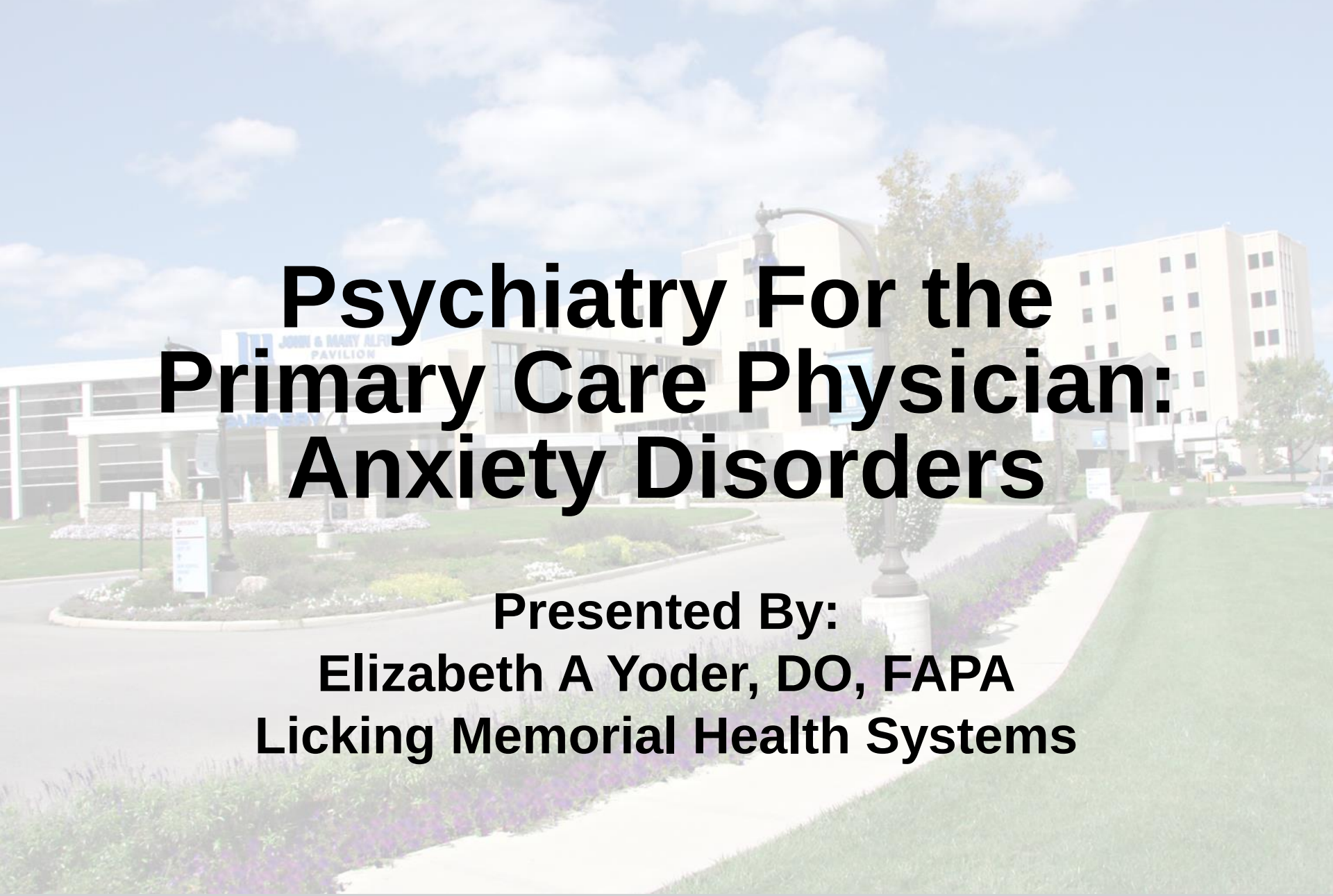

Psychiatry For the Primary Care Physician: Anxiety Disorders

Presented By:
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Licking Memorial Health Systems

Presenter Disclosure

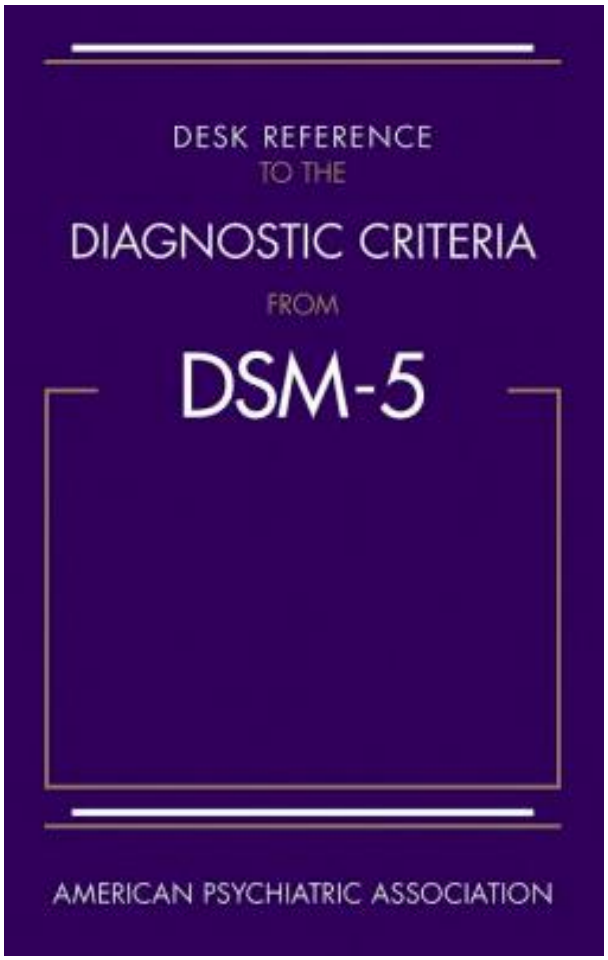
- I have no conflict of interest to disclose
- I have no financial or scientific disclosures
- I will discuss the off-label use of medications to treat various anxiety conditions

