Anxiety and Anxiety Related Disorders

Enxhi Plaku,PharmD
PGY-2 Psychiatric Pharmacy Resident
RWJBarnabas Health Behavioral Health Center

Preceptor: Henry Leach, PharmD, BCPP
Psychiatric Pharmacy Clinical Specialist
RWJBarnabas Health Behavioral Health Center

Disclosures

- The presenter and her preceptor have no relevant financial relationships with ineligible companies to disclose.

- None of the planners for this educational activity have relevant financial relationships to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling or distributing healthcare products used by or on patients.

Objectives- Pharmacists & Nurses

- Recall the pathophysiology of anxiety and anxiety related disorders
- Identify therapy options and guideline recommendations for anxiety related disorder
- Recognize “best practice” pharmacotherapy options for anxiety related disorders

Objectives - Pharmacy Technicians

- Recall the definition of anxiety and anxiety related disorders
- Identify classes of medications utilized for management of anxiety disorders
- Recognize differences in control scheduling in medications for anxiety disorder

Abbreviations

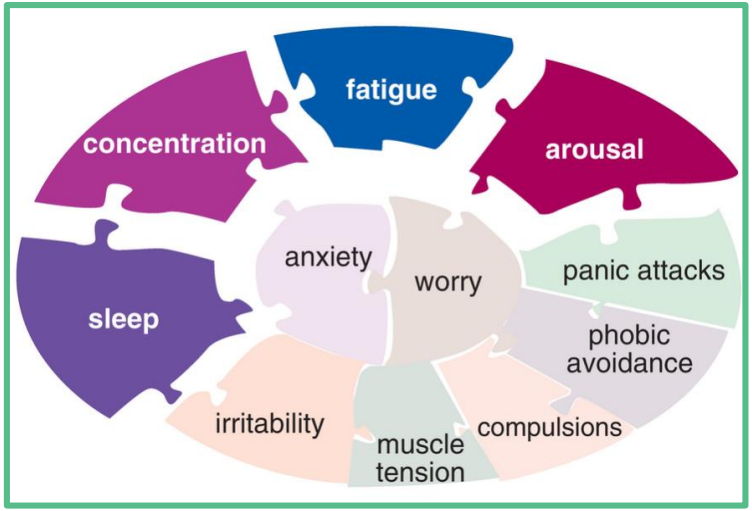
- 5-HT: serotonin
- ACTH: adrenocorticotropic hormone
- ADR: adverse drug reaction
- BZD: benzodiazepine
- CBT: cognitive behavioral therapy
- CNS: central nervous system
- CRF: corticotrophin releasing factor
- DA: dopamine
- ED: erectile dysfunction
- GABA: gamma aminobutyric acid

Abbreviations

- RCT: randomized controlled trial
- SIADH: syndrome of inappropriate antidiuretic hormone secretion
- SGA: second generation antipsychotic
- TCA: tricyclic antidepressant
- VPA: valproic acid
- HA: headache
- HPA: hypothalamic-pituitary-adrenal
- MAOI: monoamine oxidase inhibitor
- NE: norepinephrine
- NSAIDs: non-steroidal anti-inflammatory drugs

Anxiety Overview

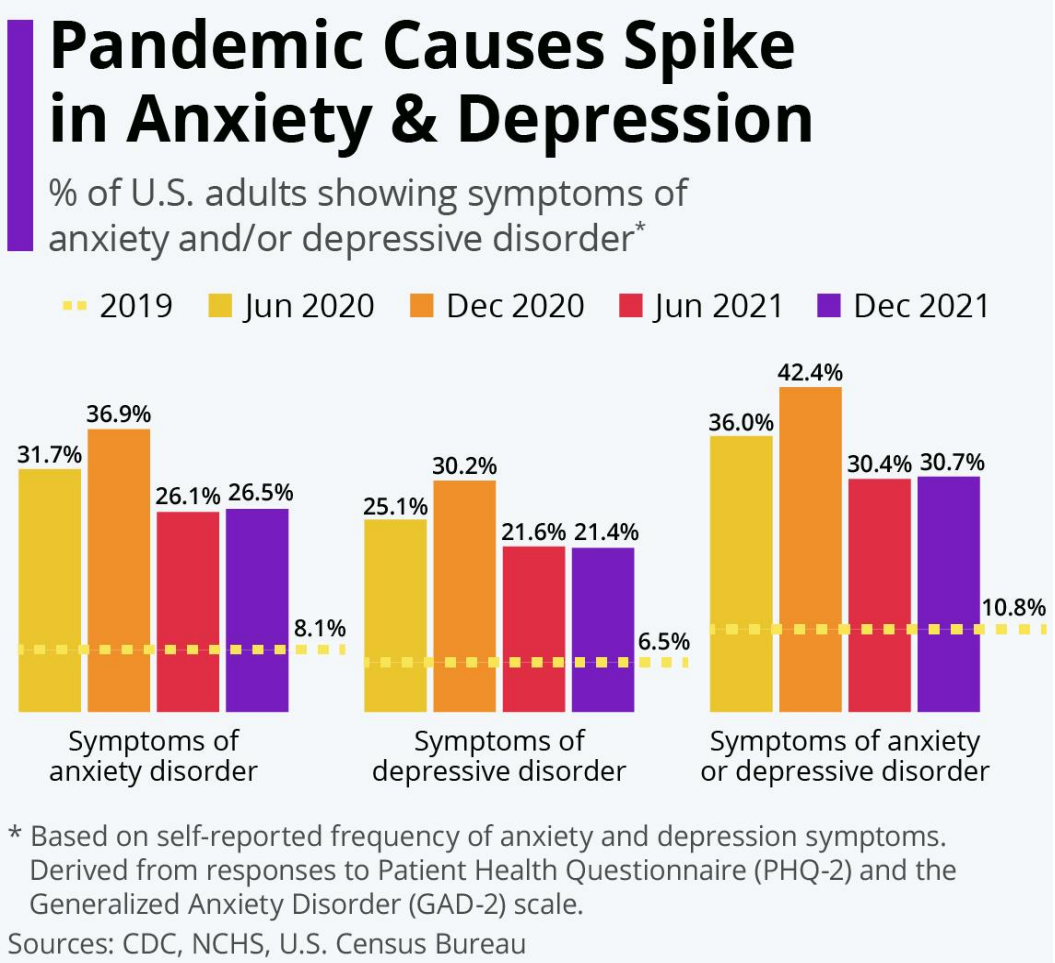
- Normal emotion under circumstances of threat
- Core symptoms of excessive fear, worry, nervousness about an imminent event or uncertain outcome
- At least 6 months
- Extensively comorbid



