Managing Depression and Anxiety in Primary Care: From Textbook to Exam Room

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Disclosure Statement:
Relevant financial relationships in the past 12 months

• Consultant/Speaker: None
Disclosure Statement:
Relevant financial relationships in the past 12 months

- Financial: I do not have any competing financial interests. In fact, I have nothing really to invest due to three primary factors:
Disclosure Statement:
Relevant financial relationships in the past 12 months

- Depression
- Somatic Symptom Disorder
- Bipolar Disorder
## State of Mental Health Care 2020

**Overall Ranking 2020**

<table>
<thead>
<tr>
<th>Rank</th>
<th>State</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>Washington</td>
</tr>
<tr>
<td>46</td>
<td>Alaska</td>
</tr>
<tr>
<td>47</td>
<td>Wyoming</td>
</tr>
<tr>
<td>48</td>
<td>Utah</td>
</tr>
<tr>
<td>49</td>
<td>Idaho</td>
</tr>
<tr>
<td>50</td>
<td>Oregon</td>
</tr>
<tr>
<td>51</td>
<td>Nevada</td>
</tr>
</tbody>
</table>
Uncertain Times 2020: Driving Depression/Anxiety?

- Burnout at work
- Sleep deprivation
- The benzo/opiate crisis
- The marijuana debate
- Increasing political discord
- Social polarization
- Covid-19/stock market volatility
Burnout

Which Physicians Are Most Burned Out?

- Critical Care 48%
- Neurology 48%
- Family Medicine 47%
- Ob/Gyn 46%
- Internal Medicine 46%
- Emergency Medicine 45%
- Radiology 45%
- Physical Medicine & Rehabilitation 44%
- Urology 44%
- Allergy & Immunology 44%
- Surgery, General 43%
- Cardiology 43%
- Otolaryngology 42%
- Pulmonary Medicine 41%
- Pediatrics 41%
- Infectious Diseases 40%
- Nephrology 40%
- Oncology 39%
- Gastroenterology 38%
- Anesthesiology 38%
- Rheumatology 38%
- Psychiatry 36%
- Public Health & Preventive Medicine 36%
- Diabetes & Endocrinology 35%
- Orthopedics 34%
- Ophthalmology 33%
- Pathology 32%
- Dermatology 32%
- Plastic Surgery 23%
Bureaucratic Tasks - Our Doom?

What Contributes to Physicians' Burnout?

- Too many bureaucratic tasks (e.g., charting, paperwork): 56%
- Spending too many hours at work: 39%
- Lack of respect from administrators/employers, colleagues, or staff: 26%
- Increasing computerization of practice (EHRs): 24%
- Insufficient compensation: 24%
- Lack of control/autonomy: 21%
- Feeling like just a cog in a wheel: 20%
- Lack of respect from patients: 16%
- Government regulations: 16%
- Decreasing reimbursements: 15%
- Emphasis on profits over patients: 15%
- Maintenance of Certification requirements: 12%
Burnout Model
(Cross-National Validation)

Background Variables
- Sex
- Age
- Children
- Solo Practice
- Academic Practice
- Work hours

Mediating Variables
- Work Control
- Work-Home Interference
- Home Support

Variable Outcomes
- Stress
- Satisfaction

Outcomes
- Burnout

Burnout Model
(Cross-National Validation)

Background Variables:
- Sex
- Age
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- Work Control
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Variable Outcomes:
- Stress
- Satisfaction

Burnout

2 Quick Tips

• “Three Good Things” exercise
  – In a trial of 148 IM residents at Duke, a 15% decrease in burnout was seen in 2 weeks and a year after the intervention, 48% remained resilient. 10 days appears to be the sweet spot.
    » www.dukepatientsafetycenter.com Sexton, B et al.

• Never forget the power of “career fit”: save 10% FTE for what you are most passionate about.
Case 1 – “Feeling Like an 80 year-old”

• Ms. A, age 25, has a gastrointestinal stromal tumor (GIST) who presents with soreness, abdominal cramping, and fatigue – which all worsened since she started chemotherapy with sunitinib. Most of all, she reports low mood.

