PTSD Pharmacotherapy- Review of Current Standards and Emerging Therapies

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Pharmacy Forward: Advancing Practice for a Healthier Tomorrow!

OPA Annual Conference & Trade Show April 9-11, 2026

OHIO PHARMACISTS ASSOCIATION

Disclosure Statement

- Chloe Matecki has no relevant financial relationship(s) with ineligible companies to disclose.
  and
- None of the planners for this activity have relevant financial relationships with ineligible companies to disclose.

Disclosure Statement

- This presentation WILL discuss off-label uses of medications and some emerging therapies

Learning Objectives

At the completion of this activity, the participant will be able to:

1. Identify symptomatic targets for the treatment of PTSD
2. Compare current pharmacologic treatment options and recommendations, including mainline therapies and augmentation agents
3. Discuss potential non-traditional agents for PTSD, including ketamine and psychedelics

Meet Patient CW

- CW is a 28-year-old female presenting to your clinic today. She initially reported she was having trouble sleeping, but on further discussion with her provider, she reports it is due to nightmares that wake her up, heart racing and sweating. She discloses that her best friend and roommate died by suicide and she found him the next morning. This occurred 3 months ago, and she has had nightmares and flashbacks since, avoiding talking about the event, and finding herself lashing out at other friends. She feels immense guilt that she did not “see the signs” and blames herself.

BACKGROUND

Epidemiology

- 3.9% of the world has/had had PTSD
- 6-7% of American adults will meet criteria in their lifetime
- Highest incidence following violent conflict and sexual violence
- More common in women
- Stigma may impact reporting figures

Risk Factors

Pre-Traumatic	Peritraumatic	Post-Traumatic
• Past psychiatric disorder • History of SUD • Lower socioeconomic status • Minority status • Low educational level • Childhood trauma • Previous trauma • Female sex • Occupational risk	• More severe trauma • Perceived threat to life • Response during trauma	• Perceived lack of social support • Dysfunctional patterns of social interaction • Other life stressors

Clinical Course

Symptom Onset

- Typically within 3 months
- Up to 25% can be delayed onset (>6 months)

Peak Symptomology

- Distress peaks in days/weeks following trauma
- Gradually declines in year following

