Pharmacologic Management of Depression & Anxiety Disorders

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- All information is considered current and accurate as of October 15, 2018
- All prescribers should fully consider scope of practice related to all medications
- Content for this presentation was prepared with assistance from PMHNP/DNP student Jessica Coker

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Learning Objectives

- Describe the clinical presentation of depressive and anxiety disorders commonly seen in primary care settings
- Identify evidence-based pharmacological treatments for depressive and anxiety disorders, including rationale for specific medication choices
- Describe safe and effective prescribing practices for treating depressive and anxiety disorders across the lifespan

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Depressive & Anxiety Disorders

Depressive Disorders

Major Depressive Disorder (MDD)

Dysthymia

Post-Partum Depression (PDD)

Anxiety Disorders

Generalized Anxiety Disorder (GAD)

Panic Disorder

Obsessive-Compulsive Disorder (OCD)

Post Traumatic Stress Disorder (PTSD)

Core Symptoms of Depression

SLEEP: increased or decreased
INTEREST: decreased for pleasure/mood**
GUILT: increased worthlessness
ENERGY: decreased
CONCENTRATION: impaired
APPETITE: increased or decreased
PSYCHOMOTOR: retardation/agitation
SUICIDE: thoughts, attempts, plans, history

Depression and Physical Health

- Cancer
- Cardiovascular Health
- Endocrine Function
  - Thyroid
  - Diabetes
    - Higher risk/Less recognition
    - May interfere with treatment adherence

Mood Disorders and Medications

DEPRESSION	MANIA
Antihypertensives Beta Blockers Ca++ channel Blockers Opiates Accutane Benzodiazepines	Synthroid Corticosteroids Stimulants INH Antidepressants

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Patient Health Questionnaire 9

- Nine items scored from 0-3
  - 0= not at all in past 2 weeks
  - 1= several days
  - 2= more than half of days
  - 3= nearly every day in past 2 weeks
- Score ranges 1-27
  - 1-4=Minimal depression
  - 5-9= Mild depression
  - 10-14 =Moderate depression
  - 15-19= Moderately severe depression
  - 20-27 =Severe depression

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Initial Treatment for MDD

Severity Level (PHQ-9 Score)	Initial Treatment
Mild (5-14)	Supportive counseling If no improvement after 4-6 weeks, consider AD and/or brief counseling
Moderate (15-19)	Start with AD, psychotherapy or both
Severe (20+)	Could start with AD or psychotherapy, but both would be better

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Pharmacological Agents for MDD

First-Line Options

- Serotonin Reuptake Inhibitors (SSRIs)
- Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)
- Bupropion (Wellbutrin®)

Secondary Options

- Tricyclic Antidepressants (TCAs)
- Monoamine oxidase Inhibitors (MAOIs)

SSRI Names and Dosing

Generic Name (Trade)	Initial Dosing (mg/day)	Dosing Range (mg/day)
Escitalopram (Lexapro®)	10	10-20
Paroxetine (Paxil®)	20	20-50
Sertraline (Zoloft®)	50	50-200
Citalopram (Celexa®)	10	20-40
Fluoxetine (Prozac®)	5	10-30
Fluvoxamine (Luvox®)	25	100-300

SNRI Names and Dosing

Generic Name (Trade)	Initial Dosing (mg/day)	Dosing Range (mg/day)
Venlafaxine (Effexor®)	37.5-75mg	75-225mg
Desvenlafaxine (Pristiq®)	50mg	50-400mg
Duloxetine (Cymbalta®)	30 or 60mg	60-120mg

SSRI/SNRI Common Side Effects

- Sleep Changes
- Nausea/Vomiting
- Diarrhea
- Weight Changes
- Sexual dysfunction
- Headache (SNRI only)
- Elevated blood pressure (SNRI only)

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Sleep Change Side Effects

"Activating" Antidepressants

- Fluoxetine
- Sertraline
- Bupropion
- Venlafaxine
- Duloxetine

Better for patients with hypersomnolence

"Calming " Antidepressants

- Citalopram
- Escitalopram
- Paroxetine

Better for patients with agitated/anxious depression

Lewis, 2015

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Weight Change Side Effects

- Most reuptake inhibitor ADs are weight neutral
- If weight changes, most report GAIN
  - Largest weight gain associated with paroxetine
  - Fluoxetine may be prescribed for weight loss or gain

