Overview of the Treatment of Post Traumatic Stress Disorder (PTSD)

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OHIO PHARMACISTS ASSOCIATION

1 VOICE VISION TEAM

Disclosure Statement

- Christopher Thomas and Mary Borovicka have no relevant financial relationship with ineligible companies to disclose.
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- The context of this presentation does not represent the views of the U.S. Department of Veterans Affairs or the United States Government.
- This presentation will include discussion of off-label, experimental, and/or investigational use of drugs or devices.

Learning Objectives

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

1. Recognize the commonality and proposed pathophysiology of the Trauma and Stress-Related Disorders;

2. Describe the symptom clusters that are required for a patient to meet diagnostic criteria of Trauma and Stress-Related Disorders;

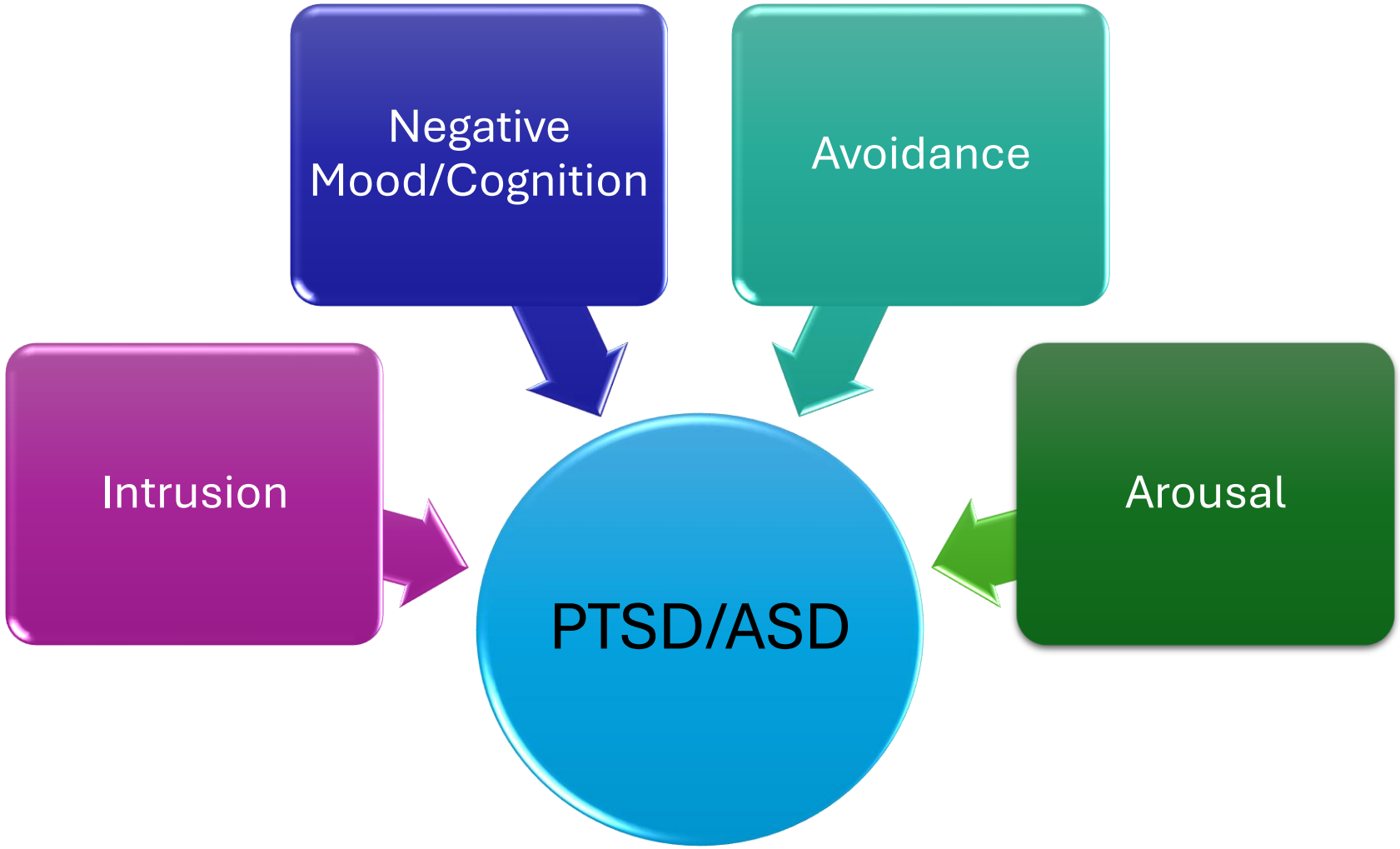
3. Examine the current literature regarding medications used to treat PTSD; and

4. Apply the PTSD literature and treatment guidelines to determine which medication option is most appropriate in treating a specific symptom in a patient with PTSD.

What is Post-Traumatic Stress Disorder (PTSD)??

- Is a trauma and stressor-related disorder
  - DSM-IV classified PTSD as an anxiety disorder
- Pattern of symptoms following a traumatic event (stressor)
- Disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of daily functioning
- The disturbance is not attributed to substance or medical condition
- Symptom severity fluctuates with co-occurring stressors, illness, life transitions

PTSD Symptom Categories



DSM-5 TR

DSM-5-TR Criteria

Exposed to actual or threatened death, serious injury, or sexual violence (1 or more):

- 1. Directly experiencing the traumatic event
- 2. Witnessing, in person, the event as it occurred to others
- 3. Learning that the traumatic event occurred to a close family member/friend
- 4. Experiencing repeated or extreme exposure to aversive details of the traumatic event

Presence of INTRUSION symptoms associated with the trauma (1 or more):

- 1. Recurrent, involuntary, and intrusive distressing memories of the trauma
- 2. Recurrent distressing dreams related to the traumatic event
- 3. Dissociative reactions
- 4. Intense psychological distress at exposure to trauma cues
- 5. Marked physiological reactivity at exposure to trauma cues

DSM-5-TR Criteria

Persistent **AVOIDANCE** of stimuli associated with the trauma (1 or more):

- 1. Efforts to avoid trauma-associated thoughts/feelings/memories
- 2. Efforts to avoid trauma-related activities/places/people/conversations

Negative **ALTERATION IN THOUGHTS/MOOD** associated with trauma (2 or more):

