Mental Health Bootcamp: Depression and Anxiety

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Disclosure

I have had no financial relationship over the past 24 months with any commercial sponsor with a vested interest in this presentation

Learning Objectives

- Identify screening tools to identify depression and anxiety, and situations for referral
- Compare and contrast antidepressants and anxiolytics to individualize patient care and counseling (pharmacist)
- Describe your personal self-stigma towards the mental health population

General Presentation Flow

- Stigma
- Depression screening
- Antidepressants
- Anxiety Screening
- Anxiolytics





WHAT DO YOU THINK OF WHEN YOU THINK ABOUT MENTAL HEALTH?

- Crazy or psycho?
- Straightjackets?
- Dangerous?
- The "stare"
- Suicide?
- People in robes shuffling around the units?

- Productive
- Chemical imbalance
- Scared and alone
- Needs help
- Actual disease

Helpful Advice



You just need to change your frame of mind. Then you'll feel better.









Article from 2002



General-alarm fire at Trenton Psychiatric

By TOM BALDWIN & JEAN LEVINE

A welder's torth sparked a prosal alarm blaze that gutted offices and a chapel at Trenton Psychiatric Hospital yesterday as it burned out of conveil for more than two hours.

Authartties said to TPH employses or patients were hart in the moving blaze. But several of the 100 firstners who responded to the acetar collapsed from best exhaustion.

Estation Chief Ceshum Smith of the Trenzon Fire Droision said the blaze broke cut in the Haines Building alactify before 5 a m.

In minutes, in the flatten shot, across the roof of the Lutaged, three-story structure, formers were calling for more halp from Trenton's fire form as well as the volunteer foremen of Exing. Hamilton and Lowrence.

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Firement initially changed one the building in the effort to best down the chanses. Fourful of a collegue, however, supervisors pulsed firefighters hack use to fight strictly from cognide with serial hows.

Officials and it was pertupa the



What Does This Do?

- Prevents patients from seeking care
 - Self medicate
 - Drugs of abuse
 - Herbals
 - Self-help shows (e.g. Dr. Oz)
 - Burn support bridges
 - Deal with it on their own

But...we all have stigma.....



- Opening Minds Scale for Health Care Providers
- Please answer honestly I'm not collecting them
- Importance is identification, not being "right"

Depression

Depression Background

- In 2021, estimated 8.3% of adults had one episode
 - Highest among 18-25 age group 18.6%
 - Female to male 1.7 to 1
 - Recent Gallup poll data shows higher:

Rising Trends: Lifetime and Current Depression Rates

Has a doctor or nurse ever told you that you have depression? Do you currently have or are you currently being treated for depression?



— % Yes, lifetime depression — % Yes, current depression

Depression Symptoms

- S sleep disturbance (insomnia or hypersomnia)
- I interest in activities decreased
- G guilt
- E energy (increase or decrease)
- C concentration impairment
- A appetite changes (increased or decreased)
- P psychomotor agitation or retardation
- S suicidal ideation or actions

Depression Screening – PHQ-2

Over the past 2 weeks, how often have you been bothered by any of the following problems?	Not At all	Several Days	More Than Half the Days	Nearly Every Day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed or hopeless	0	1	2	3

- Score of 3 is considered "positive", thus should refer
- Ask the suicide question as well
 - "Have you had thoughts of killing yourself or that you would be better off dead?"
 - If score of 1 or greater, refer

Depression Screening – PHQ-9

Questions

- Little interest or pleasure in doing things
- Feeling down, depressed, or hopeless
- Trouble falling or staying asleep, or sleeping too much
- Feeling tired or having little energy
- Poor appetite or overeating
- Feeling bad about yourself (or that you are a failure or have let others down)
- Trouble concentrating on things
- Moving or speaking so slowly others have noticed (or fidgety/restless)
- Thoughts you would be better off dead, or of hurting yourself
- Frequency questioned over past two weeks
 - Unclear cutoff for referral for mental health trained vs. non-mental health trained
 - I personally use 10 as a hard cutoff
 - Always refer on suicide question

Can Pharmacists Do This?

