More Than Stress: A Pharmacist's Guide to Addressing Anxiety

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Disclosure Statement

- The speaker 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.

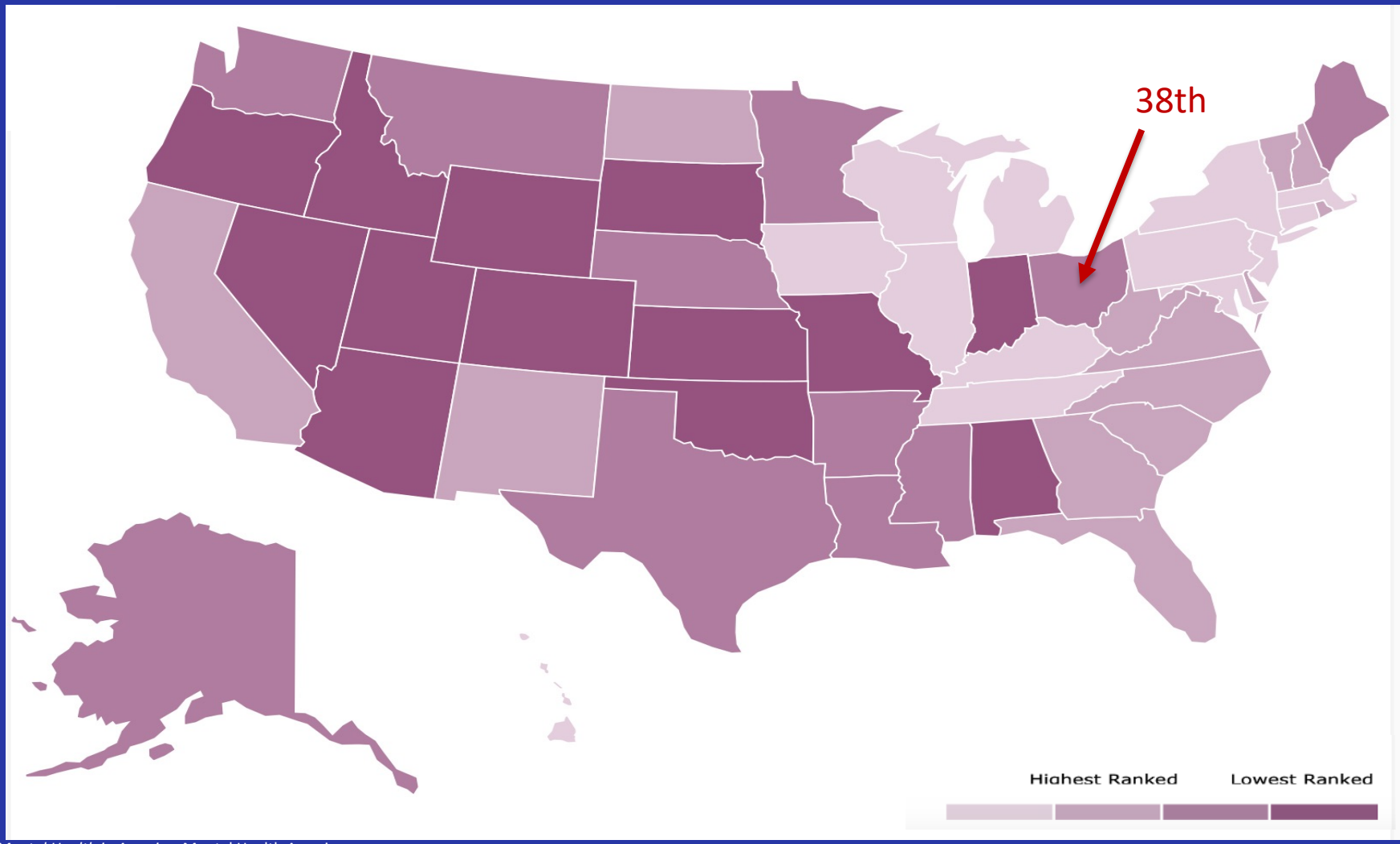
Learning Objectives

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

1. Recognize the signs and symptoms of generalized anxiety disorder (GAD)
2. Review how to screen for GAD and interpret results
3. Select an appropriate treatment and monitoring plan for GAD based on patient specific factors

