Brigham and Women's Hospital
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Depression and Anxiety

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- Clinical focus: Psychiatric Urgent Care, Primary Care-Based Psychiatry
- Research focus: Psychiatric Urgent Care, Quality Improvement, Quality Measurement, Patient Safety

DISCLOSURES

With respect to the following presentation, I have no conflicts of interest.

OBJECTIVES

1. Choose between the 4 first-line antidepressant medication classes for individual patients with depression and/or anxiety based on their symptom profiles
2. Talk to patients about novel treatments being offered for depression
3. Distinguish between Generalized Anxiety Disorder (GAD) and Adjustment Disorder based on the longitudinal course of symptoms
4. Prescribe benzodiazepines less often than might otherwise be inclined to do

Case Example

JA is a 32-year-old man who presents for his annual exam. His PHQ-9 score is 16. He reports a moderately low mood for the last 8-9 months, but mostly he just doesn't have much energy or interest in things. He spends most of his time sleeping or vegging on the couch, and he is barely getting by at work because of a lack of interest and poor concentration. He has also gained about 20 pounds in the setting of overeating and a lack of exercise. He is open to trying an antidepressant medication. He also wants to quit smoking.

Although any first-line antidepressant might be reasonable, which one is this case most likely setting you up to choose?

A. Sertraline
B. Escitalopram
C. Bupropion
D. Mirtazapine
E. Venlafaxine

Although any first-line antidepressant might be reasonable, which one is this case most likely setting you up to choose?

A. Sertraline
B. Escitalopram
C. Bupropion
D. Mirtazapine
E. Venlafaxine

SSRIs, bupropion, mirtazapine and SNRIs are all considered equally effective for treating MDD[1-3]

- If there were no other factors to consider, picking one of these agents at random would be fine
- Each class has unique effects (and side effects) that makes it more or less suitable for individual patients, given their symptom profiles
- Patient history (and family history) should also be considered

Bupropion

- Mild stimulant effects
- Suppresses the appetite
- Reduces smoking
- Not consistently helpful for anxiety

Mirtazapine

- Sedating
- Increases the appetite
- May lead to weight gain
- Optimal dosing for sleep can be unpredictable

SSRIs don’t have desirable side effects, but they have a wide range of indications

- First-line for virtually all anxiety disorders
- Well-studied for most medical conditions and pregnancy

SNRIs have a dual indication for neuropathic pain

Pharmacogenetic testing for antidepressants does not directly assess efficacy[13-14]

- Assesses rapid and slow variants of relevant P450 enzymes (2D6, 2C19)
- Theoretically can explain poor response or toxicity
- Data supporting the use at the outset of treatment is *limited*

Aim for 2-4 trials of first-line treatments before choosing an advanced therapy[15,16]

- “Treatment-resistant depression” usually defined as a failure to respond to **2 full therapeutic antidepressant trials***
- Frequency estimated ~30%
- Authorizations for advanced therapies typically require **4 failed trials**

*8 weeks at maximum approved or tolerated dose

Serotonin Modulators are newer but are not necessarily more effective[9-12]