- Clearly yes
- JAPhA 2013 study
 - 3726 patients screened in 32 grocery store pharmacies in Ohio
 - 1.8% screened positive on PHQ-2
 - 25% of them met criteria for diagnosis on PHQ-9
 - 5 patients were suicidal
 - 60% with positive scoring had therapy modified on follow-up
- 2020 International Journal of Pharmacy Practice systematic review
 - 10 articles reviewed
 - Pharmacists comfortable with the process of making referrals
 - No assessment of follow-up benefit

Let's Practice...

- How comfortable are you asking the suicide question?
- Have you ever had to ask someone if they want to kill themselves?
- Different than "hurt yourself"
- Turn to your neighbor. Let's sit with these feelings
 - It gets easier the more you ask

Referral Sources

- Advocacy organizations
 - Mental Health America
 - National Alliance on Mental Illness (NAMI)
- National Helpline (2-1-1)
 - Currently covers 93% of entire population
 - Not just for mental health (many social service support systems)
- Avera Behavioral Health
 - 605-322-4065 or 1-800-691-4336
- Local emergency department
- National Suicide Hotline (9-8-8)
- Local law enforcement if necessary (suicidality)

What's the Risk of Screening?

- Admittedly, there is some risk
- Risk is low it's open source
 - Anyone can screen themselves
- When in doubt, better to refer
 - Patients can still refuse

Antidepressants

Brief Pathophysiology

- Anatomical structural abnormalities
- Neurotransmitter involvement
 - Monoamine hypothesis
 - Deficits in 5HT, NE, and DA
 - Does not account for delayed onset of agents
 - Dysregulation hypothesis
 - Differences in monoamine concentrations results in pre-and post-synaptic receptor alterations
 - Normalization takes time, thus delayed onset
- Chronic stress model

Therapeutic Effects

- Weeks 1-2
 - Improved sleep, appetite, maybe less anxiety/agitation?
- Weeks 3-4
 - Improved energy, maybe hope returning?
- Weeks 6-12
 - Improved mood, suicidality

Black Box Warning

- Increased risk of suicidality in children, adolescents, and young adults 24 and younger
- Linked to therapeutic effects?
- Highlights importance of patient follow-up

Classes of Antidepressants

- Selective serotonin reuptake inhibitors (SSRI)
- Serotonin norepinephrine reuptake inhibitors (SNRI)
- Tricyclic antidepressants (TCA)
- Monoamine oxidase inhibitors (MAOI)
- Novel antidepressants
 - Bupropion (Wellbutrin[®])
 - Mirtazapine (Remeron[®])
 - Vortioxetine (Trintellix®)
 - Vilazodone (Viibryd®)
 - Trazodone (Desyrel[®])
 - Nefazodone (Serzone[®])

Depression Guidelines

- Fairly vague
- First line is SSRI, SNRI, bupropion, or mirtazapine
 - Add vilazodone or vortioxetine in CANMAT
- American guidelines have not been updated since 2010...

SSRIs

Agent	Half Life	CYP Substrate
Citalopram	35 hours	3A4, 2C19*, 2D6
Escitalopram	27-32 hours	3A4, 2C19*
Fluoxetine	4-6 days	2C9, 2D6*, 2C19, 3A4/5
Fluvoxamine	16 hours	1A2*, 2D6
Paroxetine	24 hours	2D6*
Sertraline	26 hours	3A4, 2C9, 2C19*, 2D6*

MOA – selectively inhibit reuptake of serotonin from the synapse

SSRICYP Inhibition

CYP Isozyme	Medication	Degree of Inhibition
1A2	Fluvoxamine	Potent
2C19	Fluoxetine Fluvoxamine	Moderate Moderate
2D6	Fluoxetine Paroxetine Escitalopram Citalopram Sertraline	Potent Potent Weak-moderate Weak-moderate Weak-moderate (dose)
3A4	Norfluoxetine	Weak-moderate

- 1A2 avoid with clozapine, warfarin, and methylxanthines
- 2C19 caution with warfarin and clopidogrel (prodrug)
- 2D6 avoid with other 2D6 drugs (metoprolol, desipramine)
- 3A4 avoid with 3A4 drugs such as statins

Drug Interactions

- NSAIDs, antiplatelets, anticoagulants
 - Increased bleeding risk secondary to platelet aggregation effects
 - Monitor for s/sx bleeding
 - Will <u>not</u> see INR increase
- Serotonergic agents
 - Increased risk of serotonin syndrome
 - Not normally clinically relevant unless multiple agents

Contraindications

- Use of MAOI within 14 days of SSRIs
 - 5 weeks if stopping fluoxetine (half-life)
 - Also includes linezolid
- Use of citalopram with other QTc prolonging agents
 - More on this next slide...