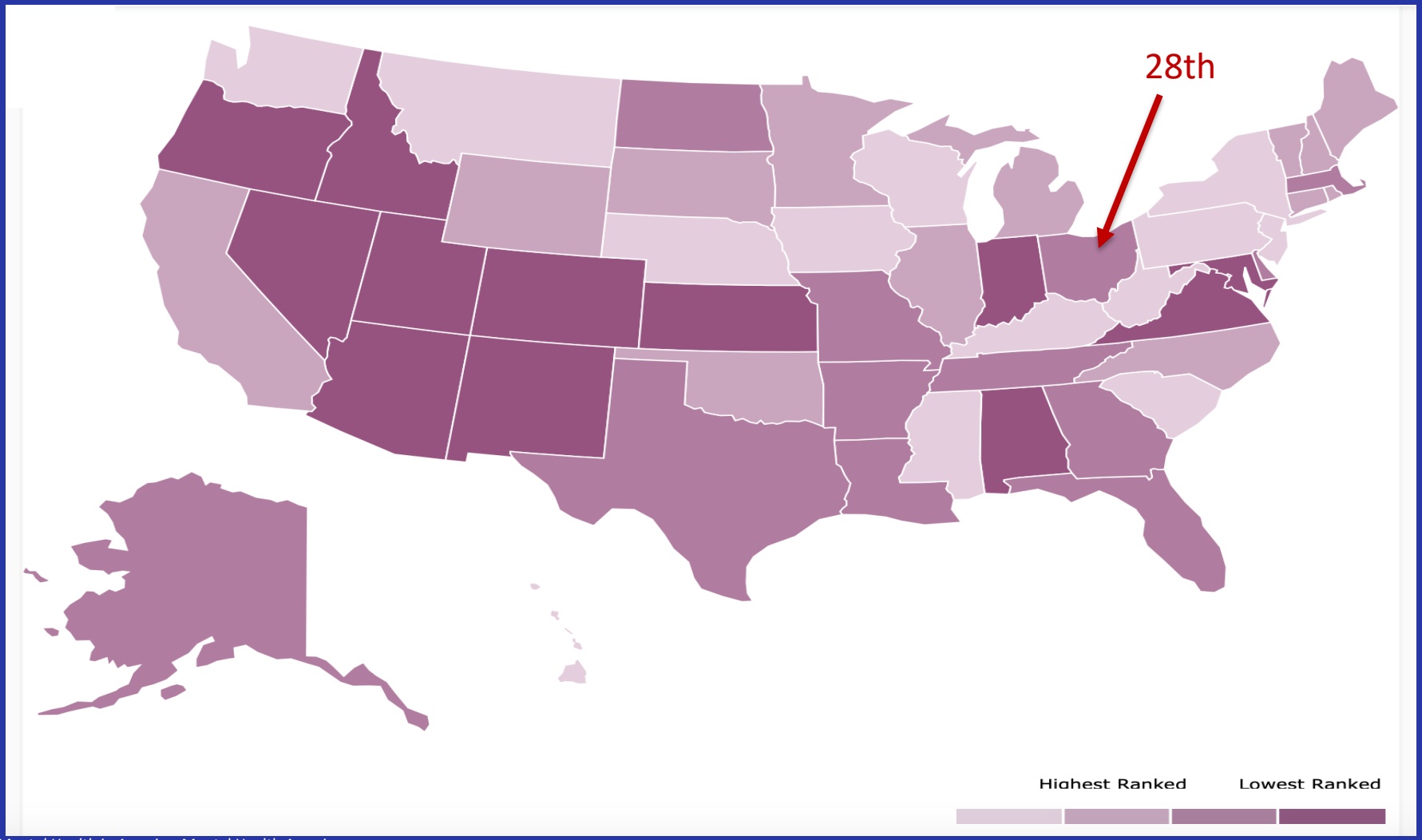
MENTAL HEALTH IN AMERICA

Adult Rankings 2023- Any Mental Illness (AMI)