- 1. Inability to remember important aspects of trauma
- 2. Persistent exaggerated negative beliefs/expectations about self/others/world
- 3. Persistent distorted cognitions re: cause/consequences of trauma that lead to blaming self/others
- 4. Persistent negative emotional state (e.g., fear, horror, anger, guilt)
- 5. Markedly diminished interest/participation in significant activities
- 6. Feelings of detachment or estrangement from others
- 7. Persistent inability to experience positive emotions

DSM-5-TR Criteria

Marked alterations in **AROUSAL / REACTIVITY** associated w/ trauma (2 or more):

1. Irritable behavior and angry outbursts w/ little provocation
2. Reckless or self-destructive behavior
3. Hypervigilance
4. Exaggerated startle response
5. Problems with concentration
6. Sleep disturbance

Duration of the disturbance is more than 1 month: YES

The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning

The disturbance is not attributable to the physiological effects of a substance or another medical condition

PTSD Prevalence

- 70% of adults worldwide experience a traumatic event in their life; 31% experience 4 or more events!!
- Lifetime prevalence is ~ 6.8% for U.S. population; differs in other countries
- 5-6% of men and 10-14% of women
- 5th most common psychiatric disorder
  - Only Major Depression, ADHD, Specific Phobias and Social Anxiety Disorder occur more often
- Must have trauma to get PTSD
  - 9% of men and 20% of women exposed to traumatic event develop PTSD
  - 22% of combat veterans develop PTSD

https://www.nimh.nih.gov/health/statistics/post-traumatic-stress-disorder-ptsd

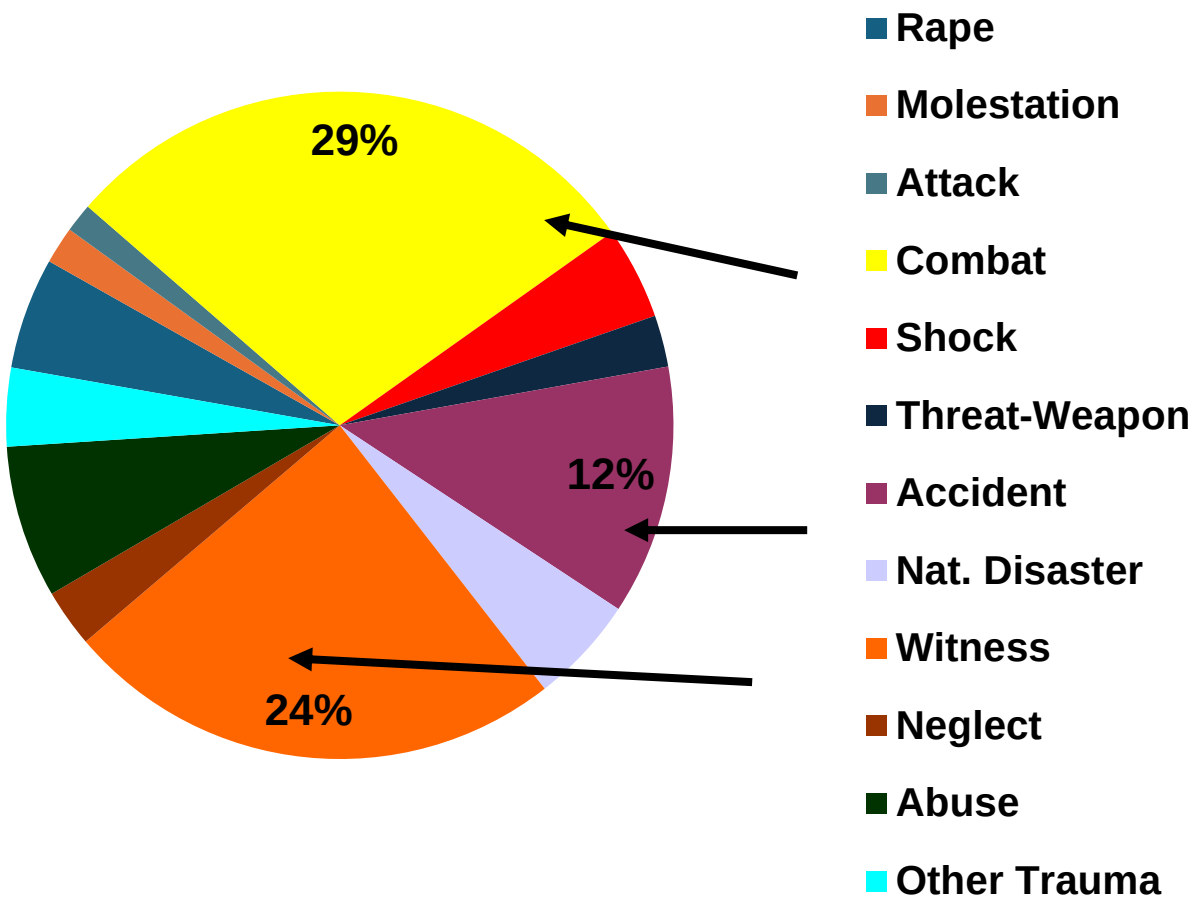
DSM-5 TR

Risk Factors for PTSD

- Female
- Less education
- Lower socioeconomic status
- Separated, divorced, or widowed
- Traumatic brain injury
- Personal and family psychiatric history
- Childhood trauma
- Poor social support
- Intensity of the traumatic event
- Exposure to 4 or more traumatic events