Warnings/Precautions

- Associated with increased fracture rate and decreased bone mineral density
- Citalopram
 - Dose-dependent QTc prolongation, thus risk of torsades de pointes
 - 20mg 8.5 msec
 - 40mg 12.6 msec (extrapolated)
 - 60mg 18.5 msec
 - Limit dose in geriatrics, poor 2C19 metabolizers, hepatic impairment, or concurrent inhibitors

Adverse Effects

- GI upset
 - Take with food
 - Move dose to bedtime
- Headache
 - Take at night
 - Use OTC pain relievers (watch NSAIDs)
- Insomnia
 - Take in AM
- Weight gain
 - Worse with paroxetine
 - Switch agents

- Sexual dysfunction
 - Switch agents
 - Add bupropion
 - Add 5-HT2A antagonist (mirtazapine)
 - Use PDE5 inhibitor
 - Drug holiday?
- Hyponatremia
 - Discontinue agent
 - Implement water restriction
 - Hypertonic saline with loop diuretic
- Serotonin syndrome

Patient Education

- Side effects will likely resolve in the first few weeks of treatment
- Delayed onset of action
- Watch for s/sx of depression/suicidality
- Abnormal bleeding s/sx
- Do not stop abruptly or withdrawal symptoms can set in

Serotonin Discontinuation Syndrome

- Worse with short half-life drugs (paroxetine)
 - Rarely happens with fluoxetine (self-tapers)
- Symptoms
 - Anxiety/irritability
 - Sadness
 - Insomnia
 - Headache
 - Nausea
 - Electric shock sensations
- Prevent by tapering agents

SNRIs

Agent	Half Life	CYP Substrate
Desvenlafaxine	10-11 hours	3A4 (minor)
Duloxetine	12 hours	1A2, 2D6
Levomilnacipran	12 hours	3A4
Venlafaxine	5 hours	2D6

- MOA inhibit reuptake of serotonin and norepinephrine from the synapse
 - Venlafaxine is more SSRI under 150mg daily, then becomes SNRI
 - Levomilnacipran more NE-selective
- Drug interactions are same as SSRIs
Contraindications

- Use of MAOI within 14 days of the agent
- Duloxetine and levomilnacipran
 - Uncontrolled narrow-angle glaucoma

Warnings/Precautions

- Black Box Warning
- Monitor for increases in blood pressure
 - Caution in patients with hx of hypertension
- Duloxetine
 - Avoid in hepatic impairment or heavy alcohol use
 - Risk of urinary retention
- Levomilnacipran
 - Risk of seizures
 - Risk of urinary retention

Adverse Effects

- Same adverse effects of SSRIs
- Cardiovascular
 - Dose reduction with increased BP/HR
- Diaphoresis
 - Dose reduction
 - Add benztropine or terazosin if necessary
- Risk of flip to mania venlafaxine

Patient Education

- Same as SSRIs
- Recommend checking BP/HR at home

Novel Antidepressants

Agent	Half Life	CYP Substrate
Bupropion	14-21 hours	2B6
Mirtazapine	26-37 hours	1A2, 3A4*, 2D6*
Vortioxetine	66 hours	2D6
Vilazodone	25 hours	3A4
Trazodone	7-10 hours	3A4
Nefazodone	2-4 hours	3A4

Bupropion

- MOA NE and DA reuptake inhibitor
- PK Interaction Potent 2D6 inhibitor
- Contraindications
 - Seizure disorder
 - Bulimia or anorexia
 - Abrupt d/c of alcohol
 - Use of MAOI
- Warnings/precautions
 - Black box warning
 - Substance dependence
 - Hypertension
 - Psychosis/mania

Bupropion

- Adverse Effects
 - Agitation
 - Insomnia
 - Dry mouth
 - Risk of seizures
 - Tremor
 - Stomach upset
 - Headache
- Patient Education
 - Similar to other agents