Source: Stahl's Essential Psychopharmacology, 5th edition (2021)

Anxiety Statistics

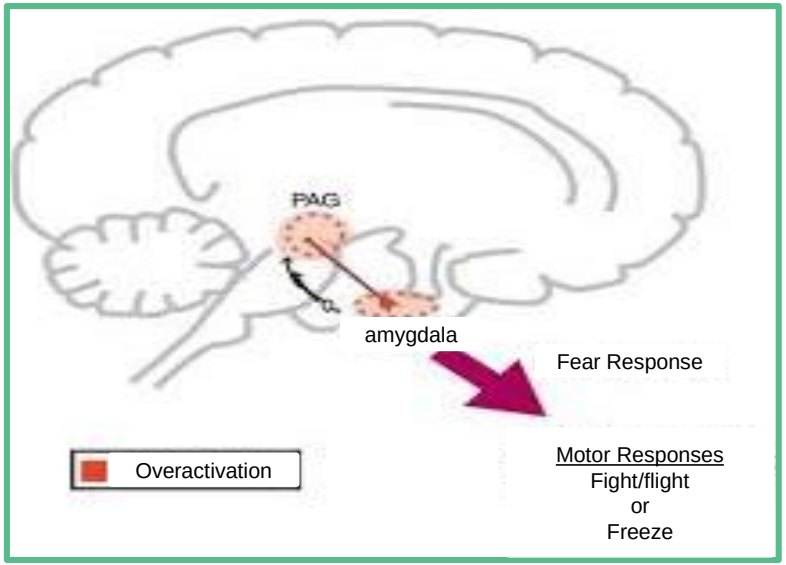
- Percentage of adults with recent symptoms of an anxiety/depressive disorder increased from 36.4% to 41.5%
- Percentage reporting an unmet mental health care need increased from 9.2% to 11.7%



Sources: www.statista.com
MMWR Morb Mortal Wkly Rep 2021;70:490–494

Amygdala and Neurobiology of Fear

- Amygdala determines fear response
- Endocrine reactions accompany fear
- Autonomic nervous system attuned to fear
- Triggered from traumatic memories
- Neurobiological regulators:
  - GABA, 5HT, NE



Source: Stahl's Essential Psychopharmacology, 5th edition (2021)

Assessment Question 1 - Pharmacy Technicians

Choose the best definition for anxiety disorder

A. Feeling of worry, nervousness, or unease, typically about an imminent event or something with an uncertain outcome occurring more days than not for at least 6 months.
B. Feeling of worry, nervousness, or unease, typically about an imminent event or something with an uncertain outcome not affecting activities of daily living.
C. Mood disorder that causes a persistent feeling of sadness and loss of interest and can interfere with your daily functioning.

Assessment Question 1 - Pharmacy Technicians

Choose the best definition for anxiety disorder

A. Feeling of worry, nervousness, or unease, typically about an imminent event or something with an uncertain outcome occurring more days than not for at least 6 months.
B. Feeling of worry, nervousness, or unease, typically about an imminent event or something with an uncertain outcome not affecting activities of daily living.
C. Mood disorder that causes a persistent feeling of sadness and loss of interest and can interfere with your daily functioning.

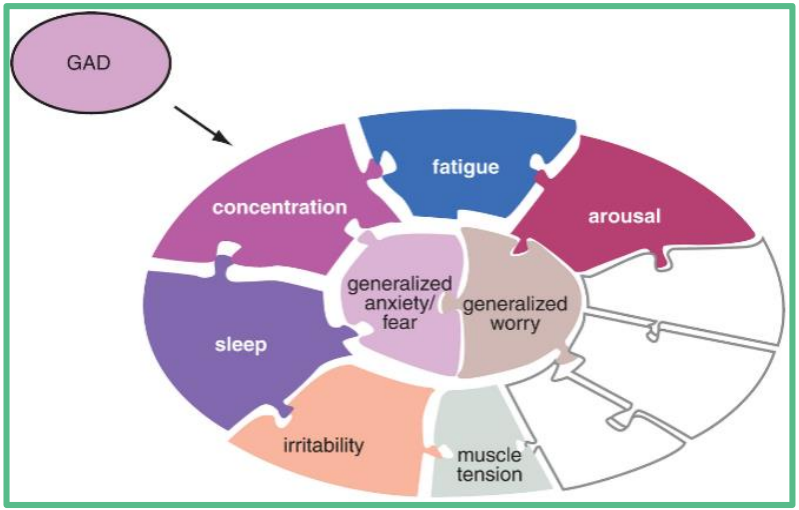
Anxiety Related Disorders

1. Generalized Anxiety Disorder (GAD)
2. Panic Disorder (PD)
3. Post Traumatic Stress Disorder (PTSD)
4. Obsessive compulsive Disorder (OCD)
5. Social Anxiety Disorder (SAD)

GENERALIZED ANXIETY DISORDER (GAD)

GAD Etiology/Risk Factors

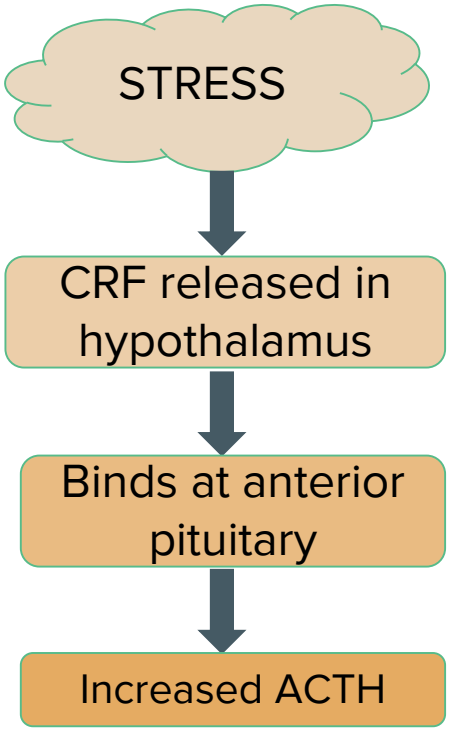
- Women 2x more likely to develop
- **Medications**: anticonvulsants, steroids, NSAIDs, stimulants, thyroid hormone
- Stressful event in susceptible people
- Mean age of onset: 21 years
- Waxing and waning clinical course



