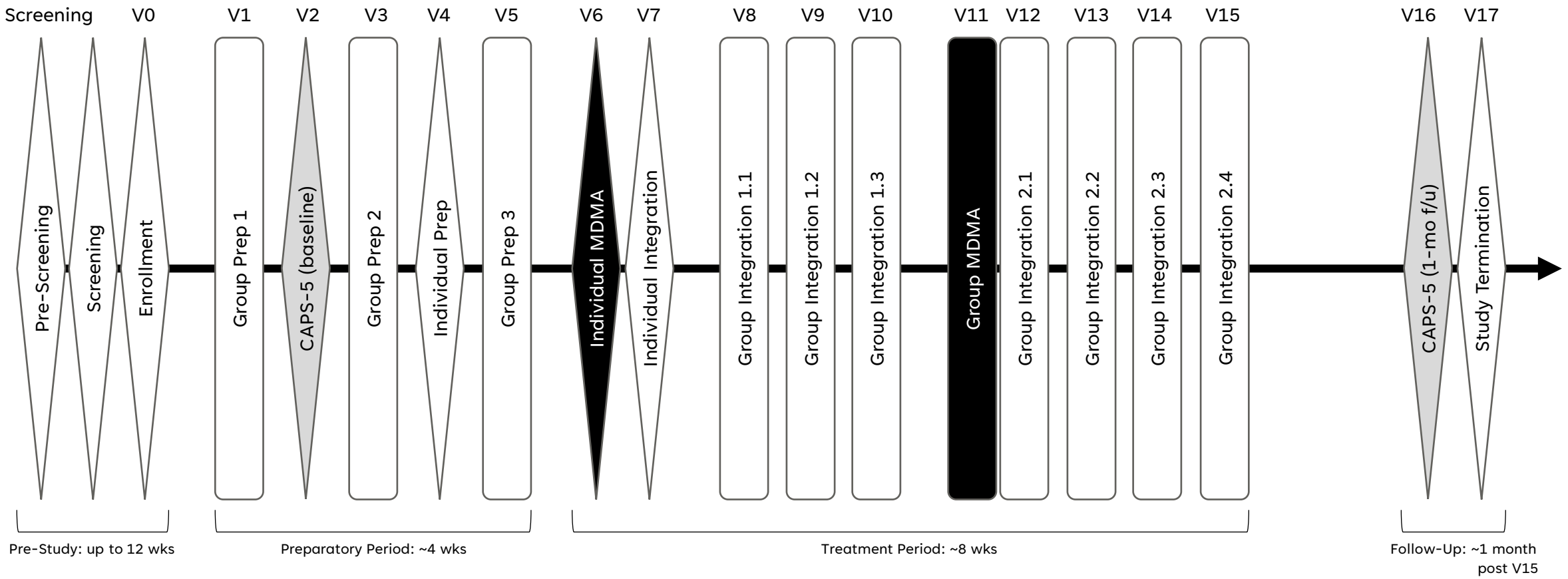


2. GROUP INTERACTION

A. Structured interaction

B. Unstructured interaction (typically groups with prior/ongoing relationships)

MDMA-ASSISTED GROUP THERAPY STUDY PROTOCOL



VA/DoD Clinical Practice Guideline for Management of Posttraumatic Stress Disorder and Acute Stress Disorder

Recommendation

12. There is insufficient evidence to recommend for or against any specific manualized group therapy for the treatment of PTSD.
(Neither for nor against | Reviewed, New-replaced)

13. There is insufficient evidence to recommend using group therapy as an adjunct for the primary treatment of PTSD.
(Neither for nor against | Reviewed, New-replaced)

Portland VA MDMA-Assisted Group Therapy Protocol

- Lykos MDMA-AT manual for all individual sessions & group MDMA session (parallel individual)
  - Includes trauma processing, if indicated
  - Additional individual integration session(s), if indicated (39% of participants)

- Psychoeducation + Present-Centered Group Therapy for group prep and integration