Objectives

- Outline evidence-based care for patients with psychiatric illness
- Practice evidence-based care for patients with psychiatry illness
- Translate information learnt at this course to improve the assessment and treatment of common psychiatric disorders by physicians

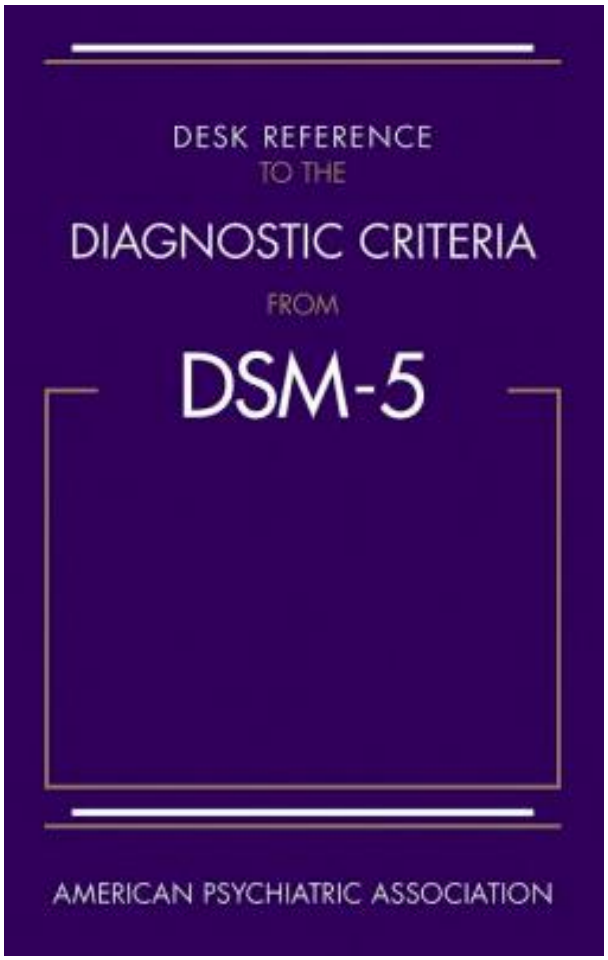
What exactly is it?

DSM-5 Anxiety Disorders



- Separation Anxiety Disorder
- Selective Mutism
- Specific Phobic
- Social Anxiety Disorder
- Panic Disorder
- Agoraphobia
- Generalized Anxiety Disorder
- Substance/Medication-induced Anxiety Disorder
- Anxiety due to GMC
- Unspecified / Other Anxiety