Sources: Stahl's Essential Psychopharmacology, 5th edition (2021)
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 5th ed.*

GAD Pathophysiology

1. Noradrenergic Model
2. GABA Receptor Model
3. Serotonin Model



Source: Stahl's Essential Psychopharmacology, 5th edition (2021)

GAD Non-Pharmacological Treatment

- Cognitive Behavioral Therapy
- Dialectical Behavioral Therapy
- Supportive Psychotherapy
- Dynamic Psychotherapy
- Relaxation Training
- Meditation Exercises

Source: American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 5th ed.*

Selective Serotonin Reuptake Inhibitors (SSRIs)

Drug Name	Dosing	Notes
Citalopram (Celexa)	20-40 mg/day Max: 40mg/day Max for elderly: 20mg/day	**Contraindications:** use with MAOi, linezolid, IV methylene blue or pimozide; (fluoxetine, paroxetine – use with thioridazine); (Brisdelle – pregnancy) **Warnings:** QT prolongation (max doses with citalopram/escitalopram); liver disease; SIADH, hyponatremia (elderly at higher risk); bleeding **Side Effects:** • Sexual (decreased libido, ejaculation difficulties, anorgasmia, ED) • Somnolence, insomnia, nausea, dry mouth, diaphoresis (dose related), weakness, tremor, dizziness, HA **Most Activating: Fluoxetine **Most Sedating: Paroxetine, Fluvoxamine **Sertraline is preferred in patients with cardiac risk
Escitalopram (Lexapro)	10 mg/day Mas: 20mg/day Max for elderly: 10mg/day	
Fluoxetine (Prozac, Sarafem)	10-60 mg/day Max 80 mg/day	
Paroxetine (Paxil, Brisdelle)	IR: 10-60 mg/day CR: 12.5 -62.5 mg/day Max: 60mg/day	
Sertraline (Zoloft)	50-200 mg/day Max: 200mg/day	
Fluvoxamine (Luvox)	50-300 mg/day (daily doses > 100 mg/day should be divided BID)	

Source: Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL

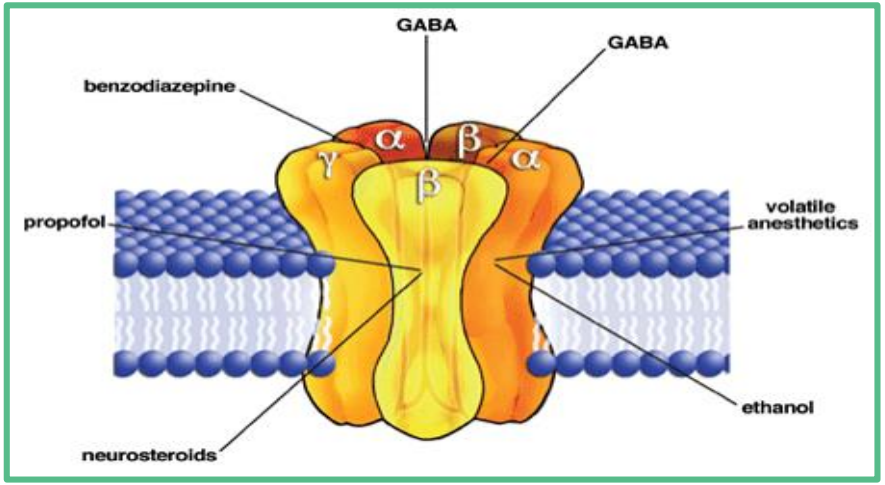
Selective Norepinephrine Reuptake Inhibitors (SNRIs)

Drug Name	Dosing	Notes
Venlafaxine (Effexor XR)	37.5 – 375 mg/day Max: 375 mg/day for IR and 225 mg/day for ER	**Contraindications:** Do not initiate in patient receiving linezolid or IV methylene blue. SNRIs and MAOis can potentially cause a lethal drug interaction : Hypersensitive crisis or serotonin syndrome → Washout period is needed **Side Effects:** similar to SSRIs • SE due to NE: increased HR, dilated pupils (can lead to episode of narrow angle glaucoma) dry mouth, excessive sweating and constipation, increased risk of bleeding • Increased BP: risk greatest with venlafaxine > 150 mg/day • Increased fall risk – use caution in frail patients
Duloxetine (Cymbalta)	40-60 mg/day Max 120 mg/day Doses > 60 mg/day not more effective	
• Venlafaxine has benefit for the psychological symptoms (ruminative worry) • Studies comparing efficacy with pregabalin and venlafaxine demonstrate mixed results • Duloxetine efficacy demonstrated in short and long term trials – decrease in relapse seen at target doses		

Source: Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL

GAD Pharmacological Treatment - Benzodiazepines

- Most frequently prescribed for **ACUTE** treatment
- Long term use not recommended
- Recommended as 2nd line after intolerance established with antidepressants
- NOT effective for depressive symptoms



Sources: NICE Clinical Guidelines, No. 113 (2019)
Alcohol Res Health. 2008; 31(3): 196–214.

Alprazolam (Xanax)

Chlordiazepoxide (Librium)

Clonazepam (Klonopin)

Diazepam (Valium)

Lorazepam (Ativan)

Temazepam (Restoril)

Schedule IV controlled substances

- **BOXED:** use with opioids: sedation, respiratory depression, coma, death
- **Contraindication:** acute narrow angle glaucoma, sleep apnea, severe respiratory insufficiency, severe liver disease (clonazepam and diazepam), myasthenia gravis (diazepam)
- **Warnings:** physiological dependence and tolerance with chronic use; CNS depression, anterograde amnesia, potential for abuse, safety risk in patients age 65 years and older, extravasation with IV use, paradoxical reactions, severe renal or hepatic impairment
- **Side effects:** somnolence, dizziness, ataxia, weakness, lightheadedness

Medication	Rate of Onset	Elimination Half Life (hour)	Equivalent Dose (mg)
Alprazolam	Intermediate	12-15	0.5
Chlordiazepoxide	Intermediate	> 100	10
Clonazepam	Slow	20-50	0.25-0.5
Diazepam	Fast	> 100	5
Lorazepam	Intermediate	10-20	1
Temazepam	Fast	10-20	10-20