State of Mental Health in America. Mental Health America. https://mhanational.org/issues/2023/mental-health-america-adult-data

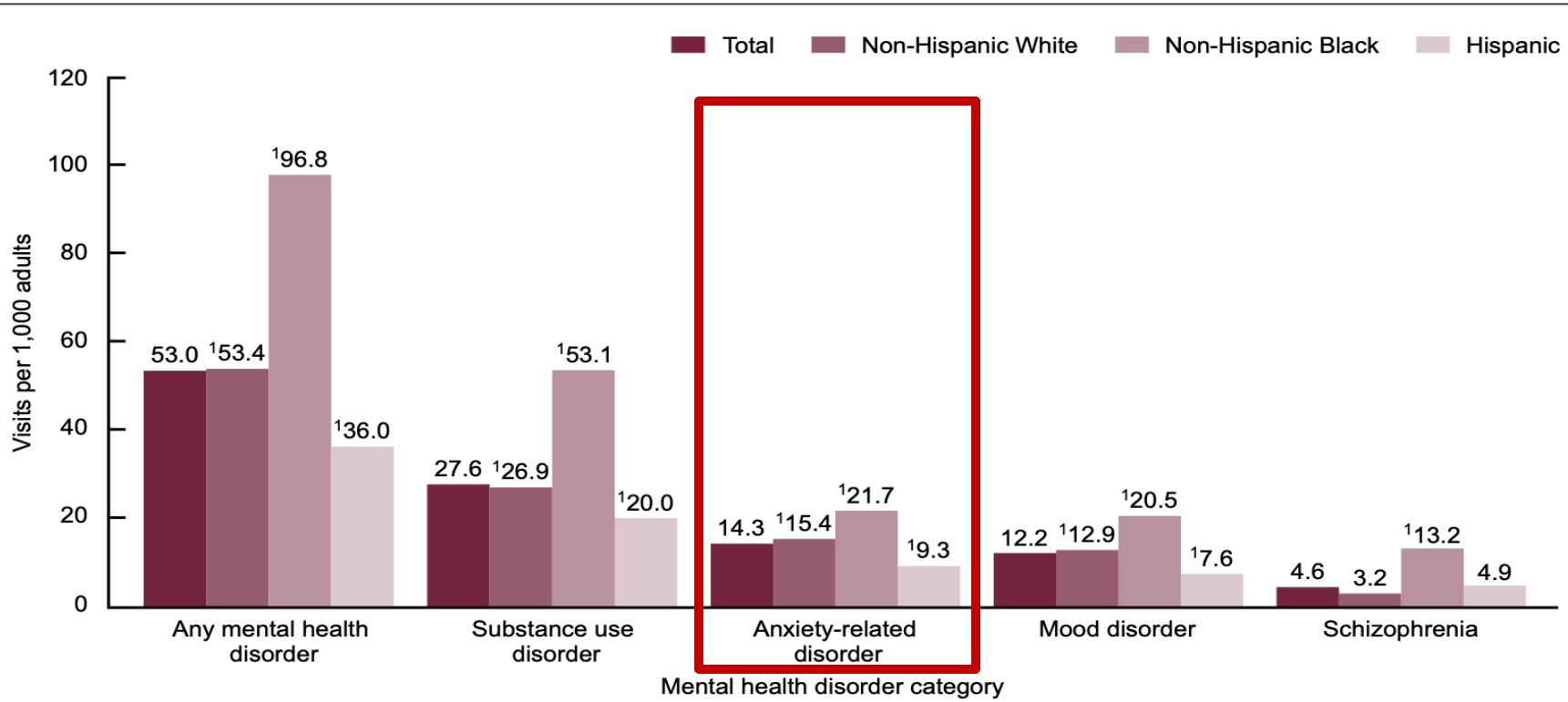
Adults Reporting Unmet Need for AMI Care 2023