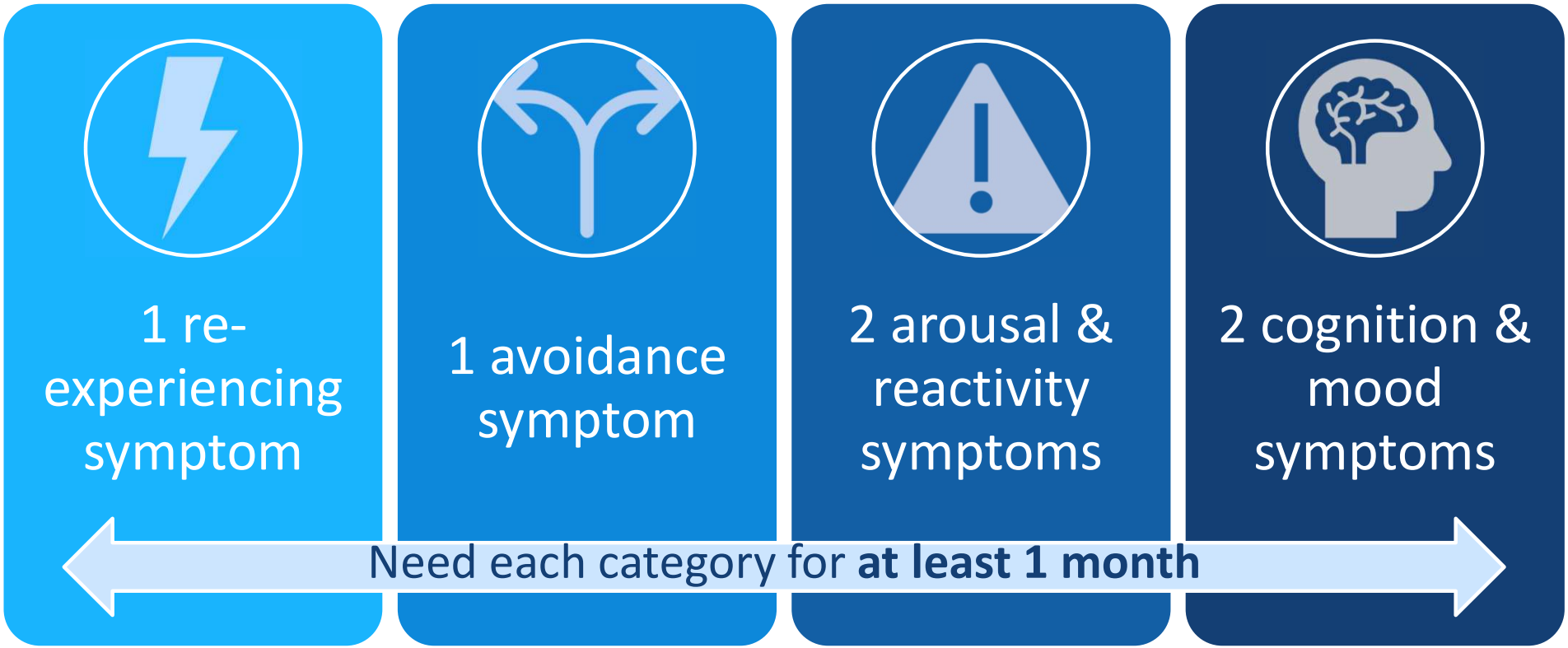
Duration

- With treatment: ~36 months
- Without treatment: ~5 years

Diagnosis

- Requires exposure to actual or threatened death, serious injury, or sexual violence in one or more of the following ways:
  - Direct experience of the event
  - Witnessing **in person** the event as it occurred to others
  - Learning the event happened to a close family member or friend
  - Experiencing repeated or extreme exposure to aversive details of traumatic events
- Symptoms cause psychological, social, or functional impairment

Diagnosis


1 re-experiencing symptom
1 avoidance symptom
2 arousal & reactivity symptoms
2 cognition & mood symptoms
Need each category for **at least 1 month**

Symptom Clusters

Re-Experiencing	Avoidance	Arousal & Reactivity	Cognition & Mood
• Flashbacks, including physical symptoms • Recurring memories or dreams • Distressing thoughts • Physical signs of stress	• Staying away from places, events, or objects that are reminders • Avoiding thoughts or feelings related to the event	• Easily startling • Feeling tense, on guard • Difficulty concentrating • Difficulty sleeping • Feeling irritable • Engaging in risky or destructive behavior	• Poor memory of the event • Negative thoughts of self or world • Exaggerated feelings of blame • Ongoing fear, anger, guilt, or shame • Loss of interest • Social isolation • Difficulty feeling positive emotions

Back to CW

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Assessment Question #1

What is true about CW's presentation at clinic?

A. CW does meet diagnostic criteria for PTSD as her symptoms have been for 3 months
B. CW does not meet diagnostic criteria for PTSD as she has only had symptoms for 3 months
C. CW does not meet diagnostic criteria for PTSD as she only has re-experiencing symptoms
D. CW does meet diagnostic criteria for PTSD as she has nightmares

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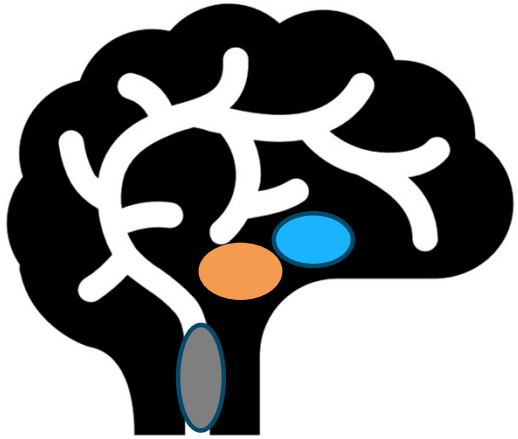
PATHOPHYSIOLOGY

Brain Circuits in Fear

- The amygdala is responsible for sensory information integration → fear memory
- Connection to the hippocampus to the periaqueductal gray (PAG) in the brainstem generates defensive behaviors
  - Freeze, flight, fawn, fight