Source: Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL

Benzodiazepine Taper

- Switch to a longer acting BZD
- Reduce dose by 50% first 2-4 weeks
- Maintain dose for 1-2 months
- Reduce dose by 25% every 2 weeks

Source: *National Center for PTSD. Effective treatments for PTSD: helping patients taper from benzodiazepines. 2013*

Benzodiazepine Taper

Alprazolam 2mg BID
Convert to Diazepam 40mg daily

Week 1		35 mg/day
Week 2	Total dose decrease by 25%	30 mg/day (25%)
Week 3		25 mg/day
Week 4	Total dose decrease by 50%	20 mg/day (50%)
Week 5-8	Hold dose	Continue at 20 mg/day for 1 month
Week 9-10	Current dose reduction of 25% every 2 weeks	15 mg/day
Week 11-12		10 mg/day
Week 13-14		5 mg/day
Week 15		Discontinue

Source: *National Center for PTSD. Effective treatments for PTSD: helping patients taper from benzodiazepines. 2013*

GAD Pharmacological Treatment - Miscellaneous

Drug Name	Dosing	Notes
Buspirone	Initial 7.5mg BID Dosage range: 15-60 mg/day	• **FDA** approved for GAD 2nd line • 5-HT1A partial agonist; moderate affinity at brain D2 receptors • **Inconsistent reports of efficacy for long term use** • Improvement in worry symptoms precedes relief of somatic symptoms • Not useful in situations requiring immediate anxiolysis
Hydroxyzine	Initial 25 mg BID Max: 400 mg/day	• **FDA** approved for anxiety in adults and children • H1 receptor antagonist and 5-HT2 receptor antagonist • 2nd line therapy due to side effect profile and **lack of efficacy for comorbid disorders** • Active metabolite: cetirizine • ADRs: anticholinergic • Sedative effects seen within 30 mins

Source: Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL

GAD Pharmacological Treatment - Miscellaneous

Drug Name	Dosing	Notes
Pregabalin	Initial: 50 mg TID Dosage range: 150-600 mg/day	• **Not** FDA approved for GAD • Rapid onset of efficacy compared with AD (~ 1 week) • Effective for **short term treatment** - comorbid w/neuropathy • Double blind, placebo controlled trial: switching to pregabalin may be safe and effective method for d/c long term BZD therapy • **Schedule V controlled substance**
Second Generation Antipsychotics	Start low dose and then increase	• **Not** FDA approved for GAD • Anxiolysis through 5-HT1A receptor agonism • Olanzapine, risperidone and quetiapine were effective as augmenting agents in treatment resistant or non-remitted GAD • Quetiapine XR monotherapy is an option
Natural Products	• **Kava**: increasing GABA binding sites; benefit seen at 8 weeks; demonstrated short term safety in clinical trials but linked to hepatotoxicity • **Valerian**: increasing GABA in CNS; reports of hepatotoxicity	

Source: Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL

	Anxiety Disorders Association of Canada (ADAC - 2014)	British Association for Psychopharmacology (BAP-2014)	NICE Generalised anxiety disorder and panic disorder in adults (2019)
1st Line	***SSRI:*** escitalopram, paroxetine, sertraline ***SNRI:*** duloxetine, venlafaxine XR *Other*: pregabalin	***Long term efficacy***: CBT, escitalopram, paroxetine, venlafaxine *BZD:* alprazolam, diazepam *Other*: imipramine; buspirone; hydroxyzine	***SSRI****:* any based on cost effectiveness
2nd Line	BZD (short term); bupropion; buspirone; hydroxyzine; imipramine; quetiapine XR; vortioxetine	Switch to another evidence based treatment after non-response to initial	Another ***SSRI or SNRI***
3rd Line	*SSRI:* citalopram, fluoxetine *Other*: divalproex; mirtazapine; trazodone; SGA augment	Consider use of BZD after non response to SSRI and SNRI Consider combo of CBT with pharmacotherapy	If cannot tolerate SSRI or SNRI consider Pregabalin **Do Not:** offer BZD except as short term during crisis or antipsychotic

Sources: BMC Psychiatry. 2014; 14(Suppl 1): S1. J Psychopharmacol. 2014 May;28(5):403-39. NICE Clinical Guidelines, No. 113 (2019)

1. **Initial Therapy:** medications, psychotherapy or combo
    - First Line: SSRIs or SNRIs
2. **IF full symptoms persist after adequate trial** → switch to another SSRI/SNRI **OR** augment with SGA, BZD, antihistamine, buspirone or pregabalin
3. **IF at least partial response at 4-6 weeks** → titrate to max tolerated dose and re-evaluate at 12 weeks
    - **Current Data:** not clear to increase the dose, augment or switch when partial response seen

Sources: BMC Psychiatry. 2014; 14(Suppl 1): S1. J Psychopharmacol. 2014 May;28(5):403-39. NICE Clinical Guidelines, No. 113 (2019)

Assessment Question 1- Pharmacists & Nurses

Which of the following neurotransmitters is not included in the main GAD pathophysiology models?

A. Serotonin
B. Acetylcholine
C. GABA
D. Norepinephrine

Assessment Question 1- Pharmacists & Nurses

Which of the following neurotransmitters is not included in the main GAD pathophysiology models?

A. Serotonin
B. Acetylcholine
C. GABA
D. Norepinephrine

Assessment Question 2- Pharmacy Technicians

Which of the following is NOT FDA indicated for generalized anxiety disorder?