• Patient Health Questionnaire-9 (PHQ-9) score is 14 out of 27 = moderate depression.
Screening For Depression
2-item PRIME-MD Screen

1. Have you had little interest or pleasure in doing things? (anhedonia)
2. Have you been feeling down, depressed or hopeless over the past month?

Patient Health Questionnaire (PHQ)-9

- 9 questions based on major depressive episode DSM IV criteria
- NOT diagnostic, but is a helpful tool for
  - Screening
  - aiding clinical diagnosis
  - monitoring severity over time
# PHQ-9 Scoring

<table>
<thead>
<tr>
<th>Score</th>
<th>Depression Severity</th>
<th>% of ANY Depressive D/O</th>
<th>Proposed Tx</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4</td>
<td>None</td>
<td>0.1%</td>
<td>None</td>
</tr>
<tr>
<td>5-9</td>
<td>Mild</td>
<td>12.6%</td>
<td>Repeat PHQ-9 at F/U</td>
</tr>
<tr>
<td>10-14</td>
<td>Moderate</td>
<td>54.9%</td>
<td>Treatment plan, considering counseling, follow-up and/or pharmacotherapy</td>
</tr>
<tr>
<td>15-19</td>
<td>Moderately Severe</td>
<td>90.6%</td>
<td>Immediate initiation of pharmacotherapy and/or psychotherapy</td>
</tr>
<tr>
<td>20-27</td>
<td>Severe</td>
<td>97.5%</td>
<td>Immediate initiation of pharmacotherapy and, if severe impairment or poor response to therapy, expedited referral to a mental health specialist for psychotherapy and/or collaborative management</td>
</tr>
</tbody>
</table>

*10 as cutoff for further investigation produces 88% sensitivity and 88% specificity*
Case 1…continued

- Ms. A, age 25, has a gastrointestinal stromal tumor (GIST) and is sore all over with abdominal cramping and fatigue – all worsened since she started chemotherapy with sunitinib. She also notes low mood.

- What labs would you order?
## Key Lab Results

<table>
<thead>
<tr>
<th>Component Results</th>
<th>Component</th>
<th>Value</th>
<th>Range</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td></td>
<td>110.00 (H)</td>
<td>0.28 – 5.00 uIU/ml</td>
<td>Fin</td>
</tr>
<tr>
<td>FREE T4</td>
<td></td>
<td>0.5 (L)</td>
<td>0.7 – 1.8 ng/dL</td>
<td>Fin</td>
</tr>
</tbody>
</table>
Treating thyroid disorders and depression: 3 case studies

Recognizing clinical nuances can improve screening and treatment of both disorders

Many endocrine disorders can manifest as depression, including relatively rare disorders such as Cushing’s syndrome (hypercortisolism) or Conn’s syndrome (primary hyperaldosteronism) as well as common ones such as diabetes mellitus. Most clinicians do not routinely screen for adrenal disorders when evaluating depressed patients because the yield is low, but do screen for thyroid disease because these disorders often mimic depression. The following 3 cases from my practice illustrate some nuances of screening and treating depressed patients with suspected thyroid abnormalities.

**CASE 1**

**Feeling ‘like an 80-year-old’**

Ms. A, age 25, has a gastrointestinal stromal tumor (GIST) and states that she feels “like an 80-year-old woman.” She is sore all over with facial swelling, abdominal cramping, and fatigue. This feeling has worsened since she started chemotherapy with sunitinib for the GIST. Her Patient Health Questionnaire-9 (PHQ-9) score is 14 out of 27, indicating moderate depression. As part of a workup for her depression, what general laboratory tests would be most helpful?