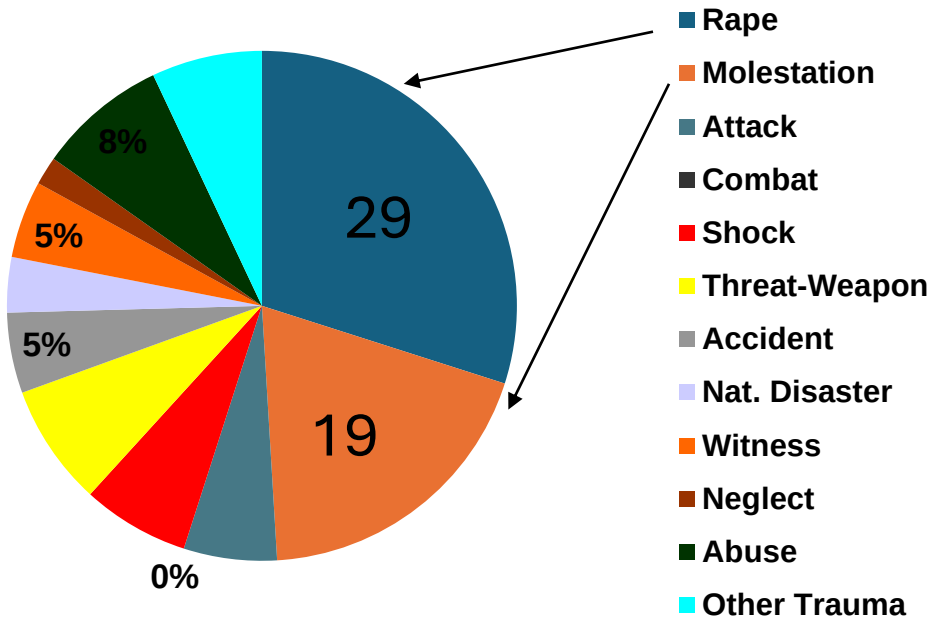
DSM-5 TR; Shalev A et al. N Engl J Med 2017

Trauma Associated with PTSD in Males



https://www.nimh.nih.gov/health/statistics/post-traumatic-stress-disorder-ptsd

Trauma Associated with PTSD in Females

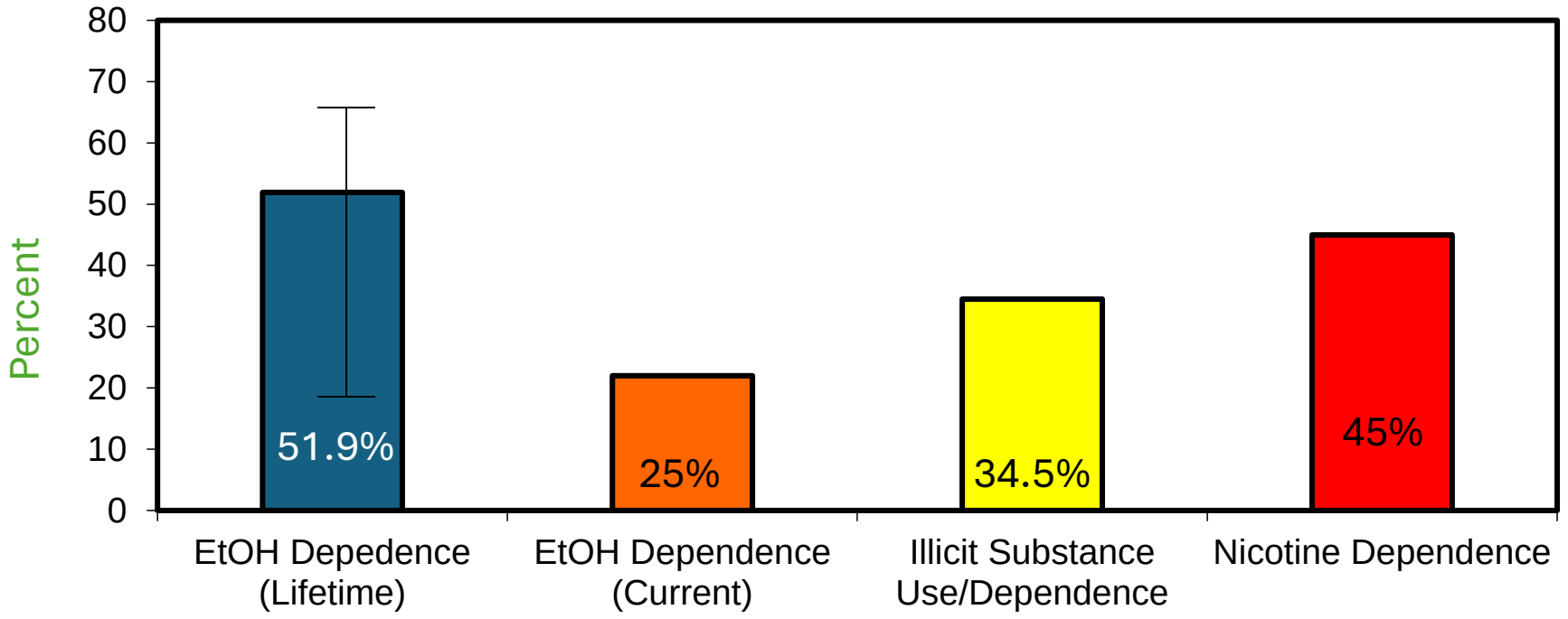


https://www.nimh.nih.gov/health/statistics/post-traumatic-stress-disorder-ptsd

Comorbid Disorders

- 50% of PTSD patients also have:
  - Anxiety disorders
  - Mood disorders
  - Substance use disorders
- 90% of people with PTSD have at least 1 lifetime comorbid mental disorder
- PTSD associated with borderline and antisocial personality disorders
- PTSD associated with bone/joint, neurological, CV, respiratory, and metabolic diseases (OR 1.5-3.0)

Substance Use in PTSD



- Lifetime prevalence of EtOH abuse ranges from 82% in vets with significant combat experience to 21.6% in civilian populations
- Patients with nicotine dependence and PTSD are less likely to quit smoking (23% compared to 45% nationwide)

McFall M, PTSD Research Quarterly 2006; Jacobson LK, et al. Am J Psych 2001

Acute Stress Disorder
vs.
PTSD

Similarities Between Acute Stress and PTSD

- Traumatic event
- Symptom categories
- Disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of daily functioning
- The disturbance is not attributed to substance or medical condition (or brief psychotic disorder)