A. Citalopram
B. Venlafaxine
C. Buspirone
D. Pregabalin

Assessment Question 2- Pharmacy Technicians

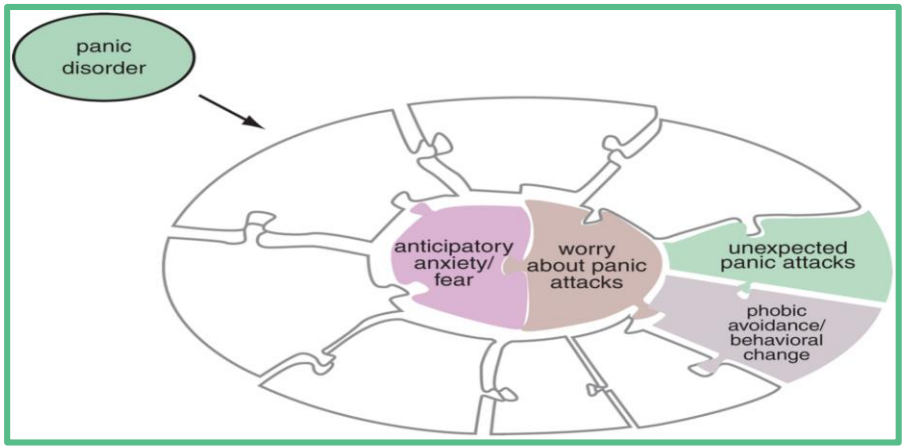
Which of the following is NOT FDA indicated for generalized anxiety disorder?

A. Citalopram
B. Venlafaxine
C. Buspirone
D. Pregabalin

PANIC DISORDER (PD)

PD Etiology/Risk Factors

- Women twice as likely to develop
- Panic attacks occur unexpectedly, but in context
- Personality Type
- Stressful Life Events
- Medical Conditions
- Clinical Course:
  - Waxing and waning over time
  - One-third achieve remission
  - Predictors of chronic course



Sources: Stahl's Essential Psychopharmacology, 5th edition (2021)
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 5th ed.*

Panic Attack Sign and Symptoms

Psychological Symptoms

- Depersonalization
- Derealization
- Fear of losing control
- Fear of going crazy
- Fear of dying

Physical Symptoms

- Abdominal/Chest pain
- Dizziness
- Hot flashes
- Palpitations
- Trembling/shaking

Sources: Stahl's Essential Psychopharmacology, 5th edition (2021)
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 5th ed.*

PD Pathophysiology

1. Neurobiology
   a. Reduced volume in amygdala and temporal lobe
   b. Decreased cerebral glucose metabolism
   c. Reductions in BZD-receptor density in amygdala

2. Psychopathology
   a. Anxiety sensitivity - can cause deleterious physical, social and psychological consequences
   b. Maintenance of panic - acute fear develops after initial panic attack

Source: Stahl's Essential Psychopharmacology, 5th edition (2021)

	Anxiety Disorders Association of Canada (ADAC - 2014)	British Association for Psychopharmacology (BAP-2014)
1st Line	***SSRI:*** citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline ***SNRI:*** venlafaxine	**CBT** ***SSRI:*** All ***SNRI:*** venlafaxine ***BZD:*** alprazolam, clonazepam, diazepam, lorazepam ***TCA:*** clomipramine, imipramine
2nd Line	*TCA:* clomipramine, imipramine *BZD:* alprazolam, clonazepam, diazepam Mirtazapine	Switch to another evidence based treatment after non-response at 12 weeks
3rd Line	Bupropion, divalproex, duloxetine, gabapentin, levetiracetam, milnacipran, SGA, phenelzine, tranylcypromine	Combination of evidence based treatment with no contraindications

Sources: BMC Psychiatry.2014;14(Suppl 1): S1. J Psychopharmacol. 2014 May;28(5):403-39.

	Anxiety Disorders Association of	British Association for

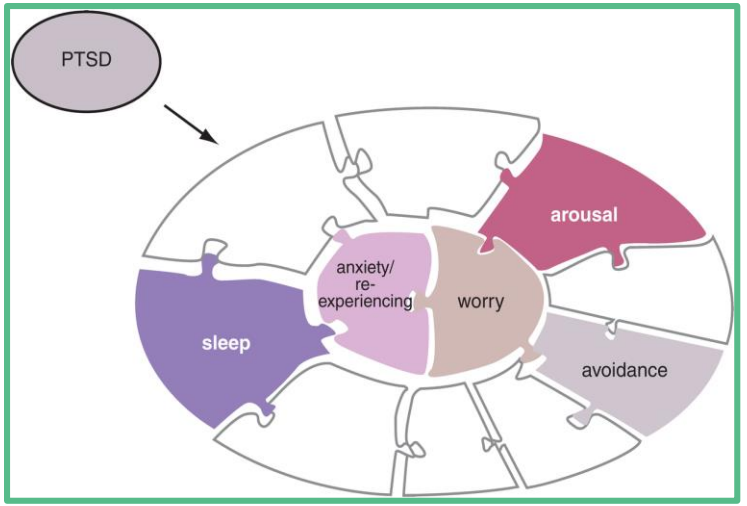
1. **Initial Therapy:** medications, psychotherapy or combo
    - First Line: SSRIs or venlafaxine
2. **BZDs:** may be used in absence of history of SUD *when rapid control needed*
3. **TCAs:** comparable efficacy to SSRI/SNRIs - less well tolerated
4. **IF full symptoms after adequate trial:** switch to another SSRI or venlafaxine **OR** augmentation w/ SGA or BZD depending on comorbid symptoms/disorders
5. **Phenelzine:** reserved for treatment resistance

Sources: BMC Psychiatry.2014;14(Suppl 1): S1. J Psychopharmacol. 2014 May;28(5):403-39.

POST TRAUMATIC STRESS DISORDER (PTSD)