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*Current Psychiatry* Vol 12(1), 2013: 17-21
Case 1…continues

- Ms. A gets better from a physical standpoint with levothyroxine dosed at 1.6 mcg/kg/day. Mood improves but later deteriorates and she asks you about antidepressant therapy. What do you “prescribe?”
Physical Activity is a Non-Pharmacological, Natural Treatment of Depression

“What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?”
Exercise Equivalent to Pharmacotherapy

- SMILE study: 16 weeks of aerobic exercise training was comparable to that of standard pharmacotherapy (sertraline) and combined exercise/meds

- 10 Month Continuation study: Remitted subjects in the exercise group had significantly lower relapse rates than subjects in the medication group.
Consensus Recommendation for Physical Activity

• Adults should accumulate at least 30 minutes of moderate-intensity physical activity (not necessarily exercise) each day
• This is equivalent to walking about 1.5 miles at a pace of 3-4 mph
• Doing more exercise and perhaps more strenuous exercise may provide additional health benefits

Statement endorsed by American College of Sports Medicine/Centers for Disease Control and Prevention, American Heart Association, NIH, the Surgeon General, and US Dietary Guidelines 2005
Are all antidepressants created equal?
STAR*D
4041 Patients
Citalopram

30% Remission
Higher dose – 41.8mg
Longer duration – 47 days
Citalopram Warning 8/24/11:

- Citalopram causes dose-dependent QT interval prolongation.
- Citalopram should not be prescribed at doses greater than 40 mg per day.
- 20 mg per day is the maximum recommended dose for patients with hepatic impairment or who are greater than 60 years of age.
**STAR*D**

4041 Patients

**Citalopram**

30% Remission  
Higher dose – 41.8mg  
Longer duration – 47 days

727 Non-Remitters Randomized for 14 weeks to:

- **Bupropion SR**  
  Out of class  
  Max: 400mg  
  25.5% Remission

- **Sertraline**  
  In-class  
  Max: 200mg  
  26.6% Remission

- **Venlafaxine XR**  
  Dual-action  
  Max: 375mg  
  25.0% Remission

STAR*D
4041 Patients
Citalopram
30% Remission
Higher dose – 41.8mg
Longer duration – 47 days

565 Non-Remitters Augmented for 12 weeks with:

Bupropion SR
DA + NE reuptake inh.
Max: 400mg
39% Remission

Buspirone
5HT-1A partial agonist
Max: 60mg
32.9% Remission

Cognitive Therapy

STAR*D says pick a med, any med… but this may not be the whole story

- 2009 study examined 117 randomized controlled trials from 1991-2007 that studied the effects of 12 antidepressants in 25,928 patients with major depression with a mean duration of studies at 8.1 weeks.

STAR*D says pick a med, any med...

- 2018 updated study: 522 trials with 116,477 patients

- **Efficacy:** agomelatine*, amitriptyline, escitalopram, mirtazapine, paroxetine, venlafaxine, and vortioxetine were more effective than other antidepressants (range of ORs 1·19–1·96),
  - Least efficacious: fluoxetine, fluvoxamine, reboxetine, and trazodone (OR 0·51–0·84).

- **Acceptability:** agomelatine*, citalopram, escitalopram, fluoxetine, sertraline, and vortioxetine were more tolerable than other antidepressants (range of ORs 0·43–0·77)
  - Highest dropout rates: amitriptyline, clomipramine, duloxetine, fluvoxamine, reboxetine, trazodone, and venlafaxine.

Treatment-Resistant Depression (TRD)

• Typically defined as inadequate or no response to the appropriate courses of at least two antidepressants* (when ECT is indicated in depression).

• Major concerns is medication non-adherence with many cases of TRD or misdiagnosis (think bipolar disorder)

• Consider cytochrome P450 genotype testing
Other Procedures

- Vagal nerve stimulator (VNS) - approved by the FDA in 2005 for TRD. Stimulates the brain via electrical signals from the implanted device.

- ECT – used of electric current to trigger a brief seizure (30-60 seconds) – boasts a 90% efficacy rate in older studies.
Transcranial Magnetic Stimulation

- TMS (transcranial magnetic stimulation) – 19 minute outpatient procedure typically done daily for 4-6 weeks approved by the FDA in October ‘08 for Treatment Resistant Depression.