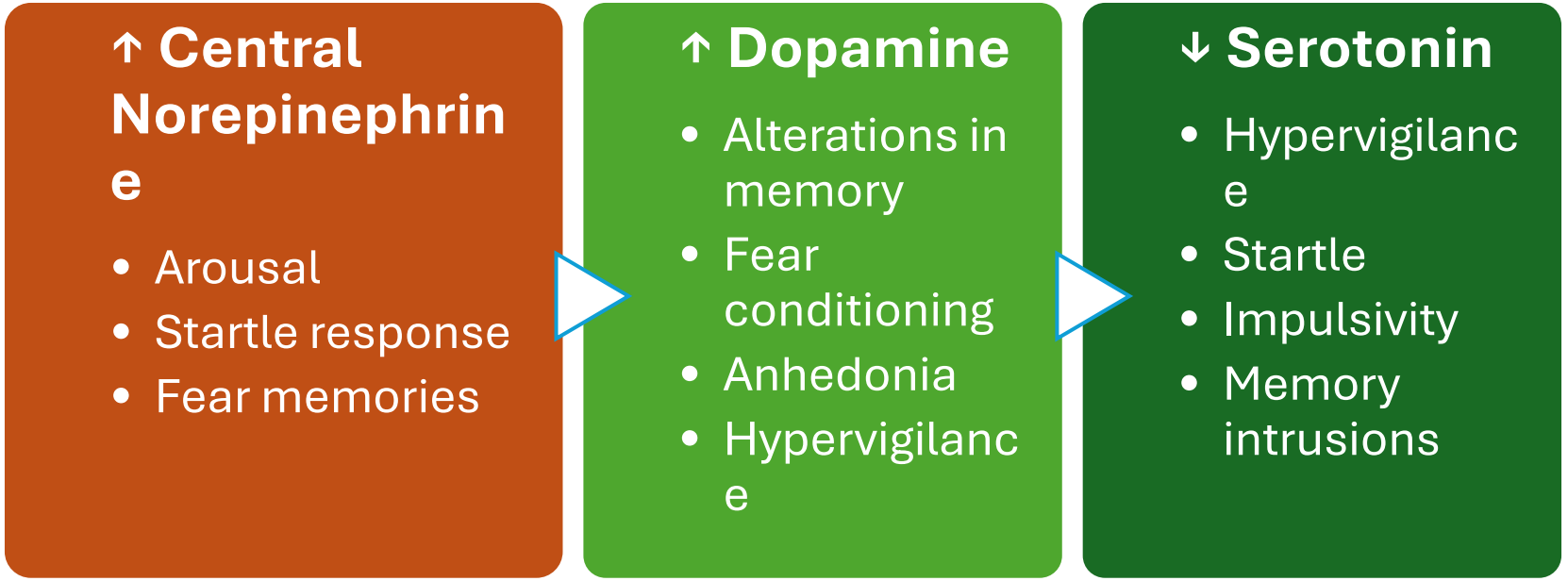
DSM-5 TR

Differences

Acute Stress Disorder	PTSD
Duration: 3 days to 1 month	**Duration: >1 month**
Presence of at least 9 of 14 possible symptoms	Presence of at least 6 of 20 possible symptoms
Less cognitive or mood symptom options	More cognitive or mood symptom options
No reckless/self-destructive behavior symptom option in arousal category	Specifier options available
	Diagnostic criteria for patients ≤6 yo

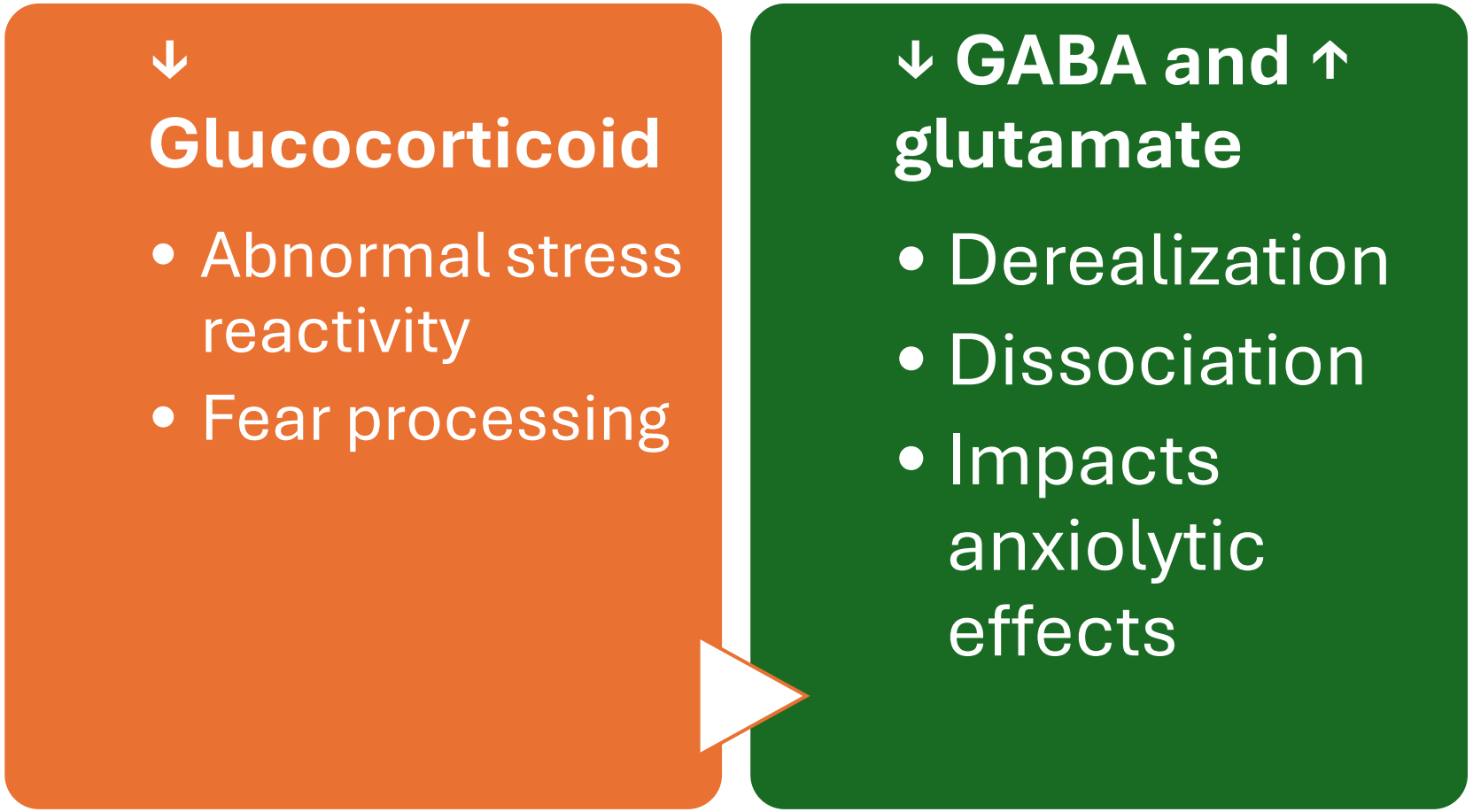
DSM-5 TR

Pathophysiology



Sareen, Jitender. UpToDate Sep 2020.
Pan, Xiongfeng, et al. Front Mol Neurosci. 2018.
Sherin, Jonathan, et al. Dialogues Clin Neurosci. 2011.