Vilazodone

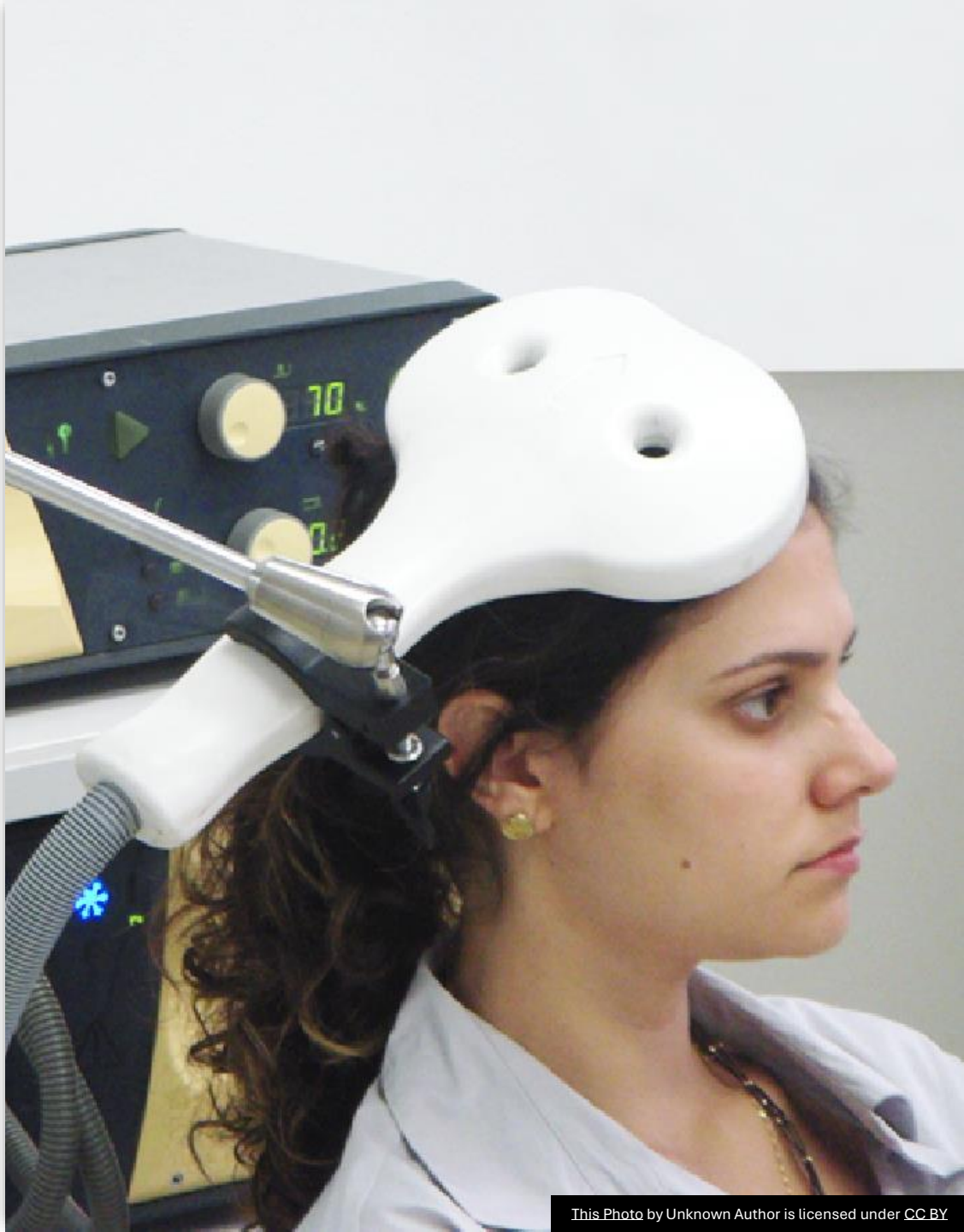
- May be less likely to cause weight gain and sexual side effects
- Must be taken with food

Vortioxetine

- May be less likely to cause sexual side effects (compared to paroxetine)

Transcranial Magnetic Stimulation (TMS) is a safe and effective ambulatory procedure[17]

- Magnetic pulses delivered to specific brain regions through the scalp via a magnetic inductor coil
- Ambulatory procedure
- Most common side effects are scalp discomfort and headache
- Avoid in patients with epilepsy
- Schedule may be inconvenient



Ketamine* and esketamine are effective for many patients, but there are caveats[18-22]

- Single dose can alleviate depression and suicidal ideation within 4 hours
- Effects last up to 1 week
- Facility should have nursing resources
- Long-term safety, efficacy, and treatment planning not well known
- Benefit requires activation of opioid receptors

*off-label use

Be on the lookout for red flags[22]

- Not a medical facility
- Patients are not medically monitored for 2 hours after admin
- Offered before first-line treatments are tried
- Promote psychedelic effects (i.e., higher doses than recommended)

Psilocybin* has been shown to improve MDD symptoms as well as depression, anxiety, and existential distress in serious illness[23,24]