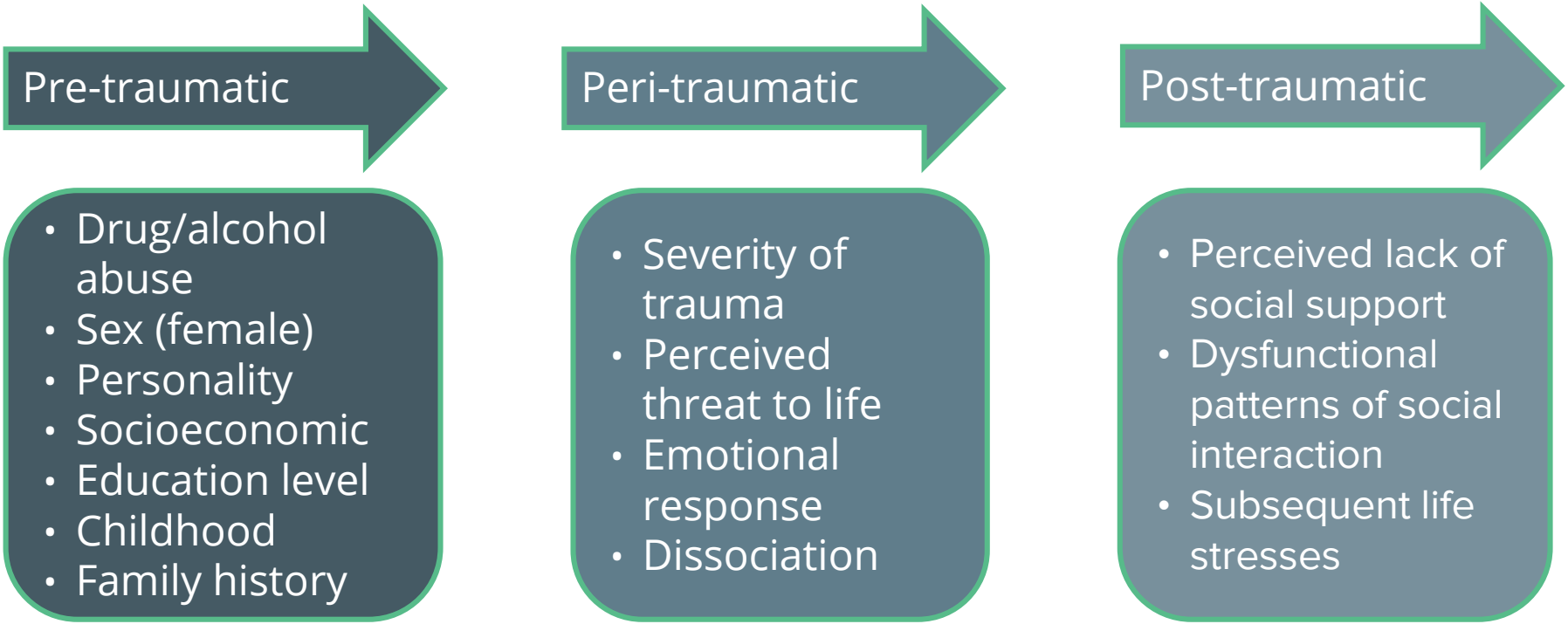
PTSD Etiology/Clinical Course

- Personal predisposition
- Biologic Perspective
- ~ 1 in 27 (3.6%) or 9.8 million in US
- Symptomatic distress peaks days/weeks after trauma and gradually decline
- Average duration if treatment: 36 months
- Average duration if no treatment: 5 years
- Rates of recovery vary by gender



Sources: Stahl's Essential Psychopharmacology, 5th edition (2021)
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 5th ed.*

PTSD Risk Factors



Sources: Stahl's Essential Psychopharmacology, 5th edition (2021)
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 5th ed.*

PTSD Concurrent Conditions

Depression
80%

Alcohol or Substance Use Disorder
50%

Attempted Suicide
20%

Sources: Stahl's Essential Psychopharmacology, 5th edition (2021)
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 5th ed.*

PTSD Pathophysiology

1. Cortisol Levels
    a. Lower than normal due to “adrenal exhaustion”
2. HPA Axis and Sympathetic Nervous System (SNS)
    a. Abnormal increases in SNS reactivity and adrenergic dysregulation
3. Alpha 1 and Alpha 2 adrenergic postsynaptic receptors
4. Acoustic Startle Response

Source: Stahl's Essential Psychopharmacology, 5th edition (2021)

	Veterans Association DOD (2017)	Agency for Healthcare Research and Quality (2018)	American Academy of Sleep Medicine (2018)	National Institute for Health and Care Excellence (2018)
1st Line	**Trauma focused psychotherapy and stress management**	**CBT** (exposure and mixed therapy) ***SSRI:*** fluoxetine, paroxetine ***SNRI:*** venlafaxine	For PTSD associated nightmares: image rehearsal therapy	Individual trauma-focused CBT including **cognitive processing therapy**, cognitive therapy for PTSD, narrative exposure therapy, prolonged exposure therapy venlafaxine; SSRIs
2nd Line	Non-trauma focused **psychotherapy** *SSRI*: paroxetine, sertraline, fluoxetine *SNRI*: venlafaxine	Cognitive processing therapy, cognitive therapy, EMDR and narrative exposure therapy	**CBT, EMDR**, exposure, relaxation and rescripting therapy *Other:* SGAs (olanzapine, risperidone and aripiprazole), clonidine, cyproheptadine, fluvoxamine, gabapentin, nabilone, phenelzine, prazosin, topiramate, trazodone, TCAs	**EMDR** following a non-combat related trauma; CBT for sleep or anger if symptoms persist or if a trauma focused intervention is not feasible *Other:* SGAs
3rd Line	imipramine; nefazodone; phenelzine	Brief eclectic psychotherapy, imagery rehearsal therapy, trauma affect regulation *Other:* prazosin, topiramate, olanzapine, risperidone, sertraline		

Sources: London: National Institute for Health and Care Excellence (NICE); 2018 Dec. AHRQ Publication No. 18-EHC011-EF PCORI Publication No. 2018-SR-01. May 2018. J Clin Sleep Med. 2018 Jun 15; 14(6): 1041–1055.. (Am Psychiatr Publ). 2018 Oct;16(4):430-448.

1. **Initial Therapy:** Trauma focused psychotherapy OR pharmacotherapy with SSRI/SNRI
2. **No response to initial AD dose:** increase the dose, consider longer duration, switch to another SSRI/SNRI or add psychotherapy
3. **Failed 2nd trial of AD:** switch to another SSRI/SNRI or mirtazapine or add psychotherapy
4. **Failure of 3 trials:** augmentation, re-evaluate diagnosis, switch to TCA or consider phenelzine
5. **All guidelines recommend AGAINST the use of BZDs** - no evidence in reducing core symptoms

Sources: London: National Institute for Health and Care Excellence (NICE); 2018 Dec. AHRQ Publication No. 18-EHC011-EF PCORI Publication No. 2018-SR-01. May 2018. J Clin Sleep Med. 2018 Jun 15; 14(6): 1041–1055.. (Am Psychiatr Publ). 2018 Oct;16(4):430-448.

PTSD Comorbid Treatment

Sleep:

- Insomnia and nightmares are core symptoms
- May respond to first line tx, however often persist
- Assess **lifestyle and sleep hygiene**
- Limit caffeine, nicotine and OTC stimulant use
- Trazodone, mirtazapine, olanzapine, quetiapine, low dose TCAs and zolpidem have shown some efficacy

Sources: Stahl's Essential Psychopharmacology, 5th edition (2021)
(Am Psychiatr Publ). 2018 Oct;16(4):430-448.