GABA and Glutamate

GABA

- GABAergic system shown to be dysfunctional in PTSD (↓ levels and receptors in brain)
- GABAergic process in amygdala → reduces fear response, reduction of anxiety
- Loss of tone → heightened anxiety

Glutamate

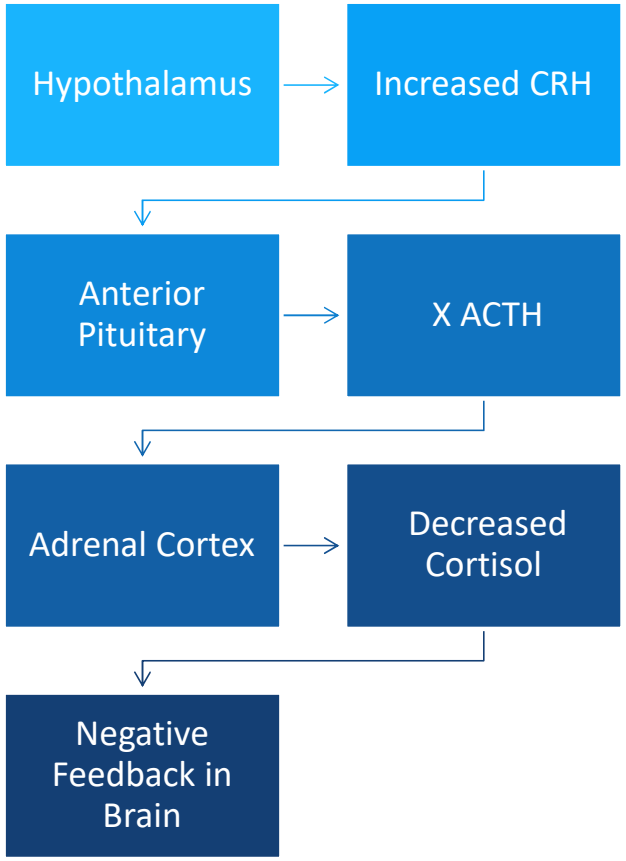
- Facilitates communication from amygdala
- Drives immediate fear responses and sustained anxiety

Serotonin, Norepinephrine, & Dopamine

Serotonin	Norepinephrine	Dopamine
• Modulates amygdala & hippocampal systems • Modulation assists with mood symptoms	• Key to arousal in fear and anxiety • Increases sensory sensitivity and vigilance • Facilitates fear memory formation	• Involved with fear extinction and aversive learning • Input may promote avoidance & aversive behavior

Physiological Response in PTSD

- Complex interplay of the HPA Axis
  - Dysregulation → inability to cope with stress
  - Cortisol
    - Ambient levels = lower – "Chronic Exhaustion"



SNS and Adrenergic Receptors

Sympathetic Nervous System

- Disassociated from the HPA axis
- Uncontrolled catecholamine release
- Abnormal increase in SNS reactivity

α1- and α2-Adrenergic Receptors

- α1- receptors → startle & sleep
- α1-receptor stimulation disturbs REM
- Excessive α activation in PTSD

Assessment Question #2

Which of the following pathways would be most specific to target for her sleep disturbances?

