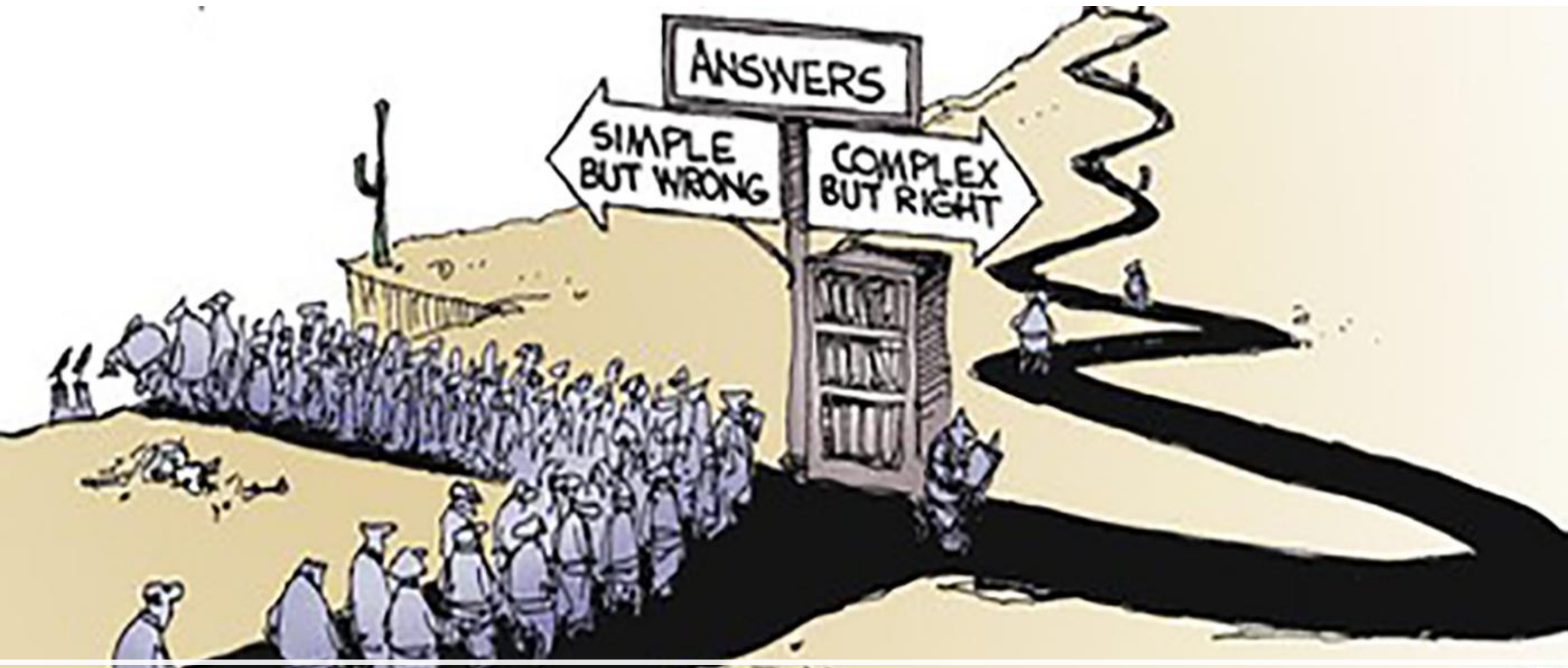


A More Detailed Look at Depression for Project ECHO

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Depression is Complex

Depression is a Symptom of What....

- No one knows...
- We don't know where, when, how, or sometimes if situational issues, genetic factors, personality issues, trauma can start or perpetuate the biological processes of Major Depression.
- The DSM approach is to categorize. It is not the "Bible" of mental illness, as often touted, but instead the Sears Catalogue of mental illness. The method used is description with very little enlightenment.
- At some point (different for every person) depression becomes a neurological illness. The most extreme manifestations of which are melancholia, catatonia, and suicide.

What does depression look like...

- Sleep: disturbances (up or down)
- Interest (Loss of, or loss of pleasure)
- Guilt (unwarranted, overblown feelings of guilt, worthlessness)*
- Energy (lower, fatigue)
- Concentration (decreased/ poor, indecisiveness)
- Appetite (up or down)
- Psychomotor (Retardation or Agitation noticeable by others, not just subjectively felt)
- Suicide (thoughts of death or suicide)

*feeling guilty about not working, being sick don't count, per DSM 5.