DSM-5 Anxiety Disorders



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- **Panic Disorder**
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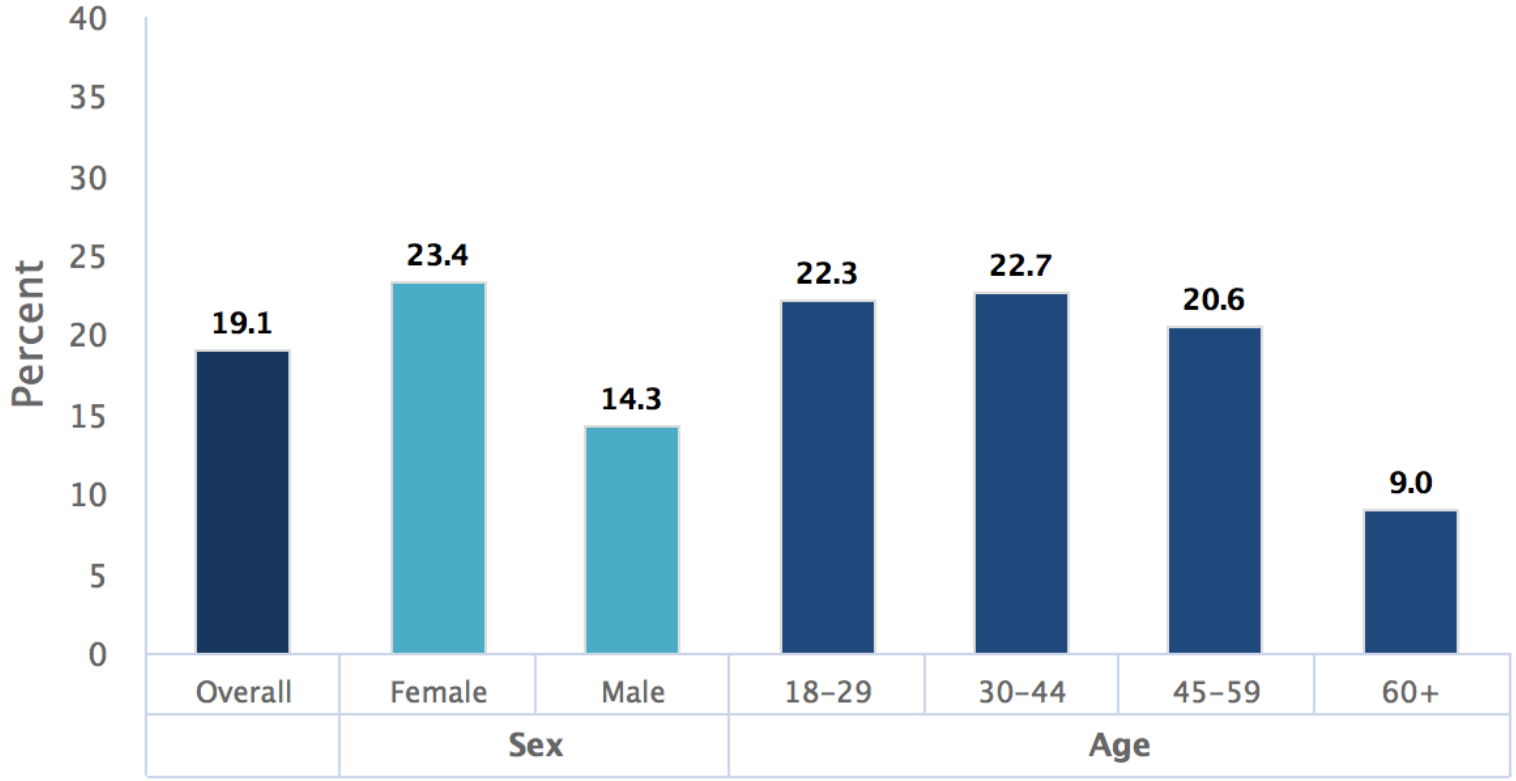
Past Year Prevalence of Any Anxiety Disorder Among U.S Adults (2001–2003)

Data from National Comorbidity Survey Replication (NCS-R)



NIMH.NIH.GOV

Anxiety Mimickers

- Endocrine
  - Hyperthyroidism ●Addison's ● Carcinoid ● Cushing's ● Diabetes ● Hypoglycemia ● Pheo
- Neuro
  - Cerebrovascular disease ● migraine ● epilepsy ● MS ● TIA ● Tumor ● Wilson's ● Infection
- Other conditions
  - Electrolyte disturbances ● B12 deficiency ● SLE ● systemic infections ● Heavy metal poisoning
- Cardiovascular diseases
  - Anemia ● Angina ● HTN ● MVP ● CHF ● MI
- Pulmonary Diseases
  - Asthma ● Hyperventilation ● PE
- Drug Intoxications
  - Amphetamines ● Anticholinergics ● Cocaine ● Marijuana ● Hallucinogens ● Nicotine
- Drug Withdrawal
  - Alcohol ● Antihypertensives ● Sedative-Hypnotics ● Opiates

Social Anxiety Disorder

- Marked fear/anxiety about one or more social situations in which the individual is exposed to possible scrutiny by others
- Individual fears that s/he will act in a way or show anxiety sx that will be negatively evaluated by others
- Social situations almost always provoke fear or anxiety
- Social situations are avoided or endured with intense fear or anxiety
- Fear/anxiety is out of proportion to the actual threat posed by the social situation
- Sx are persistent (typically > 6 months)
- Causes clinically significant distress or impairment to social/occupational functioning
- Not physiological in etiology or due to drug use
- Not due to GMC
- Specifier: Performance only

DSM-5

[WebMD Video on Social Anxiety Disorder]

Background Info

- Both heredity and environment are involved
- If sx are limited to just performance anxiety, there may be exaggerated autonomic NS
- Early studies showing HPA reactivity to social stressors associated with degree of avoidance
  - Specifically if h/o early childhood abuse
- Imaging has demonstrated specific changes
- Role of temperament
- Influence of parenting/peers
- Median age of onset = 13
  - 75% between 8-15 years
- Comorbidity:
  - Other anxiety DO, MDD, Substance Use, Bipolar, Body Dysmorphic
- Gender-related issues
- Suicide risk

Treatment

- CBT is gold standard psychotherapy, but medications have been shown to be effective
  - NICE guidelines recommend CBT as first-line
- Best evidence suggests continuing medication treatment for at least one year, if not longer

Roshanaei-Moghaddam et al, 2011 and Katzman et al 2014

COMPONENTS OF COGNITIVE BEHAVIORAL INTERVENTIONS

EXPOSURE	Encourage patient to face fears ● Learn corrective information through experience ● Extinction of fear occurs through repeated exposure ● Successful coping enhances self-efficacy
SAFETY RESPONSE INHIBITION	Patients reduce their usual anxiety-reducing behaviors (escape, need for reassurance) ● Decreases negative reinforcement ● Coping with anxiety without using anxiety-reducing behavior increases self-efficacy
AROUSAL MANAGEMENT	Relaxation and breathing control skills can help patient control increased anxiety levels
SURRENDER OF SAFETY SIGNALS	Patient relinquishes safety signals (eg: presence of a companion, knowledge of location of the nearest toilet) ● Patient learns adaptive self-efficacy beliefs