A. Dopamine
B. Cortisol
C. Norepinephrine
D. α1-Receptors

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A. Dopamine

B. Cortisol

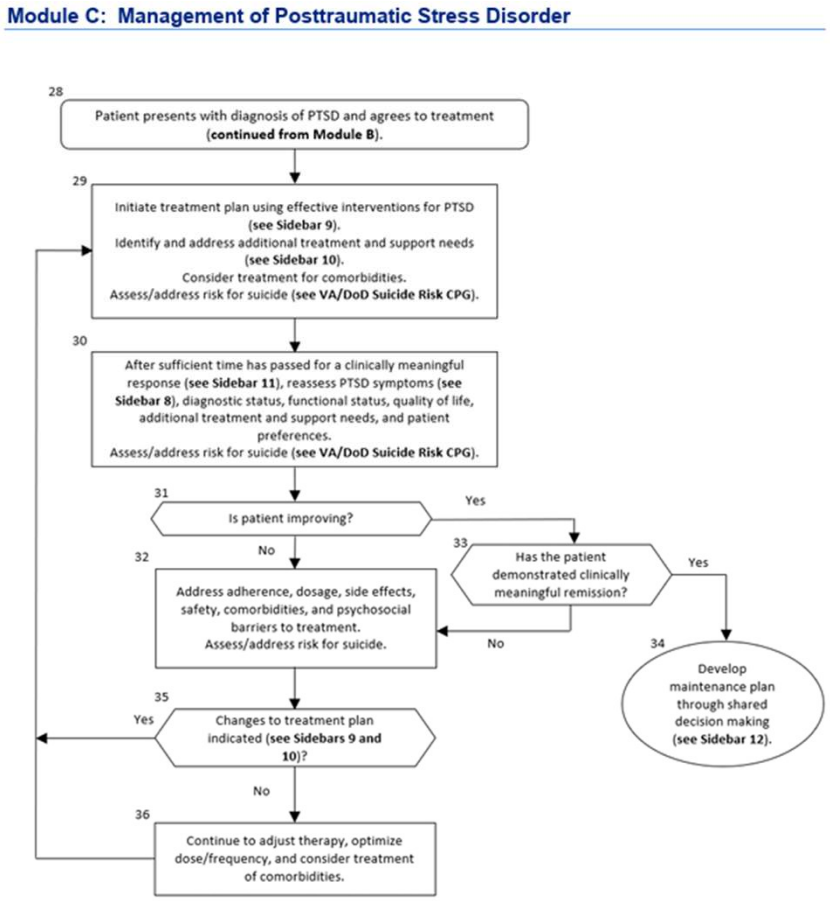
C. Norepinephrine

D. α1-Receptors

CURRENT TREATMENT

Treatment Guidelines

- VA DOD 2023
  - Most recent guideline
  - Extensive within one of the most prevalent groups with PTSD
  - Does not touch on experimental therapies



Abbreviations: CPG: clinical practice guideline; PTSD: Posttraumatic stress disorder; VA: Veteran Affairs; DoD: Department of Defense.

Non-Pharmacologic Treatment

- Eye Movement Desensitization and Reprocessing (EMDR) Therapy
- Cognitive Processing or Behavioral Therapy (CPT, CBT)
- Prolonged Exposure

Pharmacologic Treatment

SSRIs	SNRIs	TCAs
Mirtazapine	SGAs*	ASM*

*Nuance required

Antidepressant Options

SSRIs

- Paroxetine, sertraline → FDA approved
- Fluoxetine
- Overall symptom improvement

SNRIs

- Venlafaxine XR
- Overall symptom improvement
- Potentially less so for hyperarousal/vigilance

Other Antidepressants

TCAs

- Imipramine
- Amitriptyline
- Not FDA approved
- Overall symptom improvement
- Toxicity Risk

Mirtazapine

- Weak evidence alone
- Augment for sleep
- Reduction in anxiety

Phenelzine

- High efficacy for PTSD
- Side effects and DDI interfere with regular use

Second Generation Antipsychotics

- Fall most commonly in 2nd- or 3rd- line if at all
  - VA DOD has split between “insufficient evidence” and “suggest against” for different agents in the class
- Recommend AGAINST routine usage
  - Limited use benefit
  - Risperidone and olanzapine have “most” evidence for
  - Supplemental/augmentation only

Antiseizure Medications

- Adjunctive if at all
- Mind side effect profiles
- Divalproex sodium, carbamazepine, gabapentin, and topiramate have most evidence
  - Topiramate in AUD
  - VA DOD recommends against divalproex sodium

Recommend AGAINST Use

Benzodiazepines

- Notable for “causes harm” distinction
- High risk for addiction and withdrawal
- Found to increase risk for development & worsen active symptoms
- Depersonalization, memory impairment, depression

Cannabis or Cannabis Derivatives

- May cause worsening of symptoms
- Use may increase risk of development

Maintenance Medication Table

Medication	FDA Approved?	Role	Dosing	Pearls
Fluoxetine	No	Monotherapy	20-60 mg daily	Long half life
Paroxetine	Yes	Monotherapy	20 mg daily	Anticholinergic ADR
Sertraline	Yes	Monotherapy	100-200 mg daily	Good safety profile
Venlafaxine	Yes	Monotherapy	75-300 mg daily	Withdrawal issues, HTN
Amitriptyline	No	Monotherapy	50-250 mg daily	Anticholinergic ADR
Imipramine	No	Monotherapy	25-250 mg daily	Anticholinergic ADR
Mirtazapine	No	Adjunctive	15-30 mg HS	Helpful for sleep
Phenelzine	No	Monotherapy	45-75 mg/day	Drug interactions
Quetiapine	No	Adjunctive	100-300 mg HS	Mixed data, sedation
Risperidone	No	Adjunctive	2-4 mg HS	Mixed data, metabolic
Topiramate	No	Adjunctive	100-300 mg/day	Useful in AUD