Pathophysiology



Sareen, Jitender. UpToDate Sep 2020.
Pan, Xiongfeng, et al. Front Mol Neurosci. 2018.
Sherin, Jonathan, et al. Dialogues Clin Neurosci. 2011.

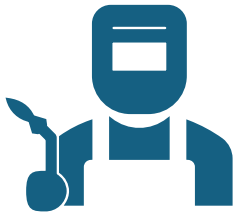
Which of the following are FDA approved for the treatment of PTSD? Select all that apply

a. Venlafaxine
b. Fluoxetine
c. Sertraline
d. Paroxetine

Treatment Guideline Summaries

Guideline/ year	1st line Non-Pharmacologic Tx	1st Line Pharmacologic Tx	Recommend tx for nightmares? Prazosin?
British Assoc for Psychopharm/ 2014	Trauma-focused CBT or EMDR	Paroxetine, sertraline, venlafaxine	Yes; prazosin as adjunct
Va/DoD/ 2017	Trauma-focused CBT including EMDR	Sertraline, paroxetine, venlafaxine - 2nd line to psychological tx	Yes; insufficient evidence for prazosin
Clinical Pract Guideline/Am Psycholog Assoc/ 2017	CPT, Trauma-focused CBT, PE	Fluoxetine, sertraline, paroxetine, venlafaxine	No; no rec
PTSD guideline/NICE/2018	Trauma-focused CBT	Venlafaxine or SSRIs (only if person has pref for drug tx)	No; no rec
Effective tx for PTSD: 3rd ed./ Int Soc Traumatic Stress Studies/ 2020	CPT, Trauma-focused CBT, EMDR, PE	Fluoxetine, sertraline, paroxetine, venlafaxine	No; no rec
Australian Guidelines/ 2020	CPT, Trauma-focused CBT, EMDR, PE	Sertraline, fluoxetine, paroxetine, venlafaxine - 2nd line to psychological tx	No; no rec

Psychotherapy for PTSD



Why? They work!!

Effects last longer than pharmacologic interventions!

What types?

Cognitive-behavioral therapy
Cognitive-processing therapy
Eye-movement desensitization and reprocessing
Prolonged exposure
Narrative processing

Pary R, et al. Prim Care Companion CNS Disord 2021

Most Common Psychotherapy?

- **Cognitive Behavioral Therapy (CBT)**
  - In this case, trauma-focused CBT (TF-CBT)
  - Based on principle that psychological problems are a result of faulty/unhelpful ways of thinking and on learned patterns of unhelpful behaviors
  - Duration: 8-25 sessions, begin within 6 mo of traumatic event
- **Goal of TF-CBT: change thinking patterns and behaviors**
  - Recognized distortions in thinking and reevaluate them in reality
  - Use problem-solving skills to cope (role playing)
  - Gradual exposure – introduce person to memories of trauma, recondition their response to triggers; ease emotional distress
  - Learn to calm mind and relax the body

Pary R, et al. Prim Care Companion CNS Disord 2021
What is Cognitive Behavioral Therapy? (apa.org)

Eye Movement Desensitization and Reprocessing (EMDR)

- **Goal:** To help heal from trauma
- **Method** involves moving your eyes a specific way while processing traumatic memories
- In PTSD flashbacks: the past becomes the present
- Children - adults can do it
- Does not require talking in detail about a trauma.
- Focuses on changing the emotions, thoughts or behaviors that result from a trauma
- Reprocess and repair: memories of a trauma event are accessed in very specific ways. Combined with eye movements and guided instructions, accessing those memories helps reprocess what is remembered from the negative event.

https://my.clevelandclinic.org/health/treatments/22641-emdr-therapy

Other Psychotherapies

- Cognitive-Processing Therapy
  - Specific type of CBT often used for combat veterans
  - Process trauma through writing, homework
  - Usually 12 sessions, 60-90 minutes each
  - Explore way trauma altered thoughts/beliefs and affects how they act
- Prolonged Exposure Therapy
  - Another form of CBT
  - Teaches individuals to gradually approach trauma-related memories, feelings, and situations in present tense (imaginal exposure)
  - Conducted weekly for 8-15 sessions, 90 minutes each
  - In-vivo exposure – confronting feared stimuli outside of therapy, in assigned homework

Paary R, et al. Prim Care Companion CNS Disord 2021;23(1):19nr02572
Cognitive Processing Therapy | Psychology Today

Psychotherapy: Treatment Guideline Recommendations

#	Recommendation	Strength
7	**We recommend individual psychotherapies, listed in Recommendation 8, over pharmacologic interventions** for the treatment of PTSD.	Strong For ***
8	We recommend the individual, manualized trauma-focused psychotherapies for the treatment of PTSD: Cognitive Processing Therapy (CPT), Eye Movement Desensitization and Reprocessing (EMDR), or Prolonged Exposure (PE).	Strong For

Australian Guidelines 2020	
Also recommends CPT, Trauma-focused CBT, EMDR, PE over pharmacologic treatments as 1st line	

https://www.healthquality.va.gov/guidelines/MH/ptsd/VA-DoD-CPG-PTSD-Provider-Summary.pdf

Harmful Psychotherapy?

Psychological Debriefing

- Conducted in days immediately following the traumatic event
  - Other names: crisis intervention approaches, group psychological debriefing, critical incident stress debriefing, process debriefing
- Goal: prevent development of PTSD
- One session, Lasts 1-3 hours
- Outcome:
  - Associated with increased PTSD symptoms relative to no treatment (Van Emmerik, et al. 2002)
- **NOT** a recommended treatment

Psychological Debriefing for Post-Traumatic Stress Disorder | Society of Clinical Psychology (div12.org)

Van Emmerik, et al. Lancet 2002.