Mirtazapine

- MOA presynaptic α_2 antagonist, thus increasing 5HT and NE release
 - Also an antihistamine
- PK Interaction clonidine/guanfacine based on mechanism
- Contraindications
 - Use of MAOIs
- Warnings/precautions
 - Black box warning
 - Agranulocytosis has been rarely reported
 - May cause orthostasis

Mirtazapine

Adverse Effects

- Weight gain/appetite increase
- Anticholinergic side effects
- Drowsiness (more sedating at lower doses)
- Less sexual dysfunction than other agents (except bupropion)
- Patient counseling
 - Watch food intake
 - Take at HS due to sedation
 - Delayed onset/suicidality

Other Antidepressant Classes

- Tricyclic Antidepressants (TCAs)
 - "Dirty" SNRI adds antihistamine, antimuscarinic, and anti-alpha MOA
 - Fatal in overdose 10mg/kg can be lethal
 - Generally not recommended in elderly
- Monoamine oxidase inhibitors (MAOIs)
 - Many dietary restrictions and DDIs
 - Recommended for treatment resistance
 - But dosed BID-TID...

Let's Practice...

See Patient Case #1

Antidepressant Summary

- Many options for the same thing
 27 to be exact
- Most are considered first line per guidelines
 All but MAOIs, nefazodone, and trazodone can be
- Agents chosen based off patient-specific factors



Anxiety Background

- Several different types
 - Generalized Anxiety Disorder
 - Social Anxiety Disorder
 - Panic Disorder
 - Post-Traumatic Stress Disorder
 - Obsessive Compulsive Disorder
- 12 month prevalence of 19.1%
 - This number is HIGHLY variable depending on source
 - Only about 37% receive treatment
- Symptoms are specific to each disorder, but overlap exists

Anxiety Symptoms

- Feeling keyed up or on edge
- Easily fatigued
- Difficulty concentrating
- Irritability and restlessness
- Muscle tension
- Sleep disturbances
- Dissociative reactions in severe disease
- Can lead to social isolation and poor medication adherence
 - Or overuse, especially of PRNs

Anxiety Screening

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all sure	Several days	Over 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's hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
Feeling afraid as if something awful might happen	0	1	2	3

Primary tool is GAD-7

Score of 10 is considered positive for screening

Referral Sources

- Similar to depression resources
- Depends on severity of anxiety
- Non-pharmacologic coping skills play a large role
 - Consider information from last presentation!



Brief Pathophysiology

- Similar serotonin hypothesis to depression
- Norepinephrine
 - Increased in locus coeruleus (alarm center)
 - Stimulates "fight or flight" mechanism
- HPA axis
 - Cortisol attempts to regulate, but depletes
- GABA/glutamate imbalance
 Too much gas, not enough brake

General Treatment Guidelines

- Many different guidelines exist
- In general, SSRI + CBT has the best evidence
 Combination has better efficacy than individual
- After initial failure, move to other serotonergic agent
- Remember non-pharmacologic treatment too!
- PRN benzodiazepines can bridge gap
 - Depends on the disorder

Benzodiazepines

Mechanism of action

- Bind to gamma subunit of the GABA_A receptor
- Increased receptor activity (ability of GABA to bind)
- More opening of the receptor = more inhibition

Efficacy

- Most prescribed drugs for anxiety
- Rapid relief of symptoms
- Do not treat underlying illness use only for short term
- Can exacerbate depression

Benzodiazepines

Generic Name	Onset of Action	Half-Life	Dose Equivalency
Alprazolam	Rapid	12-15 hours	0.5
Clonazepam	Intermediate	20-50 hours	0.25
Clorazepate	Intermediate	>100 hours	7.5
Chlordiazepoxide	Intermediate	>100 hours	10
Diazepam	Very rapid	>100 hours	5
Lorazepam	Intermediate	10-20 hours	1
Oxazepam	Slow	5-14 hours	15

Contraindications to Use

- Hypersensitivity
- Substance use history (relative)
- Myasthenia gravis (increasing muscle weakness)
- Respiratory disorders respiratory depression ceiling
- Significant hepatic disease
 - Consider?
- Acute narrow angle glaucoma (parasympathetic activation)
- Pregnancy, labor, lactation
 - Preferred agent is lorazepam
- Per guidelines, contraindicated in PTSD