Nightmares

α-Blockers

Clonidine

Antipsychotics

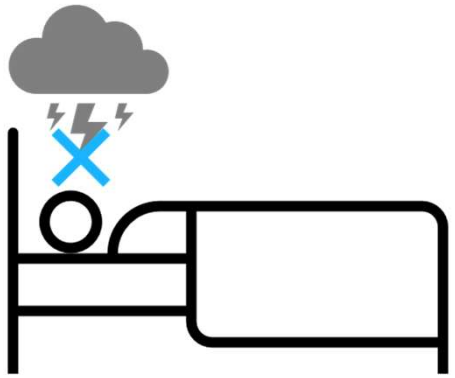
Gabapentin

Trazodone

Cyproheptadine

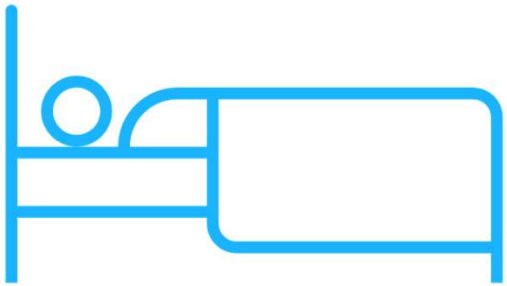
α1-Blockers

- Blocks sympathetic activity in the brain
  - Interrupts the reconsolidation of fear memories
  - Reduction in number and response when waking
- Prazosin most common, doxazosin for treatment failure
  - Prazosin indicated in VA DOD



α2-Blockers

- Clonidine is primary agent
  - Less data than α1-blockers for nightmares
  - Thought to suppress REM sleep & attenuate NE outflow
- Also used for sleep promotion



Antipsychotics

- Similar controversy as in general treatment
- ADR > Benefit
- Follow similar recommendation pattern:
  - Risperidone
  - Olanzapine, quetiapine
    - All adjunctive

Gabapentin

- Ineffective as monotherapy
- Helps with sleep duration & nightmare reduction
  - Evidence limited
  - Can use in cases of additional anxiety, comorbid pain

Trazodone

- Commonly used agent for insomnia and non-PTSD related nightmares
- Mixed data:
  - High reports of ADR (daytime sedation, priapism, worsening nightmares)
  - Best data in OSA and AUD

Cyproheptadine

- Antagonist at serotonin receptor 5-HT1A
  - REM suppression
- Low amount of evidence
  - Mostly small case series
  - Limited to veterans as study populations
- Run risk of anticholinergic side effects

Nightmare Medication Table

Medication	Dosing	Pearls
Prazosin	1-10 mg HS	Orthostatic hypotension
Doxazosin	1-6 mg HS	Comes in extended release
Clonidine	0.1-0.2 mg HS	Hypotension, drowsiness
Gabapentin	300-3600 mg/day	Can be used for anxiety & pain
Trazodone	50-200 mg HS	Daytime sedation, priapism
Cyproheptadine	4-24 mg HS	Often poorly tolerated

Evidence Not Supported

- BZDs
- Z-drugs
- Beta blockers
- Ramelteon
- Cannabis

Back to CW

- The provider asks you what might be best to start CW on as monotherapy. They offer the following information:
  - HR: 88, BP: 106/68
  - Current medications: none
  - Medication trials:
    - Bupropion XL 300 mg daily
    - Trazodone 100 mg HS
    - Paroxetine 20 mg daily

Bupropion – increased anxiety

Trazodone – did not help sleep

Paroxetine – suffered dry mouth

Assessment Question #3

Based on the clinical information, what medication would you recommend as monotherapy for CW?