STUDY THERAPISTS

Rebecca Morris

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Stephanie Rodriguez

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Alissa Bazinet

Emma Knighton

Alyssa Gursky

Gina Gratza

PARTICIPANTS

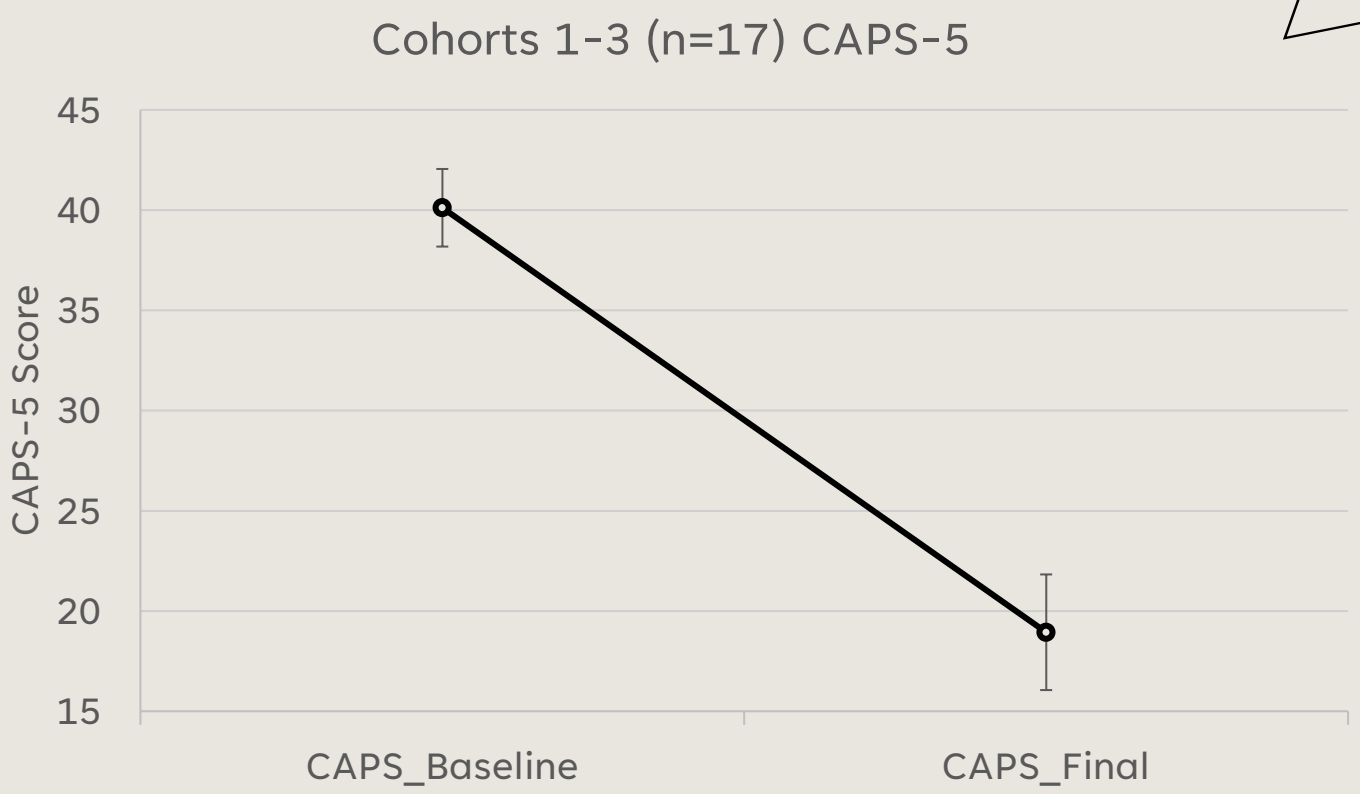
- U.S. Military Veterans (18-65yo)
- PTSD diagnosis in chart & 30-day PCL-5 ≥33
- Identify a trusted support person
- Stable living situation
- No medical contraindications
- No psychotic disorders or bipolar I
- No suicidal ideation likely to require hospitalization
- No severe alcohol or cannabis use disorder
- No illicit substance use disorder
- Unable to taper psychiatric meds