Adverse Effects

- CNS effects
 - Sedation
 - Disorientation
 - Impairment of memory and recall
 - "Freeze-dried alcohol tablet"
- Abuse and dependence?
 - Some are worse than others

BZD Discontinuation

- If they aren't needed, clean up the med list
 - Rebound anxiety, dependence/addiction risk

General taper

- 25% dose reduction first week
- 25% dose reduction second week
- 12.5% every 4-7 days based on tolerance
- >8 weeks = 2-3 weeks
- >6 months = 4-8 weeks
- >1 year = 2-4 months

Switching to longer acting agent?

Buspirone

- FDA approved for GAD
 Second line option
- Presynaptic 5HT_{1A} partial agonist
- Moderate D2 affinity
 - Not clinically significant
- Delayed onset of action = no PRN usage!
- History of BZD = poor response

Buspirone

- Short half life = BID-TID dosing
 - Max dose 6omg daily
- Not recommended in hepatic or renal impairment
- Adverse effects fairly benign

Hydroxyzine

- First generation H1 antagonist, FDA approved
 - How does this work for anxiety?
- Can use PRN
 - May be an OK sub for BZDs
- Caution in hepatic impairment decrease frequency
- Adverse effects are predictable
 - Anticholinergic
 - Antihistaminic

Other Agents?

Pregabalin

- Head-to-head studies with venlafaxine, lorazepam, and alprazolam
- May be effective
- Tiagabine
 - Multiple negative trials, though listed in some guidelines
- Antipsychotics?
 - Olanzapine, quetiapine, and risperidone may be effective
 - Especially useful in treatment resistant anxiety

Antidepressant FDA Approvals

GAD

- Paroxetine, escitalopram, venlafaxine XR, duloxetine
- Panic disorder
 - Fluoxetine, sertraline, paroxetine, venlafaxine XR
- Social anxiety disorder
 - Paroxetine, sertraline, venlafaxine XR
- Post-traumatic stress disorder
 - Paroxetine, sertraline
- Obsessive compulsive disorder
 - Fluoxetine, fluvoxamine, paroxetine, sertraline, clomipramine

Let's Practice...

See Patient Case #2

Anxiolytics Summary

- Antidepressants are still first line for treatment
 - Think of treating a wound vs bandaging
- PRNs are helpful
 - Remember indices of therapeutic effect
 - Remember to taper when they are not needed!
- Non-benzodiazepine agents may have a better role in certain patients

Key Clinical Pearls

- Screening is important
 - PHQ-2 or PHQ-9 for depression (10+ or suicidality)
 - GAD-7 for generalized anxiety (10+)
- Many different options exist to treat the same thing
 - Antidepressants are first line for depression and anxiety
 - Chosen based on patient-specific factors, DDIs, PGx, etc.
 - Remember PRNs in anxiety and remove when not needed
- Always check yourself
 - We <u>ALL</u> have stigma
 - Important to identify, name it, and put it aside to treat patients

Technician Question 1

- Any positive response on which PHQ-9 question necessitates immediate referral to a mental health facility or the police?
 - A. Question 1: little interest or pleasure in doing things
 - B. Question 4: feeling tired or having little energy
 - C. Question 7: trouble concentrating on things
 - D. Question 9: thoughts you would be better off dead

Technician Question 2

- Which class of medications is most fatal in overdose?
 - A. SSRIs
 - B. SNRIs
 - C. TCAs
 - D. Novel agents (e.g. mirtazapine)

Pharmacist Question 1

- Which of the following patients should be referred for additional depression workup? Select all that apply
 - A. 19 year old patient with a score of 2 on the PHQ-2
 - B. 37 year old patient with a score of 11 on the PHQ-9
 - C. 24 year old patient with a score of 7 on the PHQ-9
 - D. 48 year old patient with a positive response on question 9
Pharmacist Question 2

- Which of the following medications has a metabolism impacted by smoking and caffeine?
 - A. Duloxetine
 - B. Sertraline
 - C. Bupropion
 - D. Mirtazapine

Pharmacist/Technician Question 3

Using the OMS-HC, what is one area you identified to work on?

Questions?

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