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SSRI/SNRIs and Safety

- Overdose Risk
  - Relatively low risk compared with other ADs
- Use in Pregnancy
  - Most are pregnancy class C
  - Paroxetine is Pregnancy Class D
- Black Box Warning
- Syndromes
- Drug-Drug Interactions

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Black Box Warning

- Increased suicidal ideation possible for any patient under age 26
- Assess risks vs. benefits
- Proactive monitoring
  - Family involvement
  - Anticipatory guidance
- Consider need for specialty-level MH care

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Discontinuation Syndrome

- **A**gitation/Anxiety
- **B**ad dreams
- **C**oncentration problems
- **D**izziness
- **E**lectric shock-like symptoms
- **F**lu-like symptoms

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Serotonin Syndrome

- Mental Status Changes
  - Hallucinations, agitation, coma
- Autonomic Instability
  - Tachycardia, hyperthermia, BP changes
- Neuromuscular Symptoms
  - Hyperreflexia, incoordination
- GI Disturbances
  - Nausea & Vomiting

Potentially Life-Threatening

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SSRI/SNRIs and Drug Interactions

- INCREASE Effects
  - Beta Blockers, Warfarin
- DECREASE Effects
  - Digoxin
- INTERACTION Effects
  - MAOIs
  - Serotonergic Agents

Most SSRIs/SNRIs are metabolized by CYP450 system

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Bupropion (Wellbutrin®)

- Dosing:
  - Initial 150mg/day
  - Range 150-300mg/day
- Common Side Effects:
  - Nausea & Vomiting
  - Lower seizure threshold
  - Dry mouth
  - Agitation/insomnia

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Choosing Best Antidepressant

Symptom	Consider	Avoid/Caution
Underweight	Paroxetine	
Overweight/Obese	Fluoxetine	Paroxetine
Insomnia/Agitation	Paroxetine	Fluoxetine Sertraline
Psychomotor retardation	Fluoxetine or SNRI	
Pregnancy		Paroxetine
Elderly		Paroxetine
QTc Prolongation		Citalopram Escitalopram

Newton, 2016

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Choosing Best Antidepressant

Symptom	Consider	Avoid/Caution
Chronic Pain	SNRI	
Anxiety disorder	SSRI or SNRI	
Smoker	Bupropion	
Sexual dysfunction	Bupropion	
Hypertension		SNRI Bupropion
Seizure disorder		Bupropion

Newton, 2016

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Clinical Manifestations of Anxiety

Cognitive

- Worry
- Obsession
- Cognitive avoidance
- Compulsive behavior
- Behavioral avoidance

Somatic

- Hyperarousal
- Insomnia
- Agitation
- Tremor
- Sweating
- SOB
- Tachycardia
- Muscle tension

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Anxiety Disorder Treatment

Pharmacological

- SSRIs/SNRIs
- Benzodiazepines
- Tricyclic Antidepressants
- Beta Blockers
- Other Adjuncts

Psychosocial

- Anxiety Management Techniques
- Cognitive Behavioral Therapy
- Exposure Therapy

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Pharmacotherapy for Anxiety

Disorder	1st Line	2nd Line	Short-Term	Augment
Generalized Anxiety Disorder (GAD)	SSRI/SNRI	TCA	BZD	Pregabalin Hydroxyzine Buspirone
Panic Disorder	SSRI/SNRI	TCA	BZD	Buspirone
Obsessive Compulsive Disorder (OCD)	SSRI/SNRI	Clomipramine (Anafranil)		(2nd Gen antipsychotic)
Phobias	SSRI/SNRI	TCA	Beta blockers BZD	

SNRI= Serotonin Norepinephrine Reuptake Inhibitor SSRI= Serotonin Selective Reuptake Inhibitor
TCA= Tricyclic Antidepressant BZD= Benzodiazepine

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Pharmacotherapy for PTSD

Medication Class	Summary of the Evidence (Level)
SSRIs	All are First-line (A)
SNRIs	Venlafaxine is First-line (A)
Other 2nd Gen ADs	May be effective but level ranges (A-C)
TCAs/MAOIs	Secondary due to side effects (A)
Benzodiazapines	Effective but NOT advised as monotherapy (A-B)

Adapted from *Effective Treatments for PTSD*, 2nd Ed. (2016)