Adapted from Katzman et al. BMC Psychiatry 2014

FDA-Labeled Anxiety Indications

	GAD	OCD	Panic	Social Anxiety
Citalopram				
Clomipramine		X		
Duloxetine	X			
Escitalopram	X			
Fluoxetine		X	X	
Fluvoxamine		X		
Paroxetine	X	X	X	X
Paroxetine CR			X	
Sertraline		X	X	X
Venlafaxine XR	X		X	X
Buspirone	X			

PACKAGE INSERTS

Social Anxiety Pharmacotherapy

1st Line	SSRIs (typically Sertraline > Escitalopram > Fluvoxamine / CR > Paroxetine / CR > Citalopram > Fluoxetine), Venlafaxine, Pregabalin (600mg/day > placebo)
2nd Line	Benzodiazepines (alprazolam, clonazepam), gabapentin (900-3600mg/day), phenelzine
3rd Line	Atomoxetine, bupropion SR, clomipramine, divalproex, duloxetine, fluoxetine, mirtazapine, moclobemide, olanzapine, selegiline, tiagabine, topiramate
Adjunctive	aripiprazole, buspirone, paroxetine, risperidone
Specifically for performance anxiety	Beta-blockers

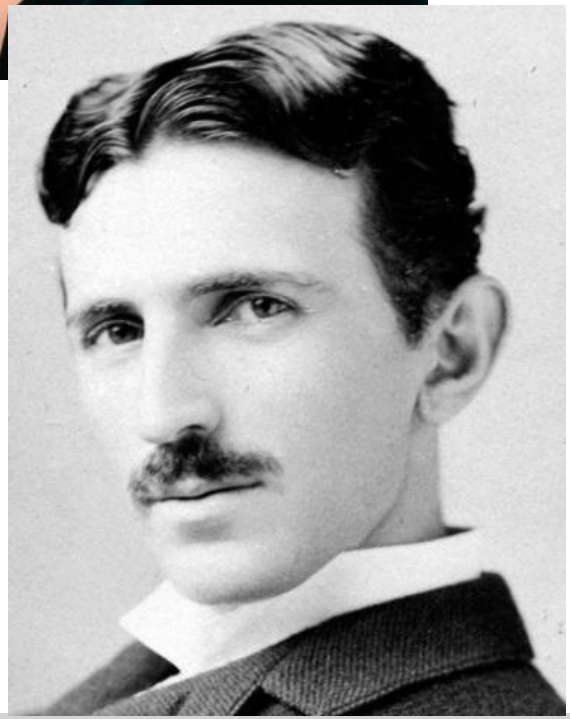
Katzman et al. BMC Psychiatry. 2014

Panic Disorder

- Recurrent unexpected panic attacks
- Panic attack: abrupt surge of intense fear or discomfort that reaches a peak within minutes, and during which time 4 or more occur (from calm or anxious state)

  - Palpitations
  - Sweating
  - Trembling/shaking
  - SOB
  - Sensation of choking
  - CP/discomfort
  - Nausesa/abomdinal distress
  - Dizziness, light-headedness
  - Chills/heat sensations
  - Paresthesias
  - Derealization / depersonalization
  - Fear of losing control or “going crazy”
  - Fear of dying