Pharmacotherapy for PTSD

Everything But the Kitchen Sink

Pharmacotherapy for PTSD

Antidepressants rarely result in complete PTSD symptom remission; they do offer some relief

Effect size small – 0.3

Risk of relapse if medication discontinued too quickly

Maintain full therapeutic dose for 6-12 months

Insufficient evidence to support combination of medication + psychotherapy

74% of PTSD patients get medication

- 89% - antidepressants
- 61% - anxiolytics or sedative-hypnotics
- 34% - antipsychotics

Pary R, et al. Prim Care Companion CNS Disord 2021; Shalev A, et al. N EngU Med 2017

Medications with Strong Evidence for PTSD Treatment

Drug	Initial dose mg/day	Response Range mg/day	Efficacy/ comments
Fluoxetine	10-20	20-80	Shown to decrease reexperiencing, avoidance, numbness, hyperarousal. Time to onset for venlafaxine slow.
Paroxetine*	10-20	20-50	
Sertraline*	25-50	50-200	
Venlafaxine XR	37.5	75-225	

* FDA approved for PTSD

NOTE: citalopram and escitalopram have less significant effect on reducing PTSD symptoms and are not recommended

Schrader C, et al. Missouri Med 2021, Pary R, et al. Prim Care Companion CNS Disord 2021

Pharmacotherapy: Treatment Guidelines

Guideline	Recommendation
Va/DoD British	**We recommend paroxetine, sertraline, or venlafaxine for the TREATMENT of PTSD.**
Am Psycholog Assoc NICE Int Trauma Soc Australian	**Recommended sertraline, paroxetine, fluoxetine, or venlafaxine**

How are PTSD Symptoms Evaluated?

- Clinician-Administered PTSD Scale (CAPS-5)
  - Gold standard in PTSD assessment
  - 30-item structured interview
  - Can be used to make current or lifetime diagnosis, and assess PTSD symptoms over the past week
  - Scores 0-80. Higher score is more severe
  - Can take 45-60 minutes to complete

Sertraline

	N	Flexible Dosing (50-200mg/d)	Statistically Sig Outcomes	Response Rate	ADRs
12-week, RDBPCT (Brady, et al. 2000)	n=187	133.3mg (±59.2mg)	CAPS-2 CGI-S CGI-I	Sertraline-53% Placebo-32%	Insomnia
12-week, RDBPCT (Davidson, et al. 2001)	n=208	146.3mg (±49.3mg)	CAPS-2 IES CGI-I CGI-S	Sertraline-60% Placebo-38%	Insomnia Diarrhea Fatigue ↓ Appetite

RDBPCT: randomized, double-blind, placebo-controlled trial; CAPS-2: Clinician Administered PTSD Scale; CGI-S: Clinical Global Impression-Severity scale; CGI-I: Clinical Global Impression-Improvement Scale; IES: Impact of Event Scale

Brady, et al. *JAMA*. 2000;283:1837-1844.
Davidson, et a;. *Arch Gen Psychiatry*. 2001;58:485-492.

FDA approved for PTSD in 1999

Paroxetine

	N	Dosing	Statistically Sig Outcomes	Response Rate	ADRs
12-week, RDBPCT (Marshall, et al. 2001)	n=551	Fixed: 20, 40mg	CAPS-2 Re-experiencing Avoidance Hyperarousal	20mg-62% 40mg-54% Placebo-37%	• Asthenia • Diarrhea • Sexual dysfunction • Impotence • Nausea • Somnolence
12-week, RDBPCT (Tucker, et al. 2001)	n=307	Flexible: 20-50mg Mean: 27.6± 6.72 mg	CAPS-2 Re-experiencing Avoidance Hyperarousal TOP-8 DTS	Paroxetine-58.8% Placebo-38%	• Nausea • Somnolence • Dry Mouth • Asthenia • Sexual dysfunction

RDBPCT: randomized, double-blind, placebo-controlled trial; TOP-8: Treatment Outcome PTSD scale; CAPS-2: Clinician Administered PTSD Scale; DTS: Davidson Trauma Scale

Marshall, et al. Am *J Psychiatry*. 2001;158:1982-1988.
Tucker, et al. *J Clin Psychiatry*. 2001;62:860-868.

FDA approved for PTSD in 2000

Venlafaxine

	N	Flexible Dosing (37.5-300mg/d)	Statistically Sig Outcomes	Remission Rate	ADRs
24-week, RDBPCT	n=329	221.5 mg/d	CAPS-2 Re-experiencing Avoidance	Venlafaxine-50.9% Placebo-37.5%	None

RDBPCT: randomized, double-blind, placebo-controlled trial; CAPS-2: Clinician Administered PTSD Scale

Majority female (~55%) population

Wide variety of traumas, but nonsexual abuse was the highest (25-30%)

Statistically significant differences in CAPS score noticed by week 4 and continued to improve through week 24

NNT for remission was 8

Davidson, et al. *Arch Gen Psychiatry.* 2006;63:1158-1165.

Fluoxetine

	N	Dosing	Significant Outcomes	Response Rate	ADRs (Higher than Placebo)
12-week, RDBPCT (Martenyi, et al. 2002)	n=301	Flexible: 20-80mg Mean: 57mg	TOP-8 CAPS CGI-S CGI-I	Fluoxetine-59.9% Placebo-43.8%	Nausea
12-week, RDBPCT (Martenyi, et al. 2007)	n=411	Fixed: 20 or 40mg	CAPS	CAPS Response Rate: 20 mg (-42.0), 40 mg (-42.8), Placebo (-36.6) - NS	None
RDBPCT: randomized, double-blind, placebo-controlled trial; TOP-8: Treatment Outcome PTSD scale; CAPS: Clinician Administered PTSD Scale; CGI-S: Clinical Global Impression-Severity scale; CGI-I: Clinical Global Impression-Improvement Scale					

Martenyi, et al. *J Clin Psychiatry.* 2002;63:199-206.
Martenyi, et al. *J Clin Psychopharm.* 2007;27:166-170

Pharmacotherapy: What to Choose Based on Routine Clinical Practice?