A. Retrial paroxetine, we do not know if it was for PTSD
B. Start sertraline, it has a more favorable ADR profile
C. Start prazosin, her chief complaint is nightmares
D. Start amitriptyline, it will help her sleep as well

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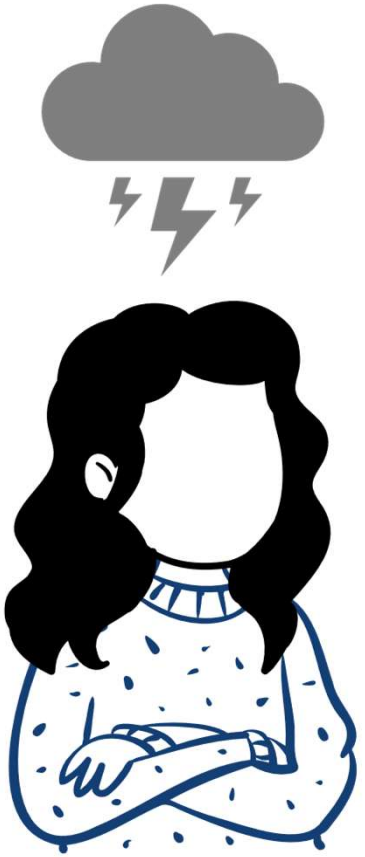
D. Start amitriptyline, it will help her sleep as well

3 Months Later

CW comes back to the clinic after titrating sertraline to 150 mg over the course of several months. She is still complaining of nightmares that interrupt her sleep. She is asking if there is something to help this specifically, as the sertraline has helped with the daytime symptoms.



Assessment Question #4

What medication recommendation would you make specifically for CW's nightmares?

1. Switch patient to risperidone 2 mg HS
2. Cross-taper the patient to venlafaxine
3. Add prazosin 1 mg HS
4. Add olanzapine 10 mg HS

Assessment Question #4

What medication recommendation would you make specifically for CW's nightmares?

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FUTURE DIRECTIONS

General Note

Medications in this section are either not supported or mentioned in the guidelines, and in other cases are not FDA approved/are experimental

Ketamine

NMDA Receptor Antagonist - Glutamate

- Rapid acting antidepressant
- Helps facilitate fear extinction
- Blocks memory consolidation

Available Data

- Small (n=41) found reduction in 3 major symptom clusters
- Effect after **single dose infusion**

Ketamine

IV

Intranasal

Memantine

Oral option

NMDA receptor antagonist

Additional receptor targets

Very small, promising studies

Highest benefit in hyperarousal & sleep

Psychedelics

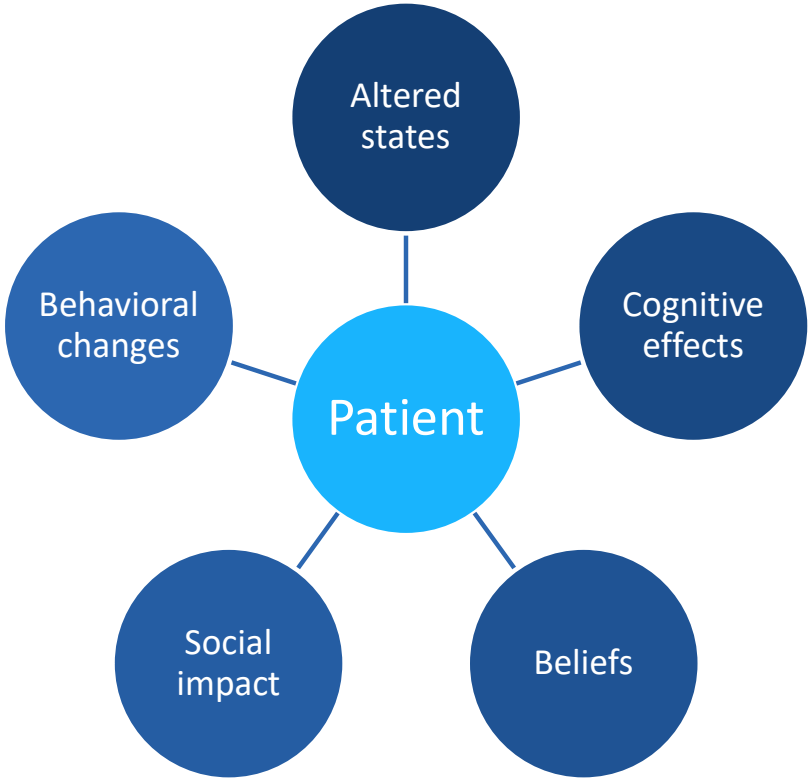
Psilocybin

- 5-HT2A agonist
- May reduce amygdala reactivity
- May reduce avoidance, increase emotional capacity

