Objective:

- Describe the DSM-5 criteria and screening tools utilized for diagnosing Major Depression, Generalized Anxiety Disorder, Panic Disorder, and Post-Traumatic Stress Disorder.
- Explain the mechanism of action, side effects, and clinical pearls in terms of prescribing antidepressants and anxiolytics in the primary care setting.
- Identify common drug interactions with antidepressants and anxiolytics.

Why Is This Important?

- In 2016, the USPSTF updated its recommendations to include routine screening for depression in adults, pregnant and post-partum women.
- Major depression is a treatable cause of pain, suffering, disability and death...
- Yet primary care clinicians detect major depression in only 1/4 to 1/2 of their patients.
Why Is This Important? (cont)
- Additionally, more than 80% of patients with depression have a medical comorbidity.
- Usual care for depression in the primary care setting has resulted in only about half of depressed adults getting treated and only 20-40% showing substantial improvement over 12 months.
- Approximately 70-80% of antidepressants are prescribed in primary care, making it critical that clinicians know how to use them and have a system that supports best practices.

Why Is This Important? (cont)
- Major depression is the 4th leading cause of disability in the world (WHO).
  - By the year 2020, it will be second only to ischemic heart disease (WHO).

Epidemiology of Depression in Primary Care
- MDD—lifetime prevalence—approx 15%
- 1 of 5 most common conditions in primary care.
- Nearly 10% of all primary care office visits are depression related.
- PCPs provide approx 50-60% of the outpatient care for depressed patients.
  - “The hidden mental health system”
Chronic Illness and Depression

- Higher prevalence in patients with comorbidities
  - Pain syndromes, DM, heart disease, neurological disorders, HIV
- History of depression appears to be a risk factor for development of CAD and DM
- Patients with comorbid illness and depression have:
  - More symptoms
  - Worse function
  - Impaired self-care and adherence
  - Higher costs

Risk Factors for MDD

- Gender
  - 2 x more in women
- Age
  - Peak onset 20-40 years
- Family history
  - Highest with 1st degree relative
  - 3 x higher risk with FHX
- Marital status
  - Higher divorced/separated

Diagnosing MDD per DSM-5

- Major depressive disorder (MDD)
  - 5 or more of the following symptoms have to be present during the same 2 week period and represent a change from previous functioning:
    - At least 1 of the symptoms is depressed mood or loss of interest/pleasure (anhedonia)
MDD (cont)
- Depressed mood most of the day, nearly every day
- Markedly diminished interest/pleasure in all activities most days
- Significant weight loss (not dieting) or weight gain and appetite increase or decrease (5% in 1 month)
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue/anergia
- Feeling worthless and/or excessive guilt
- Decreased concentration
- Suicidal or passive death wish

Use of Rating Scales
- SIGECAPS
- PHQ-9
- HAM-D
- Beck Depression Inventory

PHQ-9
- Patient self-administered
- Validated in Spanish and Chinese
- Association between increasing PHQ-9 scores and likelihood of MDD
- Useful for monitoring change over time
**PHQ-9 (cont)**

- Remember 5, 10, 15, 20
- Cut off points for depression severity
  - ≥ 5 mild
  - ≥ 10 moderate
  - ≥ 15 moderately severe
  - ≥ 20 severe
- Significant improvement = 5 point ↓
- Response = 50% ↓ or score < 10
- Remission = score < 5

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**Depression Treatment Planning Guidelines**
Adapted from MacArthur Foundation Depression in Primary Care Initiative

<table>
<thead>
<tr>
<th>PHQ-9 Severity</th>
<th>Provisional Diagnosis</th>
<th>Rx Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>Mild/minimal depressive symptoms</td>
<td>Reassurance and/or supportive counseling</td>
</tr>
<tr>
<td>10-14</td>
<td>Moderate</td>
<td>&quot;Watchful waiting&quot;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&quot;Supportive counseling&quot;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&quot;If no improvement after ≥ 1 month, consider antidepressant&quot;</td>
</tr>
<tr>
<td>15-19</td>
<td>Moderately severe</td>
<td>Patient preference for antidepressant and/or counseling</td>
</tr>
<tr>
<td>≥ 20</td>
<td>Severe major depression</td>
<td>Antidepressants alone or in combination with counseling</td>
</tr>
</tbody>
</table>

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**Monitor Progress Using the PHQ-9**

- Wouldn’t treat BP without measuring it at every visit
- Wouldn’t prescribe hypoglycemic agents without following the HgbA1C
- Why accept casual, imprecise monitoring in depression?
Psychiatric Differential Diagnoses of MDD
- Substance induced mood disorder
- Mood disorder due to a general medical condition
- Adjustment disorder with depressed mood
- Persistent depressive disorder (dysthymia)

Psychiatric Differential Diagnoses of MDD (cont)
- SCREEN FOR MANIA/HYPMANIA
- Bipolar Disorder I/II
  - Evidence or history of mania/hypomania
  - Bipolar Disorder-depressed

PCPs Adherence to Practice Guidelines for Treating MDD
- Most PCPs recognized depression and provided initial treatment
- Most did not screen for ETOH or suicide
- 46% of depressed patients received 2 or more months of treatment, when the recommended length of treatment is at least 4 to 9 months after remission of symptoms

General Principles of Antidepressant Action

- Response vs remission vs recovery
  - **Response**
  - Treatment with an antidepressant results in a 50% reduction of sx
    - This was once considered the goal of depression rx
  - **Remission**
  - Treatment with an antidepressant results in removal of essentially all symptoms for the first several months
  - **Recovery**
  - Removal of essentially all symptoms for longer than 6-12 months
  - Remission and recovery are now the goals in treating pts with depression
    - Goal of remission is not usually reached with the 1st antidepressant

Drug Continuation

- Depressed pts who have an initial treatment response will relapse at a rate of only 10-20% if their medication is continued for 6 months to a year following recovery
  - *Rationale for emphasizing need to continue med even when “feeling better”*

APA Guidelines for Treatment of Patients with MDD

- Generally, 4-8 weeks of rx are needed before concluding that a patient is partially responsive or unresponsive to a specific intervention
- If at least a moderate improvement in symptoms is not observed within 4-8 weeks of rx initiation:
  - Reappraise dx
  - Assess side effects
  - Review complicating co-occurring conditions and psychosocial factors
  - Assess compliance
SSRIs
- Introduced in the late 1980s
- Transformed the field of clinical psychopharmacology
- "Up to 6 prescriptions per second, around the clock, and around the year" are written for SSRIs
- Fluoxetine (Prozac)*
- Sertraline (Zoloft)*
- Paroxetine (Paxil)
- Fluvoxamine (Luvox)*
- Citalopram (Celexa)
- Escitalopram (Lexapro)*
- All approved for MDD with exception of Luvox
- *approved for use in patients <18

SNRIs
- Venlafaxine XR (Effexor XR)
- Desvenlafaxine (Pristiq)
- Duloxetine (Cymbalta)
- Milnacipran (Savella)
- Levomilnacipran (Fetzima)

Atypical Antidepressants
- NDRI
  - Bupropion (Wellbutrin SR/XL)
- Alpha 2 antagonist
  - Mirtazapine (Remeron)
- SRI/5HT1a partial agonist
  - Vilazodone (Vibryd)
- SRI/5HT3 antagonist/5HT1a partial agonist
  - Vortioxetine (Trintellix)
Serotonin Syndrome (SS)
- Any agent with serotonin reuptake blockade can cause this
- Increased risk when combined with MAOI
- Milder sx include:
  - Migraines, myoclonus, diarrhea, agitation, psychosis, or confusion
- Severe sx include:
  - Hyperthermia, seizures, coma, CV collapse, brain damage, or death

Meds Associated with the Development of SS
- SSRIs
- MAOIs
- TCAs
- Opioid analgesics
- Amphetamines
- Lithium
- Buspirone
- Triptans

Discontinuation Syndrome
- Can see when discontinuing any antidepressant
- Differs from classic withdrawal syndrome that results in craving and drug-seeking behavior
- Characterized by flu like symptoms
Antidepressant Pharmacokinetics
CYP 450 1A2
- Substrates of 1A2
  - Acetaminophen
  - TCAs
  - Theophylline
  - Duloxetine
  - Caffeine
  - Clozapine
- Inhibitor of 1A2
  - Fluvoxamine

Antidepressant Pharmacokinetics
CYP 450 2D6
- Substrates of 2D6
  - Atypical antipsychotics
  - TCAs
  - Thioridazine
  - Codeine
  - Some beta blockers
  - Atomoxetine
  - Vortioxetine
- Inhibitors of 2D6
  - Paroxetine
  - Fluoxetine
  - Duloxetine
  - Bupropion

Antidepressant Pharmacokinetics
CYP 450 3A4
- Substrates of 3A4
  - Ca channel blockers
  - Corticosteroids
  - Benzodiazepine's
  - Atypical antipsychotics
  - HMG-CoA reductase inhibitors
- Inhibitors of 3A4
  - Fluvoxamine
  - Fluoxetine
  - Nefazodone
  - Erythromycin
  - Ketoconazole
  - Protease inhibitors
Antidepressant Pharmacokinetics
CYP 450 2C9
- Substrates of 2C9
  - Tolbutamn
  - Diazepam
  - Phenytoin
  - Warfarin
- Inhibitors of 2C9
  - Fluvoxamine
  - Fluoxetine

Treatment Resistant Depression (TRD)
- Experts disagree on the meaning or number of different treatments that fail to achieve remission of symptoms
- What matters is degree to which treatment makes you feel better and how well you tolerate adverse effects, if any, to the medications
- Provider should:
  - Re-evaluate the diagnosis
  - Check adherence
  - Check for other causes
  - Assess S/A

Strategies for TRD
- REFER…
  - Folate
  - Thyroid hormones (T3/T4)
  - Lithium
  - Stimulants
  - brexpiprazole (Rexalti)
  - aripiprazole (Abilify)
  - quetiapine (Seroquel XR)
How to Select an Antidepressant per APA Guidelines

- Option 1
  - SSRI first line treatment of depression
- Option 2 (doesn’t matter)
  - SSRI #2, SNRI; atypical antidepressant
  - Wellbutrin, Buspar (augmentation options)
- PC—refer!
- Option 3 (doesn’t matter)
  - Remeron; TCA (switch options)
  - Lithium; thyroid (augmentation options)
- Option 4 (doesn’t matter)
  - MAOI; SNRI+Remeron

Symptom Based Algorithm for Antidepressant Selection

- Anxiety sx
  - SSRI/SNRI
  - MAOI
  - +benzo
  - +Remeron
  - +Atypical antipsychotic
- Pain
  - SNRI
  - +alpha 2 delta (gabapentin)

Symptom Based Algorithm for Antidepressant Selection (cont)

- Sexual dysfunction
  - Wellbutrin
  - Remeron
  - Buspar, Viibryd (5HT1A agonists)
  - Add stimulant
  - Discontinue SSRI/SNRI

- Sleepiness/fatigue
  - SNRI
  - Wellbutrin
  - + modafinil
  - +stimulant
  - Stop any antihistamines, antimuscarinic, or alpha 1 blockers

- Vasomotor
  - SNRI
  - Estrogen
Incidence & Prevalence of Anxiety Disorders in PC

- > than 2 times the rate of general population
- 1/3 of patients in PC
- Many report anxiety as a result of another disorder
- Anxiety disorders tend to occur in young who are at low risk for serious illness

General Anxiety Disorder (GAD)—DSM-5 Criteria

- Excessive worry/anxiety
- > 6 months
- concern general rather than specific
- Screen for with GAD-7
- At least 3/6 of the following symptoms
  - restlessness
  - easily fatigued
  - decreased concentration
  - irritability
  - muscle tension
  - sleep disturbances

Panic Disorder—DSM-5 Criteria

- Panic attack—palpitations, sweating, feelings of choking, dizziness, fear of losing control, going crazy, or death, chills, hot flashes, derealization, depersonalization (4 or more sx present that reach a peak in a 10 minute period)
- Panic Disorder
  - Recent and unexpected panic attacks are present
  - Persistent concerns about having an additional attack
  - Worry about the implications of the attack
  - Occur during a 1 month period
**Epidemiology of Panic Disorder**

- 5% of men and up to 12% of women have panic disorder and/or agoraphobia at some time in their life
- Agoraphobia develops in 50% of patients with panic disorder
- 3-5x more likely than general population if 1st degree relative has panic disorder

**Screening for Panic**

- Beck anxiety inventory (BAI)
- Severity Measure for Panic Disorder (adult)

**Post Traumatic Stress Disorder (PTSD) — DSM-5 Criteria**

- Traumatic event occurs prior to symptoms:
  - Either experienced, witnessed, or has been confronted with an event that is threatening to self or others
- Intrusions symptoms (x1)
- Avoidance (x1)
- Negative alterations in cognitions/mood (x2)
- Arousal (x2)
Screening & Epidemiology of PTSD

- **Screening for PTSD**
  - Primary Care PTSD Screen (PC-PTSD)
  - 5-item screen

- **Epidemiology**
  - Lifetime prevalence may be as high as 9%
  - Develops in 1 of 4 people who experience exposure to a severe traumatic event

Steps in Diagnosing Anxiety Disorders in PC

- Recognize anxiety as a possible cause of the presenting symptoms
- Determine if anxiety symptoms are caused by a medical disorder
- Determine if caused by substance or other psychiatric disorder such as ETOH abuse and depression

- Diagnose the anxiety disorder and the factors that precipitated the disorder
Meds Used for the Treatment of Anxiety
- SSRIs
- SNRIs
- Buspirone
- Benzodiazepines

Specific Indications for Anxiety Disorders
- Fluoxetine (Prozac)
  - OCD
  - Panic D/O
- Fluvoxamine (Luvox)
  - OCD
  - Social phobia
  - Eszopiclone (Lunesta)
- Sertraline (Zoloft)
  - OCD
  - Panic D/O
  - PTSD
  - Social phobia
- Paroxetine (Paxil)
  - OCD
  - Panic D/O
  - Social phobia
  - GAD
- Venlafaxine (Effexor XR)
  - GAD
  - Social phobia
  - Panic D/O
- Duloxetine (Cymbalta)
  - GAD

Common Benzos and Side Effects
- Alprazolam (Xanax)
- Lormazepam (Ativan)
- Clonazepam (Klonopin)
- Diazepam (Valium)
- Temazepam (Restoril)
- Sedation
- Decreased coordination
- Decreased mental acuity
  - Caution pts re: driving or operating heavy machinery
- Combining with ETOH increases side effects
- Can cause paradoxical reactions
- Tolerance, dependence, and withdrawal
Benzodiazepine Overdose

Clinical Interviewing Tips

- Normalize the experience
  - your attitude will directly effect the history you are able to elicit
- Use medical model and connect the brain and body
- Examine your own biases
- Ask the questions in terms of symptoms, not "mental illness"
- Screen for suicide
- Screen patients with non-specific somatic complaints

In Summary…

- Numerous meds to choose from
  - Use APA practice guidelines
  - Encourage lifestyle changes
  - Most importantly…
  - "You Are Only One Work Out Away From a Good Mood!"
Case Study 1

Ms. K, a 35 y/o DWF, presents to your office with a hx of Social Phobia. She has been taking Paxil 30 mg qd for the past 1 ½ years. She reports that she has been compliant with therapy and sees her therapist every 2-3 weeks. She reports that she would like to stop taking Paxil as she feels that she "no longer needs it." She does express concern re: withdrawal sx as she notes the emergence of dizziness and lightheadedness when she misses a dose.

What do you want to do?

Case Study 2

Mrs. T, a 40 y/o MWF, presents with hx of worrying about "everything." She reports DFA at night as her mind often races with worries about her children’s health, the economy, her husband’s job, etc. Describes her mood as being more irritable and sad. Also reports poor concentration and that she is easily distracted. States, “I sit on the couch in the house and then get distracted by something else.” She also endorses intermittent panic attacks. Panic attacks occur a “few times per month.” Panic symptoms consist of racing heart, difficulty catching her breath, and dizziness. Denies precipitant to panic sx. Denies that she is overly concerned re: the panic attacks or that she has changed her behavior r/t the attacks. She admits to recently drinking more at HS to aid with sleep. Denies any other substance abuse. Has not seen her PCP in several years. No past sig medical hx reported.

Reports that she took Prozac in the past "for years" and felt that it was effective but it stopped working and anxiety increased. Also had short trial of Celexa in the past but she reports that she “did not like the sexual side effects.”

What do you want to do?

Case Study 3

Jane, a 74-year-old client with depression, presented at her appointment with complaints of tremors, diaphoresis, headache, and nausea over the past week. She is currently taking Amitriptyline 50 mg po qhs, which was increased at her last visit, and Prozac 40 mg po qd. She denies depression but admits to increased confusion and memory problems.

What is your biggest pharmacologic concern at this point with the combination of medication the client is being prescribed?

What do you want to do?
John is a 33-year old MWM with a recent diagnosis of MDD and anxiety. He has been taking Zoloft 50 mg qd for the past 6 weeks and has seen a definite improvement in both mood and anxiety. He does express concern about his difficulty having an orgasm since starting Zoloft.

What do you want to do?