2018 VA Study

N = 2931

Fluoxetine, paroxetine, sertraline, topiramate, and venlafaxine

2004-2013

Available evidence-based medications for PTSD are equally effective in clinical practice

Shiner B, et al. J Clin Psychiatry 2018

2020 VA Study

N= 834

Fluoxetine, paroxetine, sertraline, topiramate, and venlafaxine

2016-2018

There may be an advantage to **venlafaxine** over other agents in achieving acute-phase remission for DSM-5 PTSD in routine clinical practice, but this finding requires further study

Shiner B, et al. J Clin Psychiatry 2020

Beyond First-Line for PTSD

- It’s a little muddy….
  - Guidelines are not in agreement
  - Studies are poorly designed, small N

Beyond First Line Pharmacotherapy VA/DoD Guideline

#	Recommendation	Strength
16	There is **insufficient evidence to recommend for or against** amitriptyline, bupropion, buspirone, citalopram, desvenlafaxine, duloxetine, escitalopram, eszopiclone, *fluoxetine*, imipramine, mirtazapine, lamotrigine, nefazodone, olanzapine, phenelzine, pregabalin, rivastigmine, topiramate, or quetiapine for the treatment of PTSD.	Neither for or against
17	There is **insufficient evidence to recommend for or against** psilocybin, ayahuasca, dimethyltryptamine, ibogaine, or lysergic acid diethylamide for the treatment of PTSD.	Neither for or against
18	We **suggest against** divalproex, guanfacine, ketamine, prazosin, risperidone, tiagabine, or vortioxetine for the treatment of PTSD.	Weak against
19	We **recommend against** benzodiazepines for the treatment of PTSD	Strong against
20	We **recommend against** cannabis or cannabis derivatives for the treatment of PTSD.	Strong against

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

Beyond First Line Pharmacotherapy

- 2nd line? TCAs such as imipramine or amitriptyline, mirtazapine
- Antipsychotics – mixed results
  - Some evidence for use of quetiapine, olanzapine, risperidone,
- Anticonvulsants
  - Mixed results for topiramate
  - Divalproex not recommended
- Ketamine - small studies, some benefit but transient lasting only 1-2 weeks

Pary R, et al. Prim Care Companion CNS Disord 2021; Shalev A, et al. N Engl J Med 2017

VA/DoD Guideline: Augmentation

#	Recommendation	Strength
21	There is insufficient evidence to recommend for or against the combination or augmentation of psychotherapy (see Recommendation 8 and Recommendation 9) or medications (see Recommendation 15) with any psychotherapy or medication for the treatment of PTSD (see Recommendation 22 for antipsychotic medications and)	Neither for or against
22	We suggest against aripiprazole, asenapine, brexpiprazole, cariprazine, iloperidone, lumateperone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone for augmentation of medications for the treatment of PTSD	Weak against

Prazosin

Raskind, et al. J Clin Psychiatry. 2002;63:565-568., Raskind, et al. Biol Psychiatry. 2007;61:928-934; Raskind et al. N Eng J Med. 2018; 378: 507-517.

	N	Flexible Dosing (1-20mg/d)	Outcomes	ADRs
Retrospective chart review of veterans (Raskind, et al. 2002)	n=59	6.3mg (±0.8mg)	CAPS: distressing dreams CGI-C P < 0.05	• Orthostasis • Dizziness • Headache • Lethargy
8-week, RDBPCT (Raskind, et al. 2007)	n=40	13.3mg (±3mg)	CAPS: distressing dreams PSQI CGI-C P < 0.05	• Transient Dizziness • Nasal Congestion
26-Week RDBPCT (Raskind 2018)	N=340	Mean dose 14.8mg +/- 6.1mg (Max Dose for men=20 mg, Max dose for Females 12 mg)	None: CAPS, PSQI, CGI CAPS B2 PR: -1.9 PL: -1.7 p = 0.38 (NS) CAPS overall PR: -11.8 PL: -13.1 **p = 0.73 (NS)**	Dizziness (34% vs 21%) Lightheadedness (34% vs 20%) Urinary incontinence (12% vs 4%)

RDBPCT: randomized, double-blind, placebo-controlled trial; CAPS: Clinician Administered PTSD Scale; CGI-C: Clinical Global Impression-Change scale; PSQI: Pittsburgh Sleep Quality Index

VA/DoD Guideline: Nightmares

#	Recommendation	Strength
32	We suggest prazosin for the treatment of nightmares associated with PTSD.	Weak For ***

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

Prospective Studies with BZD's in PTSD

- Alprazolam was studied prospectively in a 5-week crossover design in 16 patients
  - Average dose was 4.4 mg
  - There was no difference in efficacy between alprazolam and placebo
- Clonazepam was also studied in 6 patients and showed no benefit versus placebo
- In an acute stress study, 13 patients were given alprazolam or clonazepam, after a traumatic event and followed for 6 months
  - This group was compared to 13 patients that were the control group not receiving BZD's
  - At 6 months, **69% of the patients developed PTSD**, whereas only 15% of the control group developed PTSD