To be diagnosed with Major Depressive Disorder

- A major depressive episode: 2 week period, at least 5 symptoms (from below) felt almost all day on almost all of the days, 1 of which has to be depressed mood or anhedonia (loss of pleasure or interest).
 - Depressed mood (or irritable mood in children or adolescence)
 - The rest of the SIGECAPS
- The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Some Facts about Depression....

- 12 month prevalence is 7%
- Rates highest in 18-29 year-olds
- Can happen at any time (old age onset not unusual) but usually starts around puberty.
- Chronicity is bad. It usually indicates comorbidity (anxiety, personality, substance use disorders) and decreases the likelihood that a person will have a full remission.
- Having some symptoms during remission is a powerful predictor of recurrence.
- Many with depression will go on to have bipolar illness (especially with adolescence onset, family history of bipolar disorder, or psychotic features).



Depression in the elderly...

Elderly persons are more likely to have melancholic or psychotic depressions. (Younger people more likely to have “atypical depression”)

Depression can make it look like the older person has dementia: and thus the term “pseudodementia.”

A major depressive disorder (especially with lots of anxiety) can also be the first evidence of a progressive dementing process.

Descriptors of Depression

- **Melancholic Depression**
- **Psychotic Depression**
- **Catatonic Depression**
- Dysthymia
- Bipolar Depression
- Atypical Depression
- Peri-Partum Depression
- Situational depression.
- Grief that leads to depression.
- The pain and alienation of having a personality disorder that makes life hard all of the time.



Melancholia

Melancholic depression is the “cant eat” “cant sleep even though I stay in bed all day.” Melancholic patients derive no pleasure from anything and have no reactivity to usually pleasurable stimuli (receiving a complement). Classic depression. This has always been recognized as “depression” and people with Melancholia have been institutionalized with other people with severe mental illnesses as long as there have been institutions...

If you see a person who cannot (will not) eat, sleep, care for their hygiene, you have grounds to hospitalize that person under “gross inability to care for self” criteria.



Catatonia

- A feature of severe depression, but more often a manifestation of bipolar illness (either depressive or manic phase). I have seen more cases recently where catatonia was related to drug use (high potency THC/ Spice)
- Some manifestations of catatonia are extreme kinds of “psychomotor retardation” in which a person no longer moves, eats, or speaks.
- Other manifestations are related to extreme indecision, a person is literally stuck between two or more possibilities.
- Most catatonia can be broken by high doses of benzodiazepines, but the underlying mood disorder will still require treatment. This usually requires hospitalization.



Psychotic Depression

- Almost by definition, all depression is associated with some thinking errors: "my children (parents/ partner) would be better off if I was dead". "It is all my fault". "Things will never get better". "I might as well just give up now."
- These kinds of thoughts often lead to suicide.
- In severe depression, thinking errors cross the line to full blown psychotic ideas: "Someone has stolen all of my money." "My guts are rotting out of my body." "There is brain fluid dripping into the back of my throat" or "little men are moving my teeth around in my head."
- Psychosis is a marker for severe depression and, more often than not, requires hospitalization.



Bipolar Depression

- Depression in persons with bipolar disorder usually tough for the following reasons:
 - Many have not yet had a manic episode, so don't have bipolar disorder (technically) when they present with depression.
 - Often the patient can't remember or give a history of a bipolar episode, so you don't know even if they did have one in the past
 - Are less likely to respond to traditional antidepressants and these medications, may, in fact, precipitate a manic episode.
 - People with bipolar depression tend to be sicker (more likely to have peripartum, psychotic, and catatonic symptoms).
 - There aren't a lot of FDA approved medications for Bipolar Depression and those that exist are either super expensive or cause significant side effects.
 - Quetiapine (Seroquel®)
 - Olanzapine + Fluoxetine (Symbyax®)
 - Lurasidone (Latuda®)
 - Cariprazine (Vraylar®)



Suicide Risk!

- Most consistently reported risk is previous attempts or talk about suicide.
- But remember, most completed suicides happen in people who have never attempted.
- Other risks:
 - Being male
 - Living alone and/or being single
 - Prominent hopelessness
 - Owning guns and using substances increases the risk that suicidal thoughts will be translated into lethal attempts.
- There is a black-box warning for increasing suicidal thoughts in young people starting an antidepressant: this does not mean that young people should not be given an antidepressant!!

Atypical Depression: Is, actually, not too atypical...



Mood Reactivity (feeling happy when something good happens or is expected)

Plus

Two or more of the following:

- Significant weight gain or increased appetite
- Hypersomnia
- Leaden paralysis (feeling of heaviness in limbs)
- A long history of interpersonal rejection sensitivity.

Peripartum Depression

- Used to be called “post-partum” but most women actually start to have symptoms before the birth.
- 3-6% of women will have peripartum depression. Peripartum mood disorders (which include mania) include prominent psychosis in 1/500 to 1/1000 cases. The main risk of psychosis is infanticide.
- More common in first pregnancy, but very likely if prior episode of peripartum depression or if personal or family history of bipolar illness (peripartum depression is often the first mood episode in women who go on to meet criteria for bipolar disorder).





Persistent Depressive Disorder (Dysthymia)

- Persistent symptoms of depression (at least two symptoms of depression) for 2 years with only a 2 month period without symptoms.
- The symptoms cause impairment.
- Rule out medical and drug related stuff.

Level 1 Treatment

- Evidence-based psychotherapy [Cognitive-Behavioral Therapy (CBT), Interpersonal Psychotherapy (IPT), Behavioral Activation]
- *Note: Psychotherapies are preferred (where available) as first-line treatment for major depressive disorder (MDD) of mild severity.*
- Monotherapy 4-8 week trial at adequate dose and evaluate*:
Selective serotonin reuptake inhibitor (SSRI)**, serotonin-norepinephrine reuptake inhibitor (SNRI), or vortioxetine or Bupropion or mirtazapine
 - If partial response at 4 weeks, may continue for another 2 to 4 weeks or go to Level 2.
 - If no response at 4 weeks, ensure dose optimization and go to Level 2.

Regarding “evidence-based” psychotherapies

- Short term psychotherapies that are designed to administered by someone reading a manual or by a computer program like a phone app are all the rage these days.
- Insurance companies and other payers LOVE a treatment that will fix someone in 12 sessions and can be delivered by the lowest paid human or non-human. And many of them are now “evidence based” meaning that they reduced measurable symptoms over a discreet period of time compared to doing nothing.
- While I think these kinds of interventions can be very helpful over the short term, I believe that many people suffering from mental illness need a curative “relationship” with someone who will hang with them for a long time. Someone who is willing to help someone heal instead of “fix” them.



Level 2: If Level 1 is ineffective and/or not well tolerated

- Evaluate adherence
Ensure dose optimization of medication used in Level 1.
- Switch to different monotherapy agent from different or same class (SSRI, SNRI, bupropion, or mirtazapine).
Combine existing monotherapy with:
 - Evidence-based psychotherapy (e.g., CBT, IPT)
 - Second-generation antipsychotic FDA-approved for augmentation therapy for major depressive disorder (MDD) (i.e., aripiprazole or brexpiprazole)
 - An antidepressant (do not combine SSRI and SNRI)
- *Note: FDA-approved adjunctive agents for MDD are select atypical antipsychotics. Preliminary evidence evaluating comparative effectiveness of adjunctive antidepressant versus adjunctive atypical antipsychotic medications indicates superior efficacy for adjunctive antipsychotics and superior tolerability for adjunctive antidepressants.*

Level 3

- Evaluate adherence
- Seek psychiatric consultation
- (SSRI or SNRI) + quetiapine (tolerability concerns)
- (SSRI or SNRI) + (lithium or T3)
- (SSRI or SNRI) + (L-methylfolate or S-adenosylmethionine) Tricyclic antidepressant (TCA)
- Monoamine oxidase inhibitor (MAOI)
- Electroconvulsive therapy (ECT)
- Transcranial magnetic stimulation (TMS)???



Level 4

- Re-evaluate diagnosis if patient has failed to respond to 2 or more treatments
- Monoamine oxidase inhibitor (MAOI) augmentation (**AVOID CONTRAINDICATED COMBINATIONS**) L-methylfolate augmentation
- Triple drug combination (little evidence exists supporting or refuting this strategy)
 - (SSRI or SNRI) + mirtazapine + bupropion
 - (SSRI or SNRI) + mirtazapine + lithium*
 - (SSRI or SNRI) + bupropion + second generation antipsychotic (SGA)
- Other neuromodulatory approaches [e.g., vagus nerve stimulation (VNS)]
- Intravenous ketamine (at specialized centers only and in accordance with best practices)





Possible future directions

Psychedelic Assisted Psychotherapy:

- Ketamine
- MDMA
- Psilocybin
- DMT
- Ibogaine
- Ayahuasca