MDMA

- Release 5-HT, DA, NE, cortisol
- May reduce fear response
- May attenuate amygdala

Psychedelics



Psychedelic Workflow

Preparatory Meetings

- Establish study structure
- Set expectations

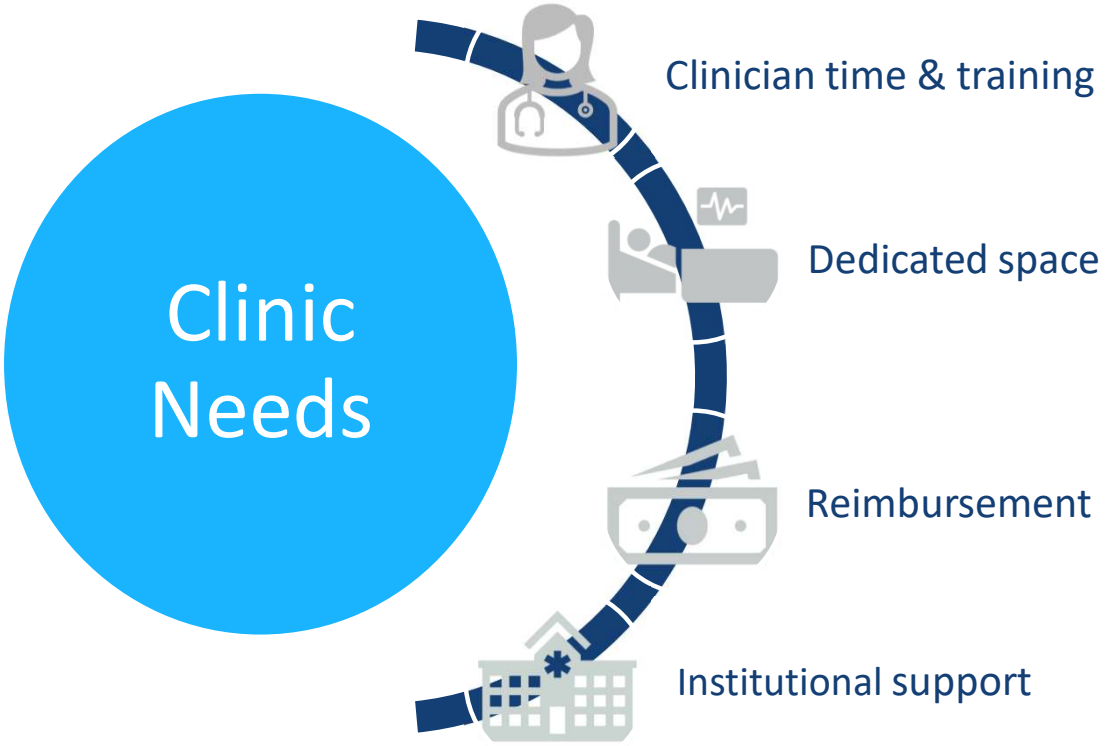
Integration

- Attend to physical and emotional needs
- Administer psychotherapy for therapeutic goals
- Accompanied by music, lighting, ambiance

Post-Sessions

- Follow-up following doses
- Discuss post-administration symptoms and attitudes

Cost to System of Psychedelics



Assessment Question #5

Which of the following does NOT represent a challenge to using more experimental therapies for PTSD?

A. Patients may require transportation to and from appointments
B. Specialty clinics would need to be set up to support administration and follow-up
C. Patients may be “too excited” for the therapy for it to work
D. New protocols would need to be developed for administration

Assessment Question #5

Which of the following does NOT represent a challenge to using more experimental therapies for PTSD?

A. Patients may require transportation to and from appointments
B. Specialty clinics would need to be set up to support administration and follow-up
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Need More Information?

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