Panic Disorder

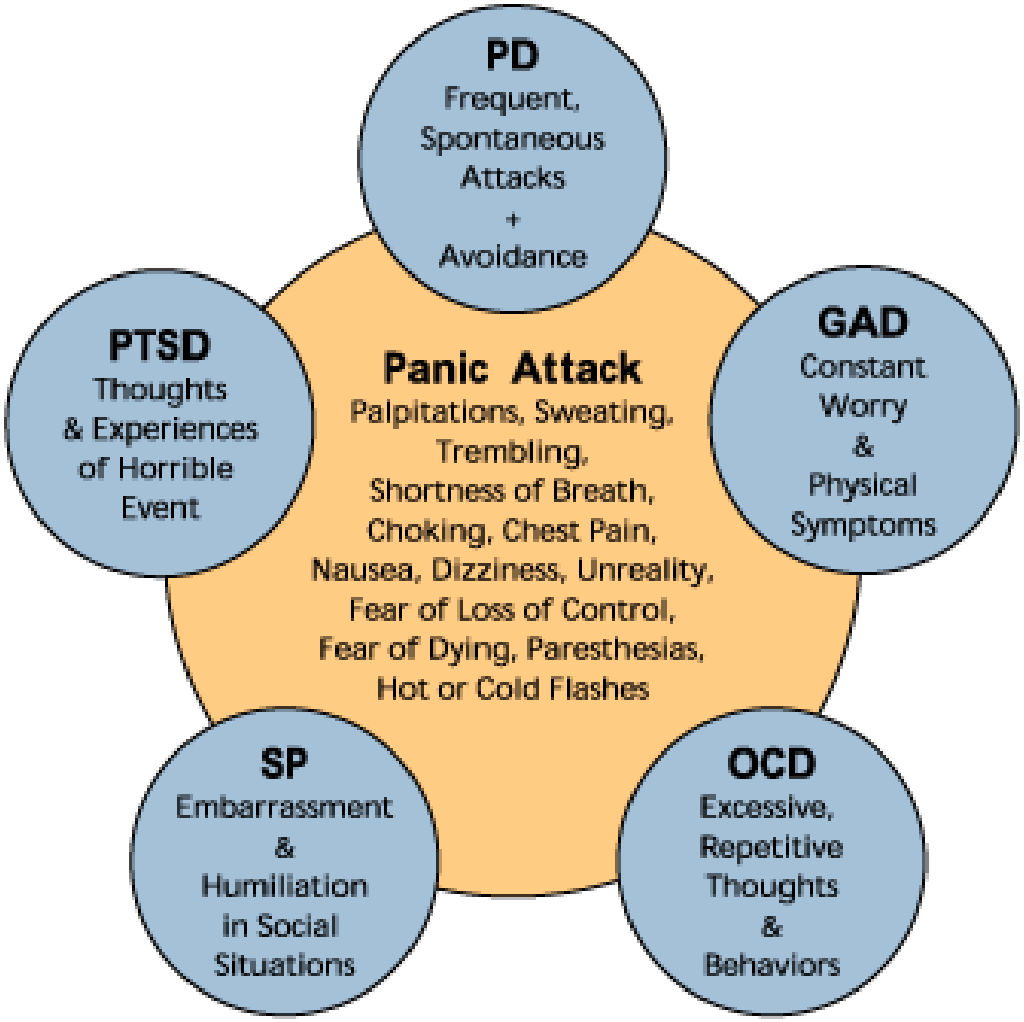


Background Info

- Lifetime prevalence of disorder ~5% versus 28% for attacks
- ~ 40-70% of PD patients will experience nocturnal panic
- RF: Women > men, middle aged, widowed/divorced, low SES
- More prevalent in medical conditions
  - Thyroid ● Cancer ● Chronic pain ● IBS ● Respiratory ● Cardiac ● Allergies
- Significant impact on QoL with ↑ risk for suicide
- Increased societal costs due to ↑ healthcare utilization and ↓ productivity
- 35-40% with comorbid MDD
- Frequently occurs with agoraphobia

Background

- Variable course with waxing / waning if untreated
- Panic attacks and Panic DO diagnosis in last 12 months associated with increased rate of suicidal ideation and suicide attempts
- Environmental RF:
  - H/o childhood physical & sexual abuse more common in PD
  - Smoking
  - Most people report identifiable stressors in month preceding first attack
- Panic attacks can occur in any anxiety or other mental disorder (eg: PTSD with panic attacks)



PD=Panic Disorder, GAD=Generalized Anxiety Disorder, OCD= Obsessive-Compulsive Disorder, SP=Social Phobia, PTSD= Post-traumatic Stress Disorder

Source: http://www.medical-look.com/Mental_health/Panic_disorder.html

Panic DO Treatment

- CBT favored significantly over medications in meta-analysis of 42 studies
  - Exposure is key component of psychotherapy
  - Typically 12-14 weekly sessions
- Minimal intervention techniques were > wait list controls
  - iCBT
  - Videoconference individual/group tx

Panic DO Treatment

- Combination CBT + benzodiazepines may be inferior to CBT alone
- CBT continues to be effective even when discontinuing medications
  - Benefits of CBT proven to last up to 3 years post treatment

FDA-Labeled Anxiety Indications

	GAD	OCD	Panic	Social Anxiety
Citalopram				
Clomipramine		X		
Duloxetine	X			
Escitalopram	X			
Fluoxetine		X	X	
Fluvoxamine		X		
Paroxetine	X	X	X	X
Paroxetine CR			X	
Sertraline		X	X	X
Venlafaxine XR	X		X	X
Buspirone	X			

PACKAGE INSERTS

Panic DO Pharmacotherapy

1st Line	SSRIs, venlafaxine
2nd Line	Clomipramine > imipramine > mirtazapine > benzodiazepines
3rd Line	Bupropion SR, divalproex, duloxetine, gabapentin, levetiracetam, milnacipran, olanzapine, phenelzine, quetiapine, risperidone, tranylcypromine
Not Recommended	Buspirone, propranolol, tiagabine, trazodone

TABLE 8. DOSING OF ANTIDEPRESSANTS AND BENZODIAZEPINES FOR PANIC DISORDER

	Starting Dose and Incremental Dose (mg/day)	Usual Therapeutic Dose (mg/day)[a]
SSRIs		
Citalopram	10	20–40
Escitalopram	5–10	10–20
Fluoxetine	5–10	20–40
Fluvoxamine	25–50	100–200
Paroxetine	10	20–40
Paroxetine CR	12.5	25–50
Sertraline	25	100–200
SNRIs		
Duloxetine	20–30	60–120
Venlafaxine ER	37.5	150–225
TCAs		
Imipramine	10	100–300
Clomipramine	10–25	50–150
Desipramine	25–50	100–200
Nortriptyline	25	50–150
Benzodiazepines		
Alprazolam	0.75–1.0[b]	2–4[b]
Clonazepam	0.5–1.0[c]	1–2[c]
Lorazepam	1.5–2.0[b]	4–8[b]

[a]Higher doses are sometimes used for patients who do not respond to the usual therapeutic dose.
[b]Usually split into three or four doses given throughout the day.
[c]Often split into two doses given morning and evening.