PTSD Comorbid Treatment

Psychosis:

- Found in as many as 40% - determine if part of PTSD or comorbid psychotic d/o
- Treat with SSRIs first to target underlying sx
- Flashbacks, hypervigilance/paranoia and dissociation may respond to antiadrenergics and anticonvulsants

Sources: Stahl's Essential Psychopharmacology, 5th edition (2021)
(Am Psychiatr Publ). 2018 Oct;16(4):430-448.

PTSD Comorbid Treatment

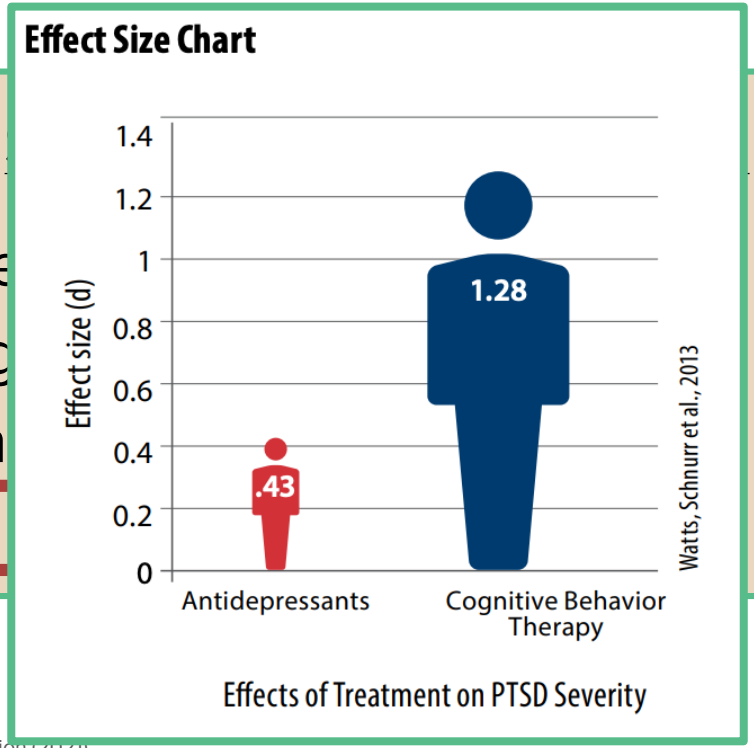
Substance Use Disorders:

- Should be abstinent for 1 week prior to beginning treatment for PTSD
- Treatment algorithm the same
- BZDs are contraindicated

Sources: Stahl's Essential Psychopharmacology, 5th edition (2021)
(Am Psychiatr Publ). 2018 Oct;16(4):430-448.
National Center for PTSD. Effective treatments for PTSD: helping patients taper from benzodiazepines. 2013

PTSD Comorbid Treatment

- Should be … to beginning …
- Treatmen …
- BZDs are …



Sources: Stahl's Essential Psychopharmacology, 5th edition (2021)
(Am Psychiatr Publ). 2018 Oct;16(4):430-448.
National Center for PTSD. Effective treatments for PTSD: helping patients taper from benzodiazepines. 2013

Assessment Question 2 – Pharmacists & Nurses

Which of the following medications is guideline recommended as first line therapy for PTSD?

A. Lorazepam
B. Sertraline
C. Venlafaxine
D. Citalopram

Assessment Question 2 - Pharmacists& Nurses

Which of the following medications is guideline recommended as first line therapy for PTSD?

A. Lorazepam
B. Sertraline
C. Venlafaxine
D. Citalopram

Assessment Question 3 - Pharmacy Technicians

Which of the following medications are controlled and need special handling based on FDA controlled substance laws? (choose all that apply)

A. Pregabalin
B. Lorazepam
C. Gabapentin
D. Escitalopram

Assessment Question 3 - Pharmacy Technicians

Which of the following medications are controlled and need special handling based on FDA controlled substance laws? (choose all that apply)

A. Pregabalin
B. Lorazepam
C. Gabapentin
D. Escitalopram

Obsessive Compulsive Disorder (OCD)

OCD Clinical Presentation/Pathophysiology

Obsessions

- Fear of contamination
- Unwanted sexual/aggressive thoughts
- Doubts
- Throwing away something valuable
- Need for symmetry

Compulsions

- Washing/cleaning
- Checking, praying, “undoing actions”
- Repeated checking behaviors
- Hoarding
- Ordering, arranging, balancing

- Recurrent and persistent
- Causes marked anxiety or distress
- Attempts to ignore or suppress such thoughts, urges or images

- Repetitive behaviors aimed at preventing/reducing anxiety or distress
- **NOT** connected in a realistic way or are clearly excessive

Sources: Stahl's Essential Psychopharmacology, 5th edition (2021)
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 5th ed.*

	BAP-2014	ADAC - 2014
1st Line	***Exposure therapy and CBT*** ***SSRIs***	***SSRI:*** escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline ***SNRI:*** venlafaxine Adjunct w/ SGA (aripiprazole, risperidone)
2nd Line	clomipramine	citalopram; clomipramine; mirtazapine; venlafaxine *Adjunctive*: memantine, quetiapine, topiramate
3rd Line	SSRI or clomipramine w/CBT Augmentation w/SGA	duloxetine; phenelzine; tramadol, tranylcypromine *Adjunctive*: celecoxib, haloperidol, mirtazapine, pindolol, pregabalin, IV ketamine, olanzapine, ziprasidone, citalopram

Response rates show 20-30% have significant improvement, 40-50% have moderate improvement and 20-40% either remain ill or symptoms worsen

Sources: BMC Psychiatry.2014;14(Suppl 1): S1.; J Psychopharmacol. 2014 May;28(5):403-39.

1. **Initial Therapy:** CBT or pharmacotherapy with SSRI - combo superior to pharmacotherapy alone but NOT to CBT alone
    a. Continue first line for at least 12 weeks and CBT trial of 13 weekly sessions before concluding inadequate response
2. **Little or no response:** try another SSRI or venlafaxine
3. **Failure of 2 SSRIs:** Clomipramine recommended

Sources: BMC Psychiatry.2014;14(Suppl 1): S1.; J Psychopharmacol. 2014 May;28(5):403-39.