State of Mental Health in America. Mental Health America.
https://mhanational.org/issues/2023/mental-health-america-adult-data

Unmet Need = ED Visits

Figure 1. Annual average rates of mental health-related emergency department visits among adults, by race and Hispanic ethnicity: United States, 2018–2020



[1]Significantly different from all other race and Hispanic-ethnicity categories.
NOTES: Data are based on 5,926 mental health-related emergency department (ED) visits in 2018–2020, representing 774,508 visits annually (12.3% of all ED visits made by adults). Other mental health disorders are included in any mental health disorder but not as their own category; these include mental disorders due to known physiological conditions, disorders of adult personality and behavior, intellectual disabilities, pervasive and specific developmental disorders, and behavioral disorders with onset in childhood or adolescence. Race categories of Asian, Native Hawaiian or Other Pacific Islander, American Indian or Alaska Native, and people with more than one race are included in the total but not as separate categories due to low sample sizes. A visit may be represented in more than one mental health disorder category.
SOURCE: National Center for Health Statistics, National Hospital Ambulatory Medical Care Survey, 2018–2020.

Peters, Z. (2023). Emergency Department Visits Related to Mental Health Disorders Among Adults, by Race and Hispanic Ethnicity: United States, 2018–2020. *National Health Statistics Report*. https://www.cdc.gov/nchs/data/nhsr/nhsr181.pdf

Epidemiology

- Lifetime prevalence ~33%
- Age of onset differs with disorder
- Women > Men
- Caucasian > other pops
- Genetic link
- Income correlation
- Stressful events

Consequences

- Chronic health conditions
- Physical disability
- Lower quality of life
- Inability to complete daily activities
- Isolation

Societal Impact

> $40 billion annually

Nearly 1/3 of healthcare costs

Indirect effect on relationships

Loss of productivity

Differentiating Our Response

FEAR

STRESS

TRAUMA

ANXIETY

Anxiety Disorders

- Generalized anxiety disorder (GAD)
- Post-traumatic stress disorder (PTSD)
- Phobia-related disorders
- Social anxiety disorder (SAD)
- Panic disorder

GENERALIZED ANXIETY DISORDER (GAD)

Symptom Onset

May occur at any age

Mean age of onset is 21

In children and adolescent, mean age if 10-14

Symptoms may wax and wane over time

Clinical Presentation

Psychological and Cognitive Symptoms

- Excessive worry
- Worries that are difficult to control
- Feeling keyed up or on edge
- Poor concentration
- Restlessness
- Irritability

Physical Symptoms

- Fatigue
- Muscle tension
- Sleep disturbance

Impairment

- Social or functional
- Poor coping skills

Links to GAD

Gender	Medications	Herbal products
Medical conditions	Socioeconomic factors	Life events

Drug-induced Anxiety

Prescription	Illicit	Herbal
• Stimulants • Carbamazepine • Phenytoin • Bupropion, SSRI, SNRI • Albuterol • Steroids • Dopamine Agonists • Pseudoephedrine • Levothyroxine	• Cocaine • Ecstasy • Marijuana • Amphetamines	• Ginseng • Kava • St. John's Wort

GAD Diagnosis (DSM-5)

Excessive anxiety and worry lasting for at least 6 months and difficulty controlling the worry

Presence of at least 3 of the following symptoms:

- Feeling keyed up or on edge; restlessness
- Becoming easily fatigued
- Mind going blank; difficulty concentrating
- Irritability
- Muscle tension
- Sleep disturbance

Focus of the anxiety and worry are not caused by another psychiatric disorder

Significant distress or functional impairment

Symptoms not caused by another substance

Generalized Anxiety Disorder Assessment- 7 (GAD-7)

- 7-item scale
- Screens for GAD and assess severity
- Self-rated
- Brief (3-5 minutes for patient to complete)

GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

Total Score ___ = Add Columns ___ + ___ + ___

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

GAD-7 Interpretation

- Scoring:
  - 5-9 = mild
  - 10-14 = moderate
  - 15+ = severe anxiety
- When used as a screening tool, further evaluation is recommended when score is $\geq$ 10

TREATMENT

Goals for Treatment

- Remission
- Resolve/minimize functional impairment
- Improve quality of life
- Prevent relapse
- Patient-specific goals

Non-Pharm Options

Cognitive Behavioral Therapy (CBT)

- Most effective psychological therapy
- Costly
- Time intensive

Supportive Therapy

- Counseling focus

Relaxation Training

- Focus on reducing stress response
- Meditation

1ST LINE

SSRI and SNRI

1st line for GAD

Class effect?

Delay in onset of action

Start low dose (1/2 of recommended starting dose)

Selective Serotonin Reuptake Inhibitor (SSRI)

Medication	Dosing	Considerations	Pearls
Citalopram*	10mg daily; max 40mg daily	Hepatic: max 20mg Older adult: max 20mg	Highest QTc risk: • 10mg ~ 8msec • 20mg ~12msec • 40mg ~ 18msec
Escitalopram	10mg daily; max 20mg daily	Hepatic: max 10mg Older adult: max 10mg	• Starting dose older adult: 5mg; max 10mg
Fluoxetine*	10-20mg daily; max 60mg daily	Hepatic: start 10mg	• Activating SSRI • Long half-life
Paroxetine	20mg daily; max 50mg daily	Hepatic/Renal: 10mg; max 40mg Older Adult: 10mg; max 40mg	• Most anticholinergic
Sertraline*	25mg daily; max 200mg daily	Hepatic: ½ dosing	

* = off-label

Serotonin and Norepinephrine Reuptake Inhibitor (SNRI)

Medication	Dosing	Considerations	Pearls
Venlafaxine	37.5-75mg; max 225mg	Hepatic: reduce dose 50% Renal: reduce dose 50%	• Consider comorbid conditions
Duloxetine	30-60mg; max 120mg*	Hepatic: Avoid Renal: CrCl <30 Avoid	• Consider comorbid conditions

Counseling Considerations

Sleep disturbances

- Sleep hygiene
- Dose in AM vs. PM

Sexual dysfunction

- Reduce dose
- Once weekly one-day drug holiday
- Add bupropion

Discontinuing Therapy

- Discontinuation symptoms
- Taper therapy over a few weeks-month
- Switching within class vs. outside of class

2ND LINE
+ AUGMENTATION

Other Options

Medication	Dosing	Considerations	Pearls
Amitriptyline*	25-50mg daily; max 150mg	Older adults and ↑ potential ADR	• Tertiary amine = ↑ anticholinergic
Nortriptyline*	25-50mg daily; max 150mg	Older adults and ↑ potential ADR	• Secondary amine = ↓ anticholinergic
Pregabalin*	150mg/day in divided doses; max 600mg/day	Controlled substance	• Short + long-term data for GAD • Quicker onset
Buspirone	10-15mg/day in divided doses; max 60mg	Hepatic: Avoid in severe impairment	• Delay to effect • Effective post-benzo use?
Hydroxyzine	50-75mg/day in divided doses	Scheduled or as needed use	• Quick onset • Effective for acute symptoms • Anticholinergic

* = off-label

Second Generation Antipsychotics (SGA)

- Evidence is limited for monotherapy with SGAs
- Evidence suggests may be beneficial in augmentation
  - Olanzapine
  - Risperidone
  - Quetiapine
- Metabolic side effects associated with SGAs
- Place in therapy likely for refractory symptoms

Limited Use

- Monoamine Oxidase-Inhibitors
  - 3rd line due to ADE and dietary restrictions
- Mirtazapine
  - Studies available in panic disorder and PTSD
  - No clinical trials for use in GAD but will see use
- Vilazodone and Vortioxetine
  - Limited evidence
- Anticonvulsants
- Natural products
  - Valerian
  - Lavender oil

BENZOS IN GAD?