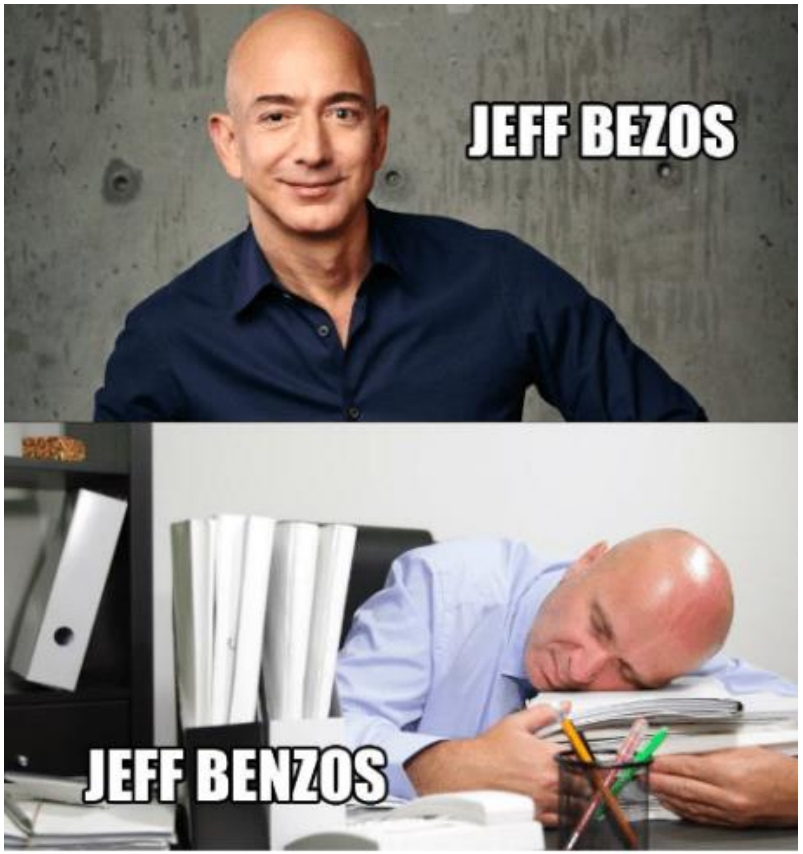
Panic DO Pharmacotherapy

- Maintenance treatment is recommended for 12-24 months or longer
- Some studies suggest that there is improvement over several years
- Discontinuation of meds should be done over weeks to months (eg: one dose step q1-2 mos) and with concurrent CBT to reduce likelihood of relapse

Important Patient Education

- Educate patient about activating potential for SSRIs
  - Insomnia
  - Restlessness / jitteriness
  - Agitation
- Initiating at low dose but will gradually move up to treatment-response dose

Let's talk about benzos…



- Benzos act rapidly for relief although panic sx likely to return quickly as medication is metabolized
- Not recommended by NICE
- APA and Canadian CPG say try SSRI / SNRI / TCA and CBT > benzo use
- No benzos if comorbid mood / substance disorder
- May be useful to treat adjunctive sx if patient is actively involved in therapy & on a base medication but must be carefully weighed
- When prescribed for panic disorder, use scheduled > prn & no longer than 2-4 weeks

Agoraphobia

- Unlinked from Panic DO as of DSM-5
- Marked fear/anxiety about two (or more) of the following 5 situations:
  - Using public transportation (e.g., automobiles, buses, trains, ships, planes)
  - Being in open spaces (e.g., parking lots, marketplaces, bridges)
  - Standing in line Being in enclosed places (e.g., shops, theaters, cinemas)
  - or being in a crowd
  - Being outside of the home alone
  - Fears that escape would be difficult or help not available
- Most commonly occurs with Panic DO
  - Lifetime prevalence 1.1% with panic v 0.8% without panic
- Risk factors: younger age, females, presence of other phobias
- 1/3 of patients have comorbid substance use disorder
- Median age of onset = 20 y/o

TREATMENT = follows Panic DO treatment

Generalized Anxiety Disorder

- Excessive anxiety and worry about multiple real-life events or activities associated with clinically significant distress/impairment
- Occurs more days than not for at least 6 months
- Worry is hard to control
- Anxiety/worry associated with at least 3/6 symptoms:
  - Restlessness or feeling keyed up or on edge
  - Being easily fatigued
  - Difficulty concentrating or mind going blank
  - Irritability
  - Muscle tension
  - Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep)

GAD Background

- Estimated 12 month prevalence = 1-4 % with lifetime ~6%
- Caucasions > other groups
- Median age of onset = 31
- Women 2-3 x more likely > men
- Highly comorbid with other anxiety disorders & MDD
- Risk of comorbid medical conditions is also higher (pain, HTN, cardiac & gastric)
- Chronic waxing and waning course

GAD-7

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
7. Feeling afraid as if something awful might happen	0	1	2	3
Add the score for each column	+	+	+	
Total Score *(add your column scores)* =				

If you checked off any problems, how difficult have these 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 _____

Source: Spitzer RL, Kroenke K, Williams JBW, Lowe B. A brief measure for assessing generalized anxiety disorder. *Arch Inern Med.* 2006;166:1092-1097.

GAD-7 Interpretation

Total Score	Interpretation
1-4	Minimal
5-9	Mild
10-14	Moderate
> 15	Severe

Using threshold of 10, the GAD-7 has a sensitivity of 89% and a specificity of 82% for GAD. More in-depth evaluation is recommended for scores ≥ 10.