Social Anxiety Disorder (SAD)

SAD Clinical Presentation/Pathophysiology

Fears	Feared Situations	Physical Symptoms	Types
• Scrutinized by others • Embarrassment • Humiliation	• Public speaking • Eating/drinking in front of others • Interacting with authority • Talking with strangers • Use of public restrooms	• Blushing • "Butterflies" in stomach • Diarrhea • Sweating • Tachycardia • Trembling	• ***Generalized***: fear and avoidance of a wide range of social situations • ***Non-generalized***: fear is limited to one or two situations

- Performance only subtype - NE system dysfunction
- DA dysfunction: decreased D2 receptor binding; low levels of DA metabolite
    - High incidence of SAD in patients w/ Parkinson's disease

Sources: Stahl's Essential Psychopharmacology, 5th edition (2021)
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 5th ed.*

	BAP-2014	ADAC - 2014	NICE (2013)
1st Line	**CBT** ***SSRI:*** escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline	**CBT** ***SSRI:*** escitalopram, fluvoxamine, paroxetine, sertraline ***SNRI:*** venlafaxine Pregabalin	**CBT** ***SSRI:*** escitalopram or sertraline
2nd Line	*SNRI:* venlafaxine *BZD:* clonazepam	*BZD:* clonazepam, alprazolam gabapentin citalopram phenelzine	*Alternative SSRI:* fluvoxamine, paroxetine *SNRI:* venlafaxine
3rd Line	Augmentation of SSRI w/ buspirone *Other:* gabapentin, pregabalin, olanzapine	atomoxetine, fluoxetine, bupropion, duloxetine, mirtazapine, divalproex, topiramate, selegiline, olanzapine, clomipramine Adjunct w/SGA, buspirone, paroxetine	phenelzine

Beta-Blockers used in performance related SAD to decrease tremor, palpitations and blushing → Propranolol 10-80 mg or atenolol 25-50 mg 1-2 hours prior

Sources: BMC Psychiatry.2014;14(Suppl 1): S1.; J Psychopharmacol. 2014 May;28(5):403-39.; NICE Clinical Guidelines, No. CG113.

1. **Initial Therapy:** individual CBT or SSRI
    a. First line pharmacotherapy should be continued for at least <u>10-12 weeks at max dosage</u> before concluding inadequate
2. **With little or no response:** try another SSRI or venlafaxine
3. **Limited evidence supports augmentation in partial response**
4. **Refractory:** phenelzine is an option

Sources: BMC Psychiatry.2014;14(Suppl 1): S1.; J Psychopharmacol. 2014 May;28(5):403-39.; NICE Clinical Guidelines, No. CG113.

Assessment Question 3 – Pharmacists & Nurses

Which medication is considered “best practice” to be used as needed for performance based anxiety?

A. Clonidine
B. Propranolol
C. Sertraline
D. Lorazepam

Assessment Question 3 – Pharmacists & Nurses

Which medication is considered “best practice” to be used as needed for performance based anxiety?

A. Clonidine
B. Propranolol
C. Sertraline
D. Lorazepam

Conclusions

- First line pharmacotherapy for most anxiety related disorders: SSRIs/SNRIs
- Dosing of SSRIs: usually start at half initial dose for depression
  - **Do not** provide immediate effect: at least 4 weeks at higher doses
- Usually trial 2-3 SSRIs before augmentation or switch
- Can utilize other antidepressants depending on comorbid disorders

References

- Abejuela HR, Osser DN. The Psychopharmacology Algorithm Project at the Harvard South Shore Program: An Algorithm for Generalized Anxiety Disorder. *Harv Rev Psychiatry*. 2016;24(4):243-256. doi:10.1097/HRP.0000000000000098
- Baldwin DS, Anderson IM, Nutt DJ, et al. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. *J Psychopharmacol*. 2014;28(5):403-439. doi:10.1177/0269881114525674
- Bandelow B, Zohar J, Hollander E, et al. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and post-traumatic stress disorders - first revision. *World J Biol Psychiatry*. 2008;9(4):248-312. doi:10.1080/15622970802465807
- Diagnostic and Statistical Manual of Mental Disorders: DSM-5. 5th ed., American Psychiatric Association, 2013. DSM-V, doi-org.db29.linccweb.org/10.1176/appi.books.9780890425596.dsm02.
- Forbes D, Creamer M, Phelps A, et al. Australian guidelines for the treatment of adults with acute stress disorder and post-traumatic stress disorder. *Aust N Z J Psychiatry*. 2007;41(8):637-648. doi:10.1080/00048670701449161
- Guideline Watch: Practice Guideline for the Treatment of Patients With Panic Disorder. *APA Practice Guidelines for the Treatment of Psychiatric Disorders: Comprehensive Guidelines and Guideline Watches*. 2009. doi:10.1176/appi.books.9780890423363.148548
- *Generalised anxiety disorder and panic disorder in adults: management*. London: National Institute for Health and Care Excellence (NICE); July 2019.
- Katzman MA, Bleau P, Blier P, et al. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. *BMC Psychiatry*. 2014;14 Suppl 1(Suppl 1):S1. doi:10.1186/1471-244X-14-S1-S1
- Lovinger DM. Communication networks in the brain: neurons, receptors, neurotransmitters, and alcohol. *Alcohol Res Health*. 2008;31(3):196-214.
- National Institute for Health and Care Excellence. (2011). Generalised anxiety disorder in adults (Clinical guideline CG113). Retrieved from: https://www.nice.org.uk/guidance/CG113
- Shapiro F. The role of eye movement desensitization and reprocessing (EMDR) therapy in medicine: addressing the psychological and physical symptoms stemming from adverse life experiences. *Perm J*. 2014;18(1):71-77. doi:10.7812/TPP/13-098
- Stahl SM. Stahl's Essential Psychopharmacology: Neuroscientific Basis and Practical Applications. Cambridge, UK: Cambridge University Press; 2021.
- VA/DOD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder: Clinician Summary. *Focus (Am Psychiatr Publ)*. 2018;16(4):430-448. doi:10.1176/appi.focus.16408

Thank you!

Enxhi Plaku,PharmD
PGY-2 Psychiatric Pharmacy Resident
Enxhi.Plaku@rwjbh.org