- ~20 trials looking at various permutations, including phase III
- Cochrane review identified 6 qualifying trials in patients with life-threatening diseases (also looking at LSD, MDMA)
- Psilocybin-based treatments associated with improved:
  - Anxiety
  - Spiritual well-being
  - QoL
  - Pain
- Few adverse outcomes

*off label/investigational use

Please don’t prescribe cannabis* as a treatment for depression[25,26]

- Some pre-clinical studies suggest theoretical basis for a benefit in some patients
- Clinical studies do not show a benefit
- Large, population-based studies suggested higher risk of developing depression (and other psychiatric disorders) in individuals with cannabis use disorder

*off label/investigational use

Case #2

GM is a 29-year-old physician who is establishing care with a new PCP after moving to Boston to start her residency. On a routine anxiety screen (the GAD-7), she scores in the mild severity range. She explains that he has always had a tendency to worry more than her peers, but she never considered this to be a significant problem in life and never considered treatment. As a child, she also had some mild compulsive tendencies (symmetry compulsions, counting compulsions), but these have resolved. Today, she is feeling a little nervous about starting residency. She denies being depressed, and her PHQ-9 was negative.

What is the correct diagnosis?

A. Generalized anxiety disorder
B. Adjustment disorder
C. Obsessive-compulsive disorder
D. Panic disorder
E. No diagnosis

What is the correct diagnosis?

A. Generalized anxiety disorder ← Maybe
B. Adjustment disorder ← Maybe
C. Obsessive-compulsive disorder
D. Panic disorder
E. No diagnosis ← Maybe

Anxiety disorders are closely linked to temperamental traits

- Generally elevated state of arousal
- Features of other anxiety disorders (e.g., OCD, social anxiety) are common, especially in childhood
- Correlates with insomnia

Diagnosing GAD involves considering the longitudinal course

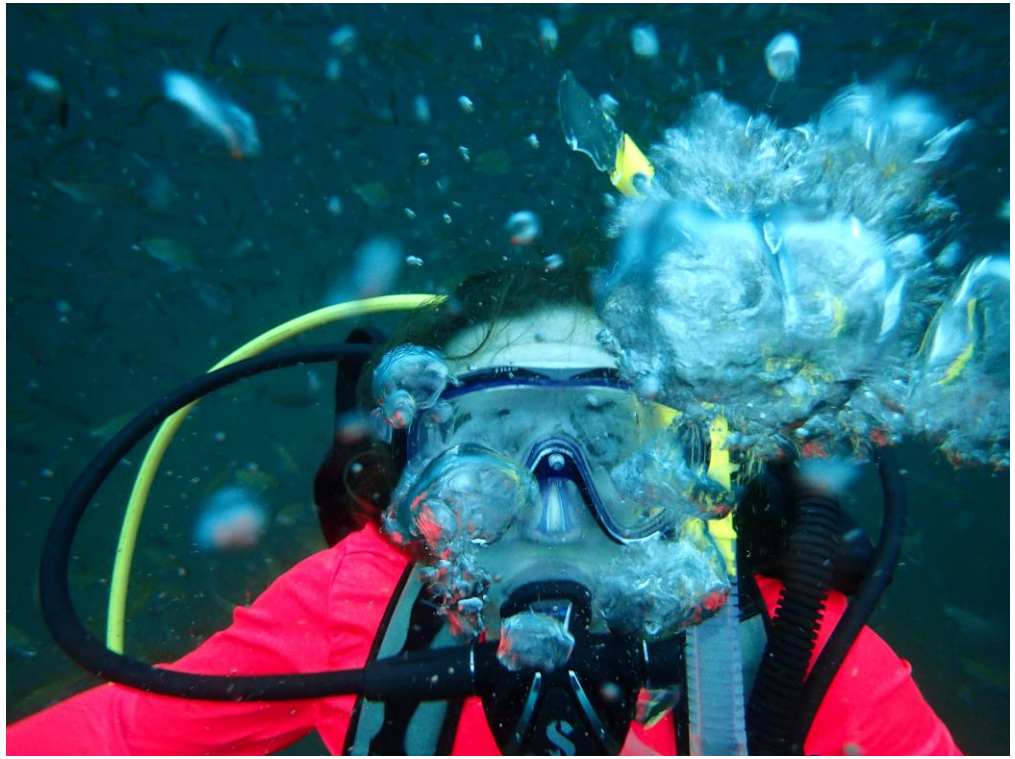
- Chronic condition
- Onset usually occurs in childhood, or at least early adulthood
- Does not emerge as a reaction to stressful life events or trauma (but individuals with GAD may cope more poorly with stress)
- Features of other anxiety disorders may also occur, but these do not necessarily indicate separate diagnoses