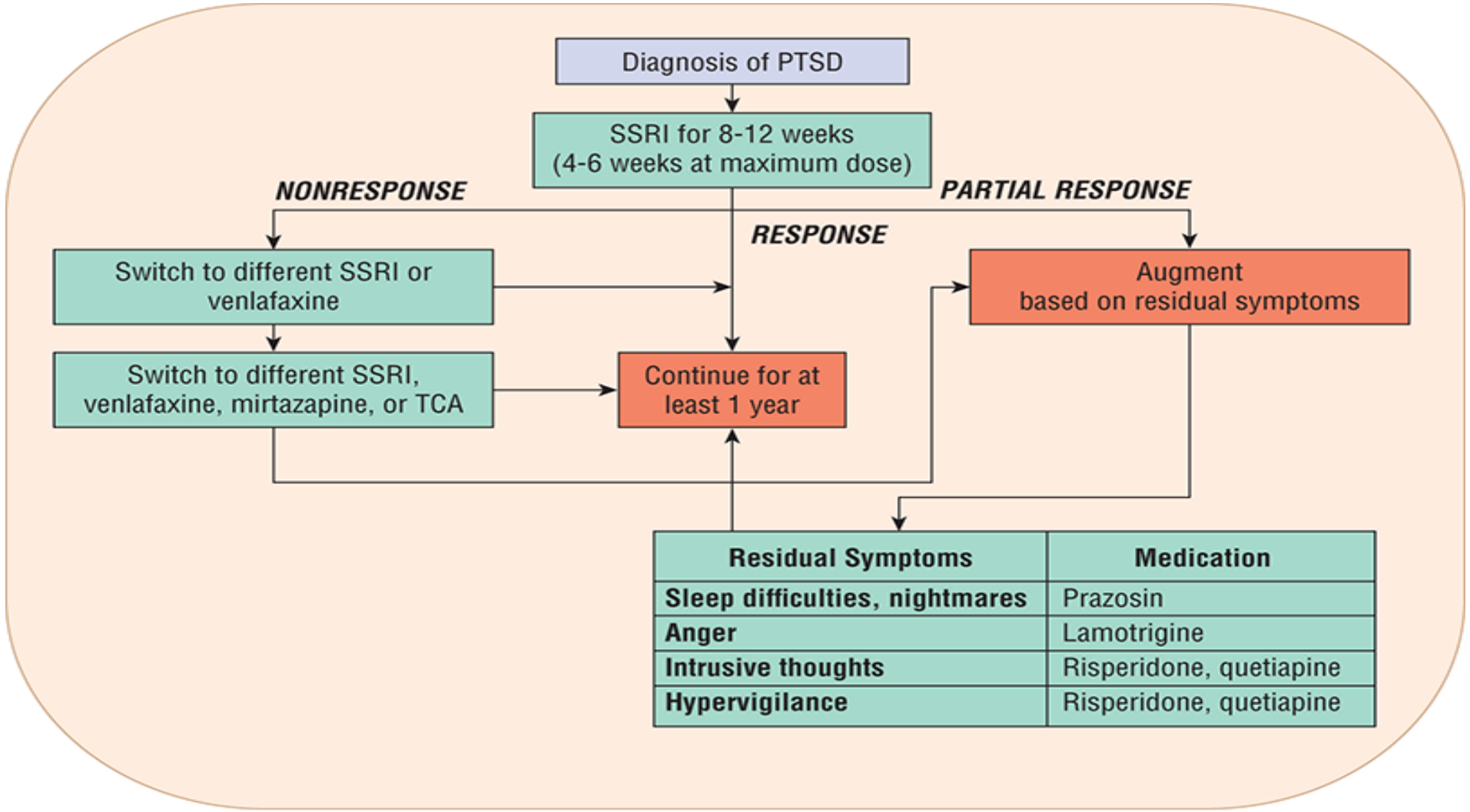
Asnis GM, et al. Drugs 2004; 64 (4): 383-404

Cates ME, et al. Ann Pharmacother 2004; 38(9) 1395-9

Benzodiazepines in PTSD

- Benzodiazepines are **NOT** recommended for the management of PTSD
- They have been shown to cause more harm than good with long term use
  - May be due to sedative, addictive, dissociative properties of the benzodiazepines when used to treat a condition in which dissociation and sedation fosters reliving traumatic events and worsens avoidant symptoms of PTSD

Schrader C, et al. Miss Med 2021



Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*
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Algorithm for the pharmacotherapy of posttraumatic stress disorder (PTSD). (SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.)

Citation: Chapter 91 Posttraumatic Stress Disorder and Obsessive-Compulsive Disorder, DiPiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey L. *DiPiro's* Pharmacotherapy: A Pathophysiologic Approach, 12th Edition; 2023. Available at: https://accesspharmacy.mhmedical.com/ViewLarge.aspx?figid=274619910&gbosContainerID=0&gbosid=0&groupID=0&sectionId=264561240&multimediaId=undefined
Accessed: March 29, 2024
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Psychedelics

Which of the following agents has had an NDA submitted to the FDA for PTSD treatment?

A. Psilocybin

B. Ibogaine

C. Lysergic acid

D. MDMA

Psychedelics for PTSD

- MDMA (3,4-methylenedioxymethamphetamine)
- Psilocybin (mushrooms)
- Lysergic Acid diethylamide (LSD)
- Ibogaine – lesser-known potent psychedelic

How do Psychedelics Work in PTSD

Psychedelics enter the brain and stimulate 5-HT2A

- The receptor necessary for the “trip”

Cause neurons to branch out quickly in the prefrontal cortex

- May be due to signaling of BDNF
- As soon as 24 hours in animal models
- Effect seems to last a long time

Some psychedelics also active dopamine receptors

- Explains the hallucinations, etc.

Reardon S. Nature 2023; Beans C, PNAS 2024

Barriers to PTSD Treatment

Fear of reporting symptoms would hurt military career
Patient afraid to admit a problem exists
Afraid to admit others that a problem with PTSD exists
Afraid that treatment will bring back the experiences and trauma
Afraid to change behaviors regarding PTSD

Referral Information Regarding PTSD

- Local mental health center or VA facility
- www. PTSD.va.gov
- PTSD hotline: 1-802-296-6300
- VA suicide hotline: 988, press 1 or
- 1-800-273-8255

Patient Case

- Patient is a 28-year-old female referred to the primary care clinic from her psychologist with ongoing concerns of “PTSD” (avoidant behaviors, hypervigilance, and hyperarousal) symptoms from a sexual assault that occurred 4 years earlier. Primary care provider referred to Psychiatry, but currently, the shortest wait time to be seen by a Psychiatrist is 3 months in your area. They are requesting a recommendation for a medication to start to assist with this patients' symptoms of PTSD.

- Which of the following medications would be most appropriate to recommend at this time?
  A. Citalopram
  B. Sertraline
  C. Vilazodone
  D. Fluoxetine

Patient Case Continued

- Patient reported back to primary care reporting that she is more social and less avoidant than before, however, she reports continuation of intense nightmares and was hoping to start a medication to assist with sleep. Which of the following medication is the most appropriate to recommend for her nightmares?
    A. Zolpidem
    B. Lorazepam
    C. Quetiapine
    D. Prazosin

Conclusions

- PTSD is often under recognized and complicated secondary to multiple diagnosis
- Psychotherapy is considered first line for PTSD to assist with the trauma that caused the PTSD symptoms
- Many pharmacological agents from several different drug classes have been explored in PTSD

Conclusions Regarding Pharmacotherapy for PTSD

- If pharmacological treatment is warranted, the 4 antidepressants that have been studied the most and recommended are sertraline, paroxetine, venlafaxine, and fluoxetine
- If adjunctive treatment is warranted, prazosin MAY be effective in treating nightmares
- Benzodiazepines are not recommended due to lack of efficacy and high comorbidity of substance abuse in this population

Need More Information?

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