I have no disclosures.

Objectives

- Improve readiness and efficacy in Primary Care treatment of depression and anxiety
- Gain Awareness of:
  - Prevalence
  - Screening tools
  - Treatment options: Pharmacological and nonpharmacological
  - STAR*D
  - Genetic testing and other labs
  - Comorbidities
**Prevalence**
- Depression is the world's fourth most prevalent health problem causing US $30-$50 billion per year in lost productivity and direct medical costs.
- PCPs are the sole contact for more than 50% of patients with mental illness.
- Symptoms consistent with depression are present in nearly 70% of patients who visit a PCP.
- GAD is one of the most common mental disorders in primary care settings with a lifetime prevalence of 5-12% in the US.

**Comorbidities**
- Arthritis
- Diabetes
- Stroke
- Obesity
- Substance Use Disorder

**Somatic symptoms that sometimes present with depression**
- Headache, migraines
- Sexual dysfunction
- Appetite changes
- Menstrual-related symptoms
- Chronic pain
- Chronic medical conditions (eg, diabetes, Parkinson’s disease, alcoholism)
- Digestive problems (eg, diarrhea, constipation)
- Fatigue
- Sleep disturbances

**Case Study**
- Mary, a 51 year old, married Caucasian female arrives early to her appointment complaining of joint pain. Later in the interview she reports that she has a bad case of the “Don’t Wannas” and rarely leaves her house these days. She doesn’t really see any purpose in her life any longer but denies SI. She insists that she isn’t depressed. “I’m not sad.”
What do you do?

A. Keep from rolling your eyes as you dismiss her complaints by telling her “There, there it will be ok.”
B. Refer her to psych, pronto!
C. Send her to the ED
D. Recommend counseling
E. Prescribe sertraline with a slow titration to avoid side effects
F. Recommend yoga or Tai Chi
G. All of the above

Also...

- Is she is psychotic, i.e., exhibiting AV/VH, delusional or disorganized thinking
- Expresses SI and a plan and unwillingness to contract for safety.
Google screening with PHQ-9 now pops up when people search “depression” on mobile devices. Google announced it will add a questionnaire to results when users in the U.S. search for “clinical depression” or other depression-related searches on mobile devices. The company said the PHQ-9 quiz — which will appear on both the Google app for iOS and Android and on mobile web browsers — is clinically validated and can assess your level of depression.

**Screening to help with diagnosis**

- Major depressive disorder
- Chronic depressive disorder
- Dysthymic disorder
- Adjustment disorder with depressed mood
- Adjustment disorder with anxiety and depressed mood
- Atypical depressive disorder
- Melancholia
- Postpartum depressive disorder

**Lots of reliable and valid screening tools**

- Beck Depression Inventory
- CUDOS/CUXOS (anxiety)
- Hamilton Depression Rating Scale
- Geriatric Depression Scale
- GAD-7 (anxiety) and PHQ-9 (depression)

**Depressive disorders that should be picked up by a screening tool for depression**

**Diagnostic criteria for major depressive disorder (DSM-5)**

At least 5 of the following symptoms have been present during the same 2-week period, represent a change from previous functioning, and include either depressed mood or loss of interest or pleasure.

- Depressed mood
- Marked diminished interest or pleasure
- Significant weight loss or weight gain
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness or excessive guilt
- Diminished ability to concentrate
- Recurrent thoughts of death or suicidal ideation
The Patient Health Questionnaire is a self-administered tool of 2 (PHQ-2) or 9 (PHQ-9) items. A meta-analysis found sensitivity to be 80% and specificity of 92%.

The PHQ-2 is a screening tool for depression that assesses the frequency of depressed mood and anhedonia over the past 2 weeks, scoring each as 0 (“not at all”) to 3 (“nearly every day”).

A PHQ-2 score of greater than 3 had a sensitivity of 83% and a specificity of 92% for major depression.

The PHQ-9 establishes the clinical diagnosis of depression and can additionally be used over time to track the severity of symptoms over time. The cut point of the PHQ-9 is equal or greater than 10, which has a sensitivity of 88% and a specificity of 88% for major depression. PHQ-9 scores of 5, 10, 15, and 20 are representative of mild, moderate, moderately severe, and severe depression, respectively.

**But first...**
- Ask about substance use
- Ask about episodes of true mania
  - Decreased need for sleep

**PHQ-9**

- 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 yourself or your family down
- Trouble concentrating on things, such as reading the newspaper or watching television
- Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual
- Thoughts that you would be better off dead, or of hurting yourself in some way

**Patient Health Questionnaire (PHQ-9)**

PHQ-9 over the last 2 weeks, how often have you been bothered by any of the following problems? Nearly every day: More than half the days: Several days: About 1 day.

- A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least one week and present most of the day, nearly every day (or any duration if hospitalization is necessary).
- B. During the period of mood disturbance and increased energy or activity, three (or more) of the following symptoms (four if the mood is only irritable) are present to a significant degree and represent a noticeable change from usual behavior:
  1) Inflated self-esteem or grandiosity.
  2) Decreased need for sleep (eg, feels rested after only three hours of sleep).
  3) More talkative than usual or pressure to keep talking.
  4) Flight of ideas or subjective experience that thoughts are racing.
  5) Distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.
  6) Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation (ie, purposeless non-goal-directed activity).
  7) Excessive involvement in activities that have a high potential for painful consequences (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).
- C. The mood disturbance is sufficiently severe to cause marked impairment in social or occupational functioning or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.
- D. The episode is not attributable to the physiological effects of a substance (eg, a drug of abuse, a medication, other treatment) or to another medical condition.

**DSM-5 diagnostic criteria for manic episode**
Sequenced Treatment Alternatives to Relieve Depression (STAR*D) is the largest prospective clinical trial of treatment of major depressive disorder ever conducted.

DEPRESSION can be treated successfully by primary care physicians under “real world” conditions.

Furthermore, the particular drug or drugs used are not as important as following a rational plan:
- giving antidepressant medications in adequate doses
- monitoring the patient’s symptoms and side effects and adjusting the regimen accordingly
- switching drugs or adding new drugs