Anxiety-related experiences:

Catastrophization

Anxiety-related experiences:

Panic

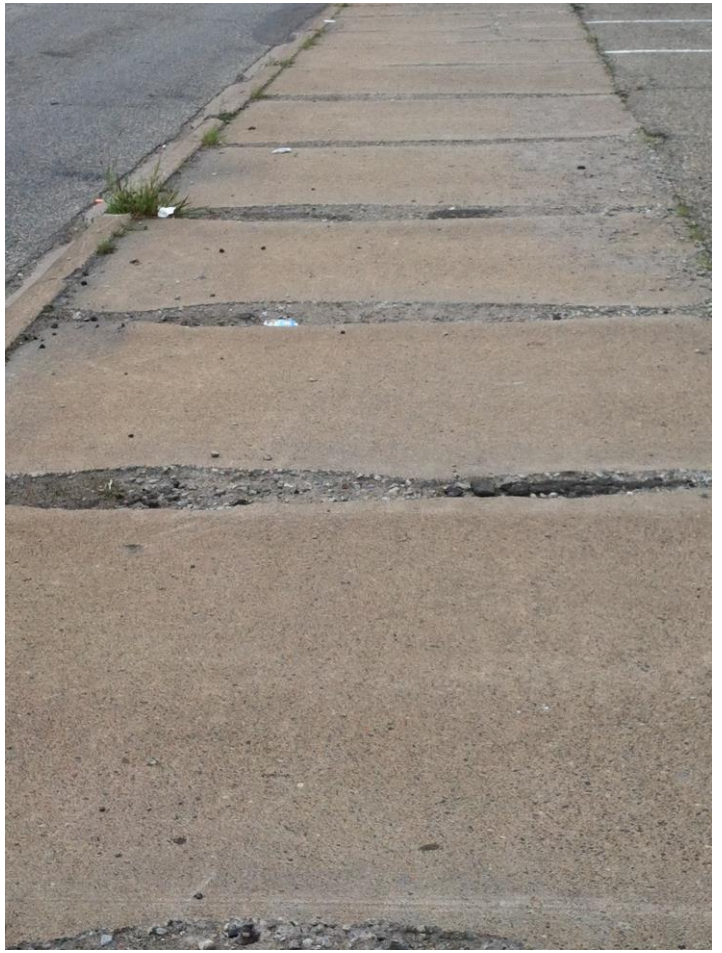


Anxiety-related experiences:

Avoidance

Anxiety-related experiences:

Compulsive behavior



First-line treatments

CBT

- Life-long benefits
- Takes a lot of effort
- May be hard to access

SSRIs (or SNRIs)

- Easier to prescribe than CBT
- Benefits go away when the medication is discontinued

Benzodiazepines do not improve long-term outcomes and are associated with serious problems

- Reduce severe symptoms in the short-term
- Usually* safe to use sparingly
- Avoid for chronic anxiety disorders
- Avoid in patients who are most at risk of adverse events
  - Elderly
  - Substance use disorders
  - Medical conditions affecting cognition or pulmonary functioning

SUMMARY

1. SSRIs, SNRIs, bupropion, and mirtazapine are all reasonable first choices for treating major depressive disorder
2. First-line treatment for anxiety disorders are SSRIs and CBT.
    1. SNRIs and mirtazapine can also be considered
    2. Bupropion is less predictable for anxiety
3. Benzodiazepines are useful for short-term or sparing use, but their risks should not be taken lightly

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