	Mean (SD)
Age (years)	42.3 (9.8)
	***n* (%)**
Sample Size	23 (100)
Gender	
Man	12 (52.2)
Nonbinary	2 (8.7)
Trans Man	1 (4.3)
Trans Woman	3 (13.0)
Woman	5 (21.7)
2SLGBTQIA+	10 (43.5)
Race	
American Indian	1 (4.3)
Asian	2 (8.7)
Black	1 (4.3)
Mixed	2 (8.7)
White	17 (73.9)
Hispanic Ethnicity	6 (26.1)
Trauma Exposure	
Combat	18 (78.3)
Military Sexual Trauma	8 (34.8)

OUTCOMES

- PTSD (CAPS-5 & PCL-5)
- Disability (SDS)
- Depression (BDI-II)
- Posttraumatic growth (PTGI)
- Attachment insecurity (ECR-S)
- Group Cohesion (GQ)
- Treatment expectancy (SETS)
- Perceptions of touch (TOMI)
- Epistemic Trust (ETMCQ)
- Synchrony (PES)
- Spiritual Transcendence (STS)
- Emotion Regulation (ERQ)
- Inflammatory markers

PRIMARY CLINICAL OUTCOME



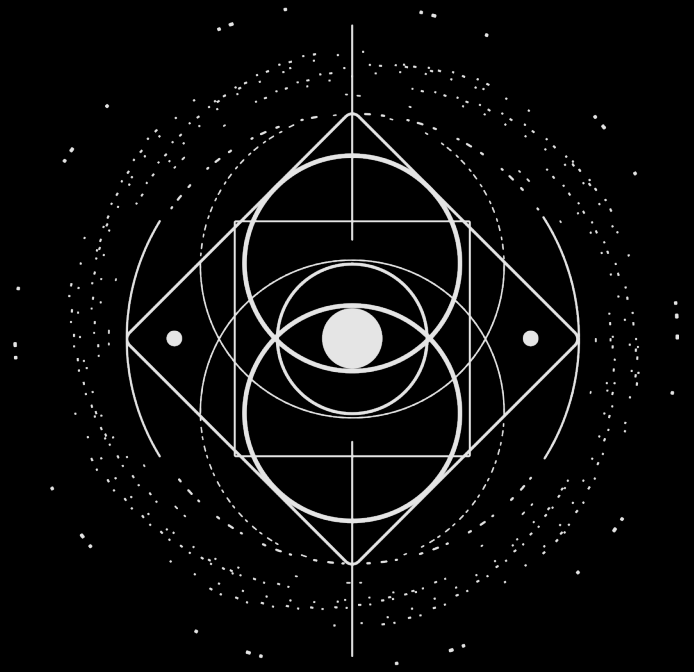
- **Clinically significant improvement** (↓ ≥10 points)
  - **13/17 (76.5%)**
- **Loss of PTSD diagnosis** (based on CAPS-5)
  - **12/17 (70.6%)**
- **Remission** (Loss of PTSD diagnosis and CAPS-5 score ≤11)
  - **3/17 (17.6%)**

COST EFFECTIVENESS

	Individual therapy		Group model		Difference (savings from grp = negative numbers)	
Clinician type	Clinician - hours	Dollars	Clinician-hours	Dollars	Clinician-hours	Dollars
Supervising therapist	2.0	$284	1.0	$138	(1.0)	($147)
Primary therapist (psychologist)	34.0	$2,291	16.4	$1,106	(17.6)	($1,185)
Adjunct therapist (NP)	17.0	$1,382	8.2	$667	(8.8)	($715)
Adjunct therapist (Vet. peer specialist)	17.0	$404	8.2	$195	(8.8)	($209)
	70.0	**$4,362**	**33.8**	**$2,106**	**(36.2)**	**($2,256)**
				Reduction of clinician time	**51.7%**	
				Percent savings of clinician cost	**51.7%**	
				Reduction of overall variable costs	**19.5%**	

- Marseille E, Stauffer CS, Agrawal M, Thambi P, Roddy K, Mithoefer M, Bertozzi SM, Kahn JG. (2023). Group psychedelic therapy: empirical estimates of cost-savings and improved access. Frontiers in Psychiatry. Volume 14. https://doi.org/10.3389/fpsyt.2023.1293243.

THANK YOU!



SNaPLAB

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