GAD Psychotherapy

- CBT & pharmacotherapy appear to be equally effective
- Strongest evidence is for CBT
- Developing evidence for other modalities of psychotherapy:
  - Short term psychodynamic psychotherapy
  - Relaxation therapy
  - Acceptance based behavioral therapy
  - iCBT
  - Mindfulness Based CBT
  - Adjunctive Motivational Interviewing
- Balneotherapy?

FDA-Labeled Anxiety Indications

	GAD	OCD	Panic	Social Anxiety
Citalopram				
Clomipramine		X		
Duloxetine	X			
Escitalopram	X			
Fluoxetine		X	X	
Fluvoxamine		X		
Paroxetine	X	X	X	X
Paroxetine CR			X	
Sertraline		X	X	X
Venlafaxine XR	X		X	X
Buspirone	X			

PACKAGE INSERTS

GAD Pharmacotherapy

1st Line	SSRIs ~ SNRIs (although escitalopram may be < venlafaxine) *Maudsley's suggests that fluoxetine is most effective & sertraline best tolerated*
2nd Line	Buspirone, imipramine, quetiapine XR, vortioxetine, hydroxyzine, benzos, bupropion XL
3rd Line	Divalproex, mirtazapine, trazodone
Adjunctive	Pregabalin, aripiprazole, olanzapine, quetiapine / XR, risperidone
Not Recommended	Beta-blockers, tiagabine, ziprasidone

Katzman MA et al. BMC Psychiatry 2014; Maudsley's Prescribing Guidelines in Psychiatry 2019

GAD Pharmacotherapy

Anticonvulsants:

- Pregabalin: holds approval in Europe for GAD
  - 4-placebo-controlled studies (Pande et al, 2003; Pohl et al, 2005; Rickels et al, 2005; Montgomery et al, 2006)
  - Effective dose ranges: 150-600 mg/day
  - Initially 150mg daily, increased gradually to max of 600mg in 2-3 divided doses
    - Don’t stop abruptly due to risk of precipitated seizures
- Gabapentin: case report data suggests benefit but not as monotherapy

Alternative GAD Treatments

- rTMS
  - Small, open label trial showed efficacy as monotherapy or adjunctive with SSRIs; improvements were maintained 6 months after completion
- Herbal supplements
  - Lavender oil & *Galphimia glauca* extract have been demonstrated to be as efficacious as lorazepam
  - Cochrane meta-analyses found two studies of passiflora (passion flower) indicating it was as effective as benzodiazepines and one study of valerian which found no significant differences between placebo, valerian, or diazepam
  - Unfortunately, because these preparations are poorly standardized and have substantial variation in proportion of the active ingredient in different products, they cannot be widely recommended

Alternative GAD Treatments

- RCT of adjunctive weight training or aerobic exercise > wait list treatment
- Meditation and Yoga are demonstrating increasingly powerful results but studies have limitations
- Bright Light Therapy is not recommended

Question #1

- 34 y/o WF presents to your office with c/o headaches and muscle tension that are worsening in past 7 months. She acknowledges being a “worry wart” since childhood but anxiety has only increased since she moved & started a new job. She finds that while she likes her job, her performance has slipped because she can’t concentrate, often noting that her thoughts drift off to state of American politics, financial stability of her family, eventual death of her parents, and if she consumes too much red meat. She acknowledges restlessness, insomnia, and inability to control worry. Denies overt symptoms of depression. Physical examination and lab evaluation is unremarkable.

What is the most likely diagnosis?

1) Panic Disorder
2) Obsessive Compulsive Disorder
3) Generalized Anxiety Disorder
4) ADHD, inattentive type

What is the most likely diagnosis?

1) Panic Disorder
2) Obsessive Compulsive Disorder
3) **Generalized Anxiety Disorder**
4) ADHD, inattentive type

You are super savvy & administer the GAD-7. Her score is 19. What is your next treatment choice?

1) Prescribe Cyclobenzaprine 10mg PO qHS for muscle tension
2) Refer for individual CBT & start Sertraline 25mg x 7 days, then 50mg daily. Re-eval in 3-4 weeks.
3) Refer to Wellness Program through LMH
4) Tell her to “Don’t worry, be happy.”

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3) Refer to Wellness Program through LMH
4) Tell her to “Don’t worry, be happy.”

She returns to your office in 1 month with reduction in GAD-7 score to 14 but is still c/o residual sx. Sertraline dose is 50mg daily with good tolerance. She has met therapist once so far. What is your next move?

1) Increase dose of Sertraline to 100mg daily
2) Increase dose of Sertraline to 150mg daily
3) Leave dose of Sertraline at 50mg daily
4) Add on Gabapentin 100mg TID
5) Watch and wait

She returns to your office in 1 month with reduction in GAD-7 score to 14 but is still c/o residual sx. Sertraline dose is 50mg daily with good tolerance. She has met therapist once so far. What is your next move?

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5) Watch and wait

Case #2

- 41 y/o WM presents to your office with CC of episodes chest pain, palpitations, sweating, dizziness and SOB that have been occurring when he thinks about occupational stressors and marital discord. Episodes last ~ 20 minutes and cause him to feel “exhausted and crazy.” He has had to leave work and finds himself worrying that he will have another episode when in front of colleagues. Denies other significant worries but finds that he is starting to feel depressed as a result of these attacks. Has increased alcohol use since these attacks began from 1-2 beers per week to 5-6 as it’s the only thing that will “help me calm down.” No PMHx. Labs including UDS and EKG are WNL.