Google: “AM Northwest TMS”
Augmentation Strategies in Severe or Treatment-resistant Depression: Which are you most scared to prescribe?

- 2nd Antidepressant (bupropion common)
- Lithium
- Atypical antipsychotics - FDA says aripiprazole, quetiapine XR, brexpiprazole, olanzapine*
- Lamotrigine
- Thyroid hormone
- Esketamine intranasal

Therapy: Is Lithium Still an Option?

• In the USA, prescription of lithium for outpatients nearly halved between 1992 and 1996, and 1996 and 1999, whereas the rate of prescription of valproate almost tripled.

Therapy: Is Lithium Still an Option?

- Many studies consistently support the impression that risks of suicide and of life-threatening attempts are far lower during treatment with lithium (and even with a placebo) than without treatment.

- What NNT would you guess there is with Li+ as it pertains to avoiding 1 life-threatening or fatal suicidal act? 23
Lithium’s Medical Risks

- Hypothyroidism – annual TSH needed
- Nephrogenic diabetes insipidus – irreversible
- Multiple neurological side effects: sedation, decreased concentration, tremor
- Weight gain/Acne
- **Avoid** these meds which increase risk of lithium toxicity: NSAIDS, ACE-I, ARBs, diuretics (thiazide > loop), tetracycline
- Ebstein’s anomaly in 1st trimester
ALWAYS Screen for Bipolar before treating Depression

• Rule of 3’s: If someone has had 3 jobs, 3 marriages, or has failed more than 3 different antidepressants, suspect bipolar disorder

• Irritability can be a mania equivalent

• Think bipolar if a patient first exhibited mood symptoms earlier than age 25.
Case 2 – benzos and opiates

- Ms. B is 48 with significant anxiety/depression and chronic pain (on COT).
- She talks calmly at first then later asks you for a benzo prescription for anxiety. When you discuss your concerns about mixing benzos with opiates, she starts yelling at you for being “just another one of those providers who doesn’t care about people!”
- What is your next move?
• A. Go into “limit setting” mode and quickly wind the discussion down.
• B. Listen to her diatribe on the evils of the “medical system” for a few more minutes uninterrupted.
• C. Excuse yourself politely but then head over to a clinic social worker or nurse like a heat-seeking missile!
• D. Just give her the benzo. It ain’t worth the fight (or low patient satisfaction survey numbers).
Personality

- Predispositions
- Temperament
- Biological Factors (hormones, etc)

- Addictions
- Psychoanalytic (defenses)

- Monkey see, monkey do

- Trauma
- Life stresses
Borderline Personality Disorder
(Emotionally Unstable Personality Disorder in the ICD-10)

A. Significant impairments in personality functioning manifest by:
   • a. Empathy: Compromised ability to recognize the feelings and needs of others
   • b. Intimacy: Intense, unstable, and conflicted close relationships

1. Negative Affectivity, characterized by:
   – a. Emotional lability
   – b. Anxiousness
   – c. Separation insecurity: think abandonment
   – d. Depressivity

2. Disinhibition, characterized by:  a. Impulsivity  b. Risk taking

3. Antagonism, characterized by:  Hostility
Boundary Pearls

- Setting Limits (empathically) is very important but so is listening in a supportive manner.
- Use “time statements” to naturally wind conversation down – helps with long-winded patients as well.
- Sometimes, leaving the room to allow for “de-escalation” can be effective.
Case 2 continued

…she constantly worries about the health of her parents (on top of her own health) especially since her father had a myocardial infarct.

She knows that the worries are mostly unfounded but she can’t stop worrying. Her social contacts have diminished because of “nerves.”
Differential Diagnosis

- Illness Anxiety Disorder
  - High health concerns, low somatic symptoms
- Somatic Symptom Disorder
  - High health concerns, high somatic symptoms
- Conversion Disorder
  - High health concerns, functional neurological symptoms
Generalized Anxiety Disorder

• Anxiety disorders are among the most prevalent of mental disorders, and GAD is the most common* impairing anxiety disorder.

• The degree of disability attributable to GAD compares with that of major depression and is similar to that of chronic physical illnesses such as diabetes.

• Low levels of professional help-seeking

  » Mackenzie CS et al. Am J Geriatric Psych 19:4, April 2011
Normal vs. Abnormal Anxiety

The “right” amount of anxiety

Too much anxiety
Generalized Anxiety Disorder

think TICKES

Three of the following over 6 months

- Tension in muscles
- Irritability
- Concentration is poor
- Keyed up/Restless
- Easily Fatigued
- Sleep disturbance

The Generalized Anxiety Disorder (GAD)-7 scale. The first 2 items constitute the GAD-2 subscale.

<table>
<thead>
<tr>
<th>Problem</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feeling nervous, anxious, or on edge</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Not being able to stop or control worrying</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Worrying too much about different things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Having trouble relaxing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Being so restless that it is hard to sit still</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Becoming easily annoyed or irritable</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Feeling afraid as if something awful might happen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Total Score = Add Columns

Question: Generalized Anxiety Disorder

Which of the following medications does not have FDA indication but is reasonable for GAD?

A. Escitalopram (Lexapro)
B. Duloxetine (Cymbalta)
C. Hydroxyzine (Atarax/Vistaril)
D. Buspirone (Buspar)
E. All have FDA indication
Question: Generalized Anxiety Disorder

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  C. Hydroxyzine (Atarax/Vistaril)
  D. Buspirone (Buspar)
  E. All have FDA indication
Hydroxyzine: A Suitable Anxiolytic

- European hydroxyzine vs. buspirone RCT data
  - Advantages of hydroxyzine:
    - Cheap
    - Non-addicting
  - Disadvantages of hydroxyzine:
    - Sedating
    - Could lead to anticholinergic delirium

Adding Long-term Benzos for Anxiety:
A Few Words About The Benzos

- Best if used for a SHORT period of time
- Multiple risk factors for dependence
  - Alcoholic use disorder
  - Use of benzos with short half lives/rapid onset of action (xanax, valium, halcion, tranxene)*
  - Use of higher potency benzos (klonopin, xanax, ativan, valium)*
- Associated with Falls in the elderly
- Suppress REM sleep and stage 3 and 4 sleep

* Brand names used for purposes of easy identification
So you’re telling me no benzos…

- Other agents that are not BZDs that may have a role in anxiety management
  - Propranolol – helps physiologic triggers off-label, does not treat emotional component of anxiety
  - Hydroxyzine – FDA indication for GAD
  - Gabapentin – Off-label evidence for SAD & PD
  - Pregabalin – Off-label evidence for SAD & GAD
  - Buspirone – FDA indication for GAD
  - Clomipramine – FDA indications for OCD & Panic
What do Contractors and Doctors Have in Common
(besides both ending in “ctors”)

[Images of a contractor and a doctor]
High Suicide Rates
CDC Occupational Mortality Report 2016

• Males and females in the “construction and extraction industries” had the highest suicide rates: 49.4 per 100,000 and 25.5 per 100,000 respectively.

• Physicians are 2.5 times more likely to die by suicide than general population. Black, female physicians are at highest risk: 5 times higher. White males 2 times higher.*
Suicide rates rose across the US from 1999 to 2016.
Suicide Rates from ’99 -‘16

- Most deaths by suicide were men (77%)
- Most (51%) were aged 45-64 years.
- The median suicide rate per county rose from 15 per 100,000 (1999-2001) to 21 per 100,000 (2014-2016)
- Counties with the highest risk of suicide:
  - Western states (e.g., Colorado, New Mexico, Utah, and Wyoming)
  - Appalachia (e.g., Kentucky, Virginia, and West Virginia)
  - Ozarks (e.g., Arkansas and Missouri)
Coupling
Alcohol-related deaths from ’99 - ’17

- Rate doubled overall in the US (72,558 in 2017 from 35,914 in 1999) – 3rd leading cause of preventable death
- Men accounted for 76.4% of the deaths
- Women experienced a 135.8% increase in the number of EtOH-related deaths over the study period.
Challenge of Impulsivity

• Nearly 80% of suicide attempts are impulsive acts.
• 24% of those who made near-lethal suicide attempts decided to kill themselves less than five minutes before the attempt.
• 70% made the decision within an hour of the attempt.
• 90% of people who survive a suicide attempt do not go on to die by suicide.

Systematic Suicide Assessment

- Assess for delirium
- Assess for psychosis – hallucinations
- Assess for mood disorders
- Quote what the patient plans to do – perhaps offer a suggestion if needed
- Collateral from a third party
Summary Statement

- Patient says that she is no longer feeling suicidal. There is no evidence of delirium or psychotic features. She acknowledges her family problems and says that counseling makes sense. She has agreed to a follow-up appointment at the mental health center tomorrow and plans to call her employer today to say she will be back at work next week. She has discussed these plans with her husband who agrees to be seen with her at the initial psychiatric assessment following discharge. Pt no longer needs constant observation.

SSRI Pearls By Drug

• Fluoxetine (Prozac)
  – Longest half-life (7 days vs ~ 24 hours for all others)
  – Good for co-morbid eating disorders and non-adherent patients

• Paroxetine (Paxil)
  – Only Pregnancy Category D (others are C)
  – Most anticholinergic
  – Most sexual side effects
  – Most likely SSRI to cause discontinuation syndrome
SSRI Pearls By Drug

- Fluvoxamine (Luvox)
  - Only FDA approved for OCD in US
- Sertraline (Zoloft)
  - SADHART study in cardiac patients
  - Least expressed in breast milk
- Citalopram (Celexa)
  - FDA warning about QTc prolongation
  - STAR*D starting drug
SSRI Pearls By Drug

• Escitalopram (Lexapro)
  – S-Isomer of Celexa – fewer side effects?
  – Most prescribed antidepressant in the country

• Vilazodone (Viibryd)
  – FDA approved 2011
  – Must take with food for absorption
    • AUC and Cmax doubles with even a light meal
  – Better sexual side effect profile?
    • Reported rates similar to other SSRIs
    • The 2 studies using sexual function scales had conflicting data
SNRI Pearls by Drug

• Venlafaxine (Effexor)
  – Notorious discontinuation syndrome
• Desvenlafaxine (Pristiq)
  – R-Isomer of venlafaxine – less side effects?
• Duloxetine (Cymbalta)
  – FDA approved for diabetic neuropathic pain
  • almost equal serotonin/norepinephrine (compared to about 3 orders of magnitude preference for serotonin in the other 2 SNRIs); thus receptor profile more like TCAs
• Levomilnacipran (Fetzima) – newer option; cousin of milnacipran (Savella) for fibromyalgia
Newer Antidepressants

• Vortioxetine (Trintellix)
  – Promising data in reducing progression of cognitive decline
  – Multimodal serotonin receptor activity
  – Minimal effects on weight/sex drive

• Vilazodone (Viibryd)
  – Faster onset of action and helpful in anxiety
  – Multimodal serotonin receptor activity
  – Minimal effects on weight/sex drive
Common “Other” Antidepressants

- Bupropion (Wellbutrin)
  - Helpful in smoking cessation (Zyban)
  - Seizure risk (avoid in at-risk patients)
  - “Stimulant-like”
    - No sexual side effects
    - Can be used to treat mild ADHD sx
    - May exacerbate HTN
    - In short term (first several weeks of treatment), may exacerbate anxiety. However, it is anxiolytic after therapeutic window reached (6-12 weeks)

- Trazodone – yes, it is an antidepressant
  - Typically used as a sleep aid b/c effective dose for depression is about 300-400 mg daily (extremely sedating)
  - Adds to serotonergic load in a patient
  - Warn male patients about priapism risk
Common “Other” Antidepressants

- Mirtazapine
  - Fewer sexual side effects than SSRI/SNRIs
  - Induces sleep at lower doses (start at hs)
  - Increases appetite (avg weight gain 6 lbs)
  - Although rare, there is evidence of blood dyscrasias (neutropenia, agranulocytosis)
General Take on the TCAs

- Monotherapy in younger patients – reasonable, especially when cost is an issue or with a comorbid pain syndrome
- Tremendous anticholinergic load…dry mouth is a bear!
- Elderly patients: more concerning from a cardiac conduction/sedation/toleration standpoint*
- Watch out for “augmentation” strategies – especially involving SSRIs like prozac – that lead to high TCA levels. When in doubt, check a TCA level.

QRS > 100 has been associated with seizures (34%) and arrhythmia (14%)
Selegiline (EMSAM), not...

- Transdermal MAO-I inhibitor (remember them?): hypertensive crisis, 2-week “wash-out”
- No dietary constraints with 6mg/24hr patch
- Higher doses (9mg/12mg): diet restriction of tyramine – aged cheeses, tap beer mentioned specifically but soy often overlooked
- $$$$$$
Reminder: Three Warnings with SSRIs

- Suicide Warnings
- Serotonin Syndrome
- Increased Bleeding
SSRIs may increase the risk of abnormal bleeding

- Case-control data from 1992-2000
- Cases = 196 of 64,647 new antidepressant users hospitalized for abnormal bleeding; Controls = 5/case matched for age and sex (73% were women)
- Showed that bleeding cases increased with degree of serotonin reuptake inhibition (18 low, 75 intermediate, 103 high)
- Uterine bleeding, upper GI bleeds were most common

» Arch Intern Med 2004;164:2367-2370
Bleeding Risk?

• Take into account the increased risk of bleeding associated with SSRIs, particularly for older people or people taking other drugs that can damage the gastrointestinal mucosa or interfere with clotting (for example, NSAIDS or aspirin). Consider prescribing a gastroprotective drug in these circumstances.

» Guidelines from the United Kingdom’s National Institute for Health and Clinical Excellence (NICE)
Does CBD Really Work For Anxiety?
Here’s what you need to know.
*Huffington Post*; May 14, 2018

- “Strong data is lacking with CBD. There have been only small research trials some showing benefit, others showing no benefit with CBD,” said Pritham Raj, an internist-psychiatrist in Portland, Oregon. “So, in short, the jury is still out. This doesn’t mean CBD doesn’t work for anxiety, it just means that we don’t have enough information to make a strong argument for CBD in the treatment of anxiety.”

- However, CBD use is better than patients self-medicating with marijuana in a bid to treat anxiety, Raj added.

- Among most cannabis components, “CBD is the best of all options in reducing anxiety,” Raj said. “THC has been shown more definitively to increase anxiety, which is why self-medicating with traditional marijuana products often leads to increased overall anxiety.”
Newest Approved Options for TRD

- Phase 3 double-blind, active-controlled study in non-responders to 2 prior antidepressants
- 227 adults randomized (1:1) to flexibly dosed intranasal esketamine (56 or 84 mg twice weekly) and a new oral antidepressant or intranasal placebo and a new oral antidepressant
- Result: More than half of the esketamine-treated TRD patients achieved remission by the 4-week endpoint. Common AEs – dysgeusia, nausea, vertigo, dizziness (>2-fold higher than placebo)

Fair and Balanced?

• Forty-nine of 227 in the only successful efficacy trial had failed just one class of oral antidepressants. “They weeded out the true treatment-resistant patients”
  » Erick Turner, MD

• Only modest evidence it works with no information about the safety for long-term use beyond 60 weeks.

• Three patients died by suicide during clinical trials, compared with none in the control group.
Esketamine (Spravato)

- In Study 2 (long-term), 39% of patients received the 56-mg dose, and 61% received the 84-mg dose of SPRAVATO™
- SPRAVATO™ does not require daily dosing and should be administered in conjunction with an oral AD
Thank You

*Fortune Favors the Prepared Mind*

- Louis Pasteur