Benzodiazepine Options

Alprazolam (Xanax®)	Chlordiazepoxide (Librium®)	Clonazepam (Klonopin®)	Clorazepate (Tranxene®)
Diazepam (Valium®)	Estazolam (ProSom®)	Halazepam (Paxipam®)	Lorazepam (Ativan®)
Midazolam (Versed®)	Oxazepam (Serax®)	Flurazepam (Dalmane®)	Quazepam (Doral®)
	Temazepam (Restoril®)	Triazolam (Halcion®)	

Place in Therapy

- Symptomatic relief during delay to effect with antidepressant
  - Less effective than antidepressants
  - Relapse rates higher than antidepressants
  - Work more quickly than antidepressants
  - Limit use to 2-4 weeks
- Short term distress – ie: air travel, prior to procedure
- VERY rarely used long-term for refractory anxiety

Benzodiazepine Selection

- **Onset of action**
  - Related to lipid solubility
- **Half-life**
  - Long ½ life preferred in anxiety disorders
- **Metabolism**
  - Avoid: liver disease and the elderly
  - **LOT →** lorazepam, oxazepam, and temazepam

Misuse Potential

Risk Factors for Misuse

- High benzodiazepine doses
- Use of potent or short acting benzodiazepines
- Long duration of therapy

Minimizing Misuse Potential

- Ensure adequate dosing intervals
- Use controlled substance agreements
- Short-term use

Discontinuation of Benzo

- Rebound Anxiety
- Relapse
- Withdrawal

Tapering Benzodiazepines

- Consider starting/titrating first line anxiety medication or CBT
- Adjunctive use of pregabalin may be beneficial
- Slow Taper : may take months-years
- May switch to long-acting benzodiazepine
- Consider use of benzodiazepine with active metabolites
- Consider available strengths of benzodiazepines

Taper Considerations

As the dose gets smaller, decrease dose reduction

- ~25% reduction per 1-2 weeks until 50% of dose reached
- Smaller reduction thereafter

Try never to go backwards (increase the dose)

May still experience withdrawal symptoms

- At lower doses, withdrawal symptoms may worsen

SPECIAL POPULATIONS

Older Adults

- Special attention to max doses
- Minimize number and dose of drugs
- Citalopram and escitalopram QTc risk
- ⇧ risk of hyponatremia
- AVOID paroxetine (most anticholinergic)
- If benzo needed, remember LOT

Pregnancy

- Weigh risk of untreated anxiety vs. risk of medication
- Minimize number and dose of drugs
- DOC: citalopram, fluoxetine, and sertraline
- AVOID paroxetine
- AVOID benzos during 1st trimester

PEARLS FOR MANAGEMENT

GAD Treatment

1st Line:

- SSRI
- SNRI

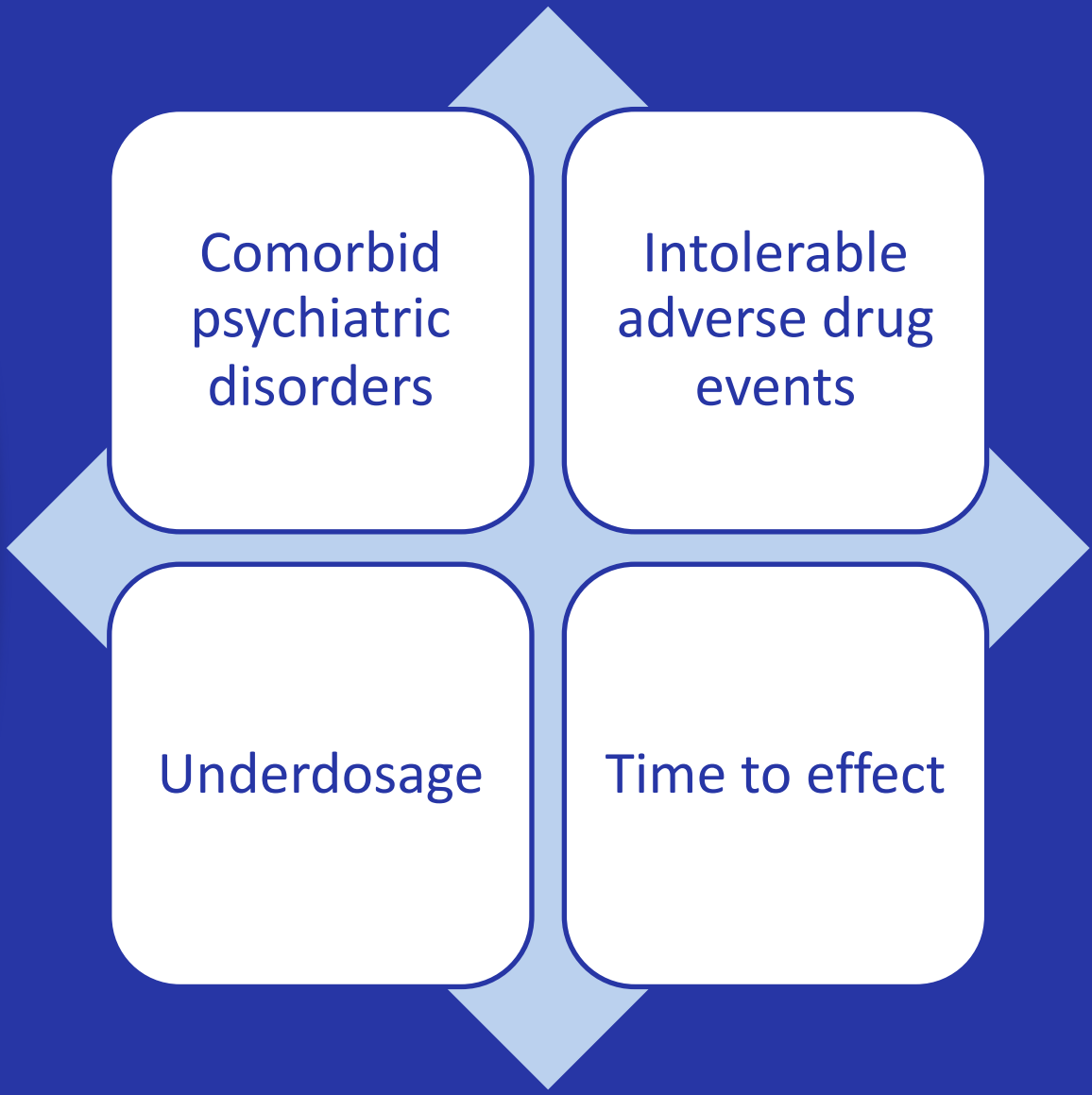
2nd Line/Augmentation:

- TCA
- Pregabalin
- Benzodiazepines
- Buspirone
- Atypical antipsychotics
- Hydroxyzine
- Mirtazapine
- Anticonvulsants

Last Line:

- MAO-I

Addressing Treatment "Failure"



Partial Response

- Ensure adequate time for response
- Maximize dose
- Add psychotherapy
- Add additional agent
- Augment based on symptoms

Lack of Response

- Ensure trial of 4-6 weeks
- Evaluate for comorbidity
- Switch to another first line agent
- Add psychotherapy

Take Home Points

- Generalized anxiety disorder is a common disorder in the general population
- Pharmacists can screen for GAD with the GAD-7 questionnaire across settings
- SSRI and SNRI's remain 1st line for GAD
- 2nd line and augmentation should be personalized to specific patient factors

Benzo Tapering Resources

- PL Detail-Document, Benzodiazepine Toolbox. Pharmacist's Letter/Prescriber's Letter.
- Bostwick JR, et al. Current Psychiatry 2012;11(4):55-64
- Lader, M, et al. CNS drugs 23.1 (2009): 19-34
- The Ashton Manual. Available at: http://www.benzo.org.uk/manual/contents.htm

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