You've diagnosed Panic Disorder and the patient is open to a medication. Your next step is:

1) Alprazolam 1mg BID

2) Venlafaxine ER 150mg daily + refer to therapy

3) Cannabidiol

4) Venlafaxine ER 37.5mg daily x 7 days, then 75g daily

You've diagnosed Panic Disorder and the patient is open to a medication. Your next step is:

1) Alprazolam 1mg BID

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3) Cannabidiol

4) Venlafaxine ER 37.5mg daily x 7 days, then 75g daily

The patient returns to you in one month & has only noticed partial improvement. You decide to:

1) Refer directly to one of the Yoders
2) Refer for individual therapy & increase Venlafaxine ER to 150mg daily
3) Begin Pregabalin 150mg BID
4) Watch and wait

The patient returns to you in one month & has only noticed partial improvement. You decide to:

1) Refer directly to one of the Yoders
2) Refer for individual therapy & increase Venlafaxine ER to 150mg daily
3) Begin Pregabalin 150mg BID
4) Watch and wait

At the next month's follow up appointment, the patient's BP is now 138/108 and GAD-7 has not improved. What would you do next?

1) Increase Venlafaxine ER to 225mg daily
2) Add on Lisinopril 10mg daily
3) Cross taper to Fluoxetine
4) Leave dose and recheck in one month

At the next month's follow up appointment, the patient's BP is now 138/108 and GAD-7 has not improved. What would you do next?

1) Increase Venlafaxine ER to 225mg daily
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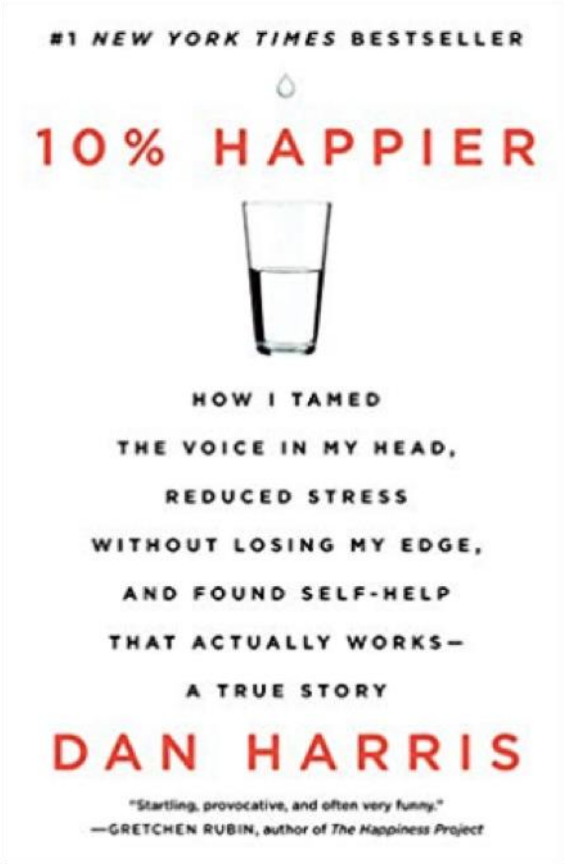
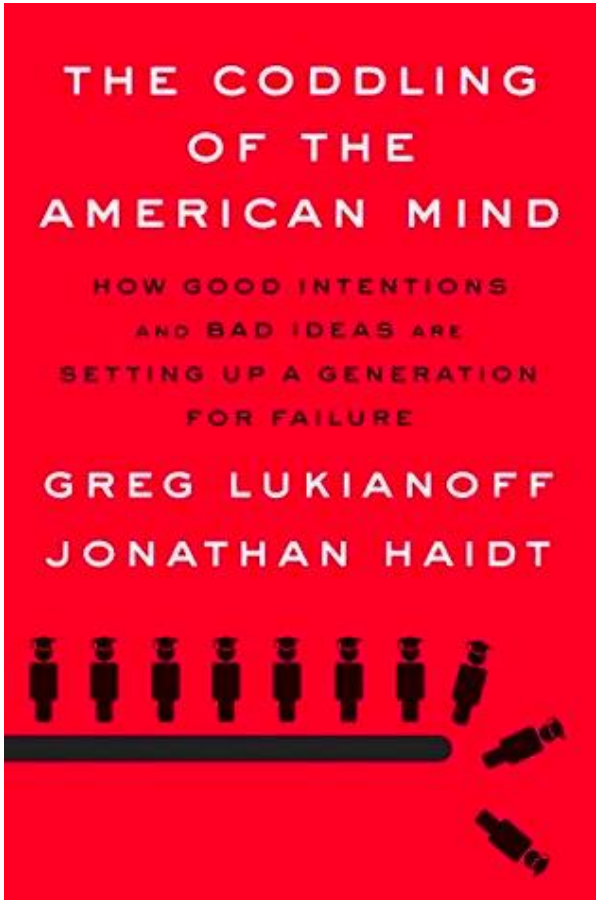
Bonus Material

- How to Meditate
- Apps for Mindfulness:
  - 10% Happier
  - Head Space
  - Insight Timer
- Maybe even consider doing a 1 minute meditation with the patient?

Dr. Yoder's Book Club Recommendations





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