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Benzodiazepine Dosing

Medication	Oral Dose Onset	Half-Life	Duration of Action	Notes
Alprazolam	30 min	12h	3-4hr	High abuse potential Rebound anxiety
Lorazepam	30-60min	15h	4-6hr	No active metabolites
Clonazepam	1hr	34h	6-8hr	Relative easy to taper
Diazepam	30min	100h	4-6hr	Caution with elders
Chlordiazepoxide	2hr	100h	4-6hr	EtoH withdrawal Caution with elders

http://www.thecarlatreport.com/sites/default/files/2011%20TCPR%20Benzo%20Table.pdf

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FDA Approved Uses

Medication	GAD	Insomnia	Alcohol Withdrawal	Seizure	Other
Alprazolam	X				Panic Disorder
Chlordiazepoxide			X		
Clonazepam	X			X	Panic Disorder Neuralgia
Diazepam	X		X	X	Muscle spasm Sedation
Lorazepam	X			X	Sedation Chemo-related N/V
Temazepam		X			

Source: Guina & Merrill (2018) *Journal of Clinical Medicine*

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Benzodiazepine Interactions

- INCREASE Effects
  - Concomitant Use
  - Alcohol/CNS Depressants
- DECREASE Effects
  - Caffeine
  - Smoking

Black Box Warning
Potentially fatal interaction between Benzodiazepines and Opioids

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Benzodiazepines & Safety

- Slow taper after long-term use
  - 25% dose reduction q 1-2weeks
- Risk for injury while under influence
  - Driving
  - Operating machinery
  - Falls
- Pregnancy & Lactation
  - Avoid

Safe Pediatric Prescribing

- Depressive Disorders
  - BBW since 2004 has influenced practice
  - Largest body of evidence for SSRIs, SNRIs
- Anxiety Disorders
  - OCD: studied more than other ADs
  - Only 1 FDA approved agent for GAD
  - Very limited data for PTSD

Locher et al (2017) Efficacy and safety of SSRIs, SNRIs, and placebo for common psychiatric disorders among children & adolescents: Systematic review and meta-analysis. *JAMA Psychiatry*; 74 (10), 1011-1020

FDA Pediatric Labeling*

Medication	Depression	Anxiety
Fluoxetine	MDD 8-17 years	OCD 7-17 years
Escitalopram	MDD 12-17 years	
Duloxetine		GAD 7-17 years
Sertraline		OCD 6-17 years
Fluvoxamine		OCD 8-17 years

MDD= Major Depressive Disorder **GAD**- Generalized Anxiety Disorder **OCD**= Obsessive Compulsive Disorder

*FDA indications current as of July 2018

Safe Prescribing in Pregnancy

- Psychosocial interventions may be 1st-line treatment
- FDA approved SSRIs are preferred
- Untreated depression impacts mother and baby
- Other considerations
  - Fluoxetine: longer half-life=less frequent dosing
  - Escitalopram: least effect on CYP450 enzymes= less drug-drug interaction

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SSRI Use during Pregnancy

Medication	Evidence Summary
Sertraline (Zoloft) **1ST LINE**	Evidence includes RCTs with non-pregnant patients May be slightly more effective than other SSRIs Good choice for breastfeeding Little to no risk of teratogenicity
Citalopram (Celexa)	**Good 1-Line alternative** Little to no risk of teratogenicity
Fluoxetine (Prozac)	**NOT 1st Line** Possible teratogenicity risk Long half-life can lead to accumulation in newborn
Escitalopram (Lexapro)	**NOT 1st Line** (too few studies)
Paroxetine (Paxil)	**AVOID (Category D)** Associated with small increased risk of congenital cardiac defects

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Antidepressants & Breastfeeding

- SSRIs should be tried first (lowest risk of toxicity, side effects)
  - **Sertraline, paroxetine, fluvoxamine** have lowest passage into breast milk
  - **Sertraline** is most studied agent (considered 1st line)
- Highest infant plasma levels reported in **fluoxetine, citalopram, venlafaxine, desvenlafaxine**
- Recommended to start at half dose, then increase as tolerated to minimize side effects

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Depression Treatment in Elders

- SSRIs are first-line
  - Fluoxetine has longer half-life
  - Paroxetine has strong anticholinergic effects
- Additional risks
  - Overdose
  - Common health conditions
  - Drug-Drug Interaction
  - Hyponatremia/Increased ADH Secretion

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References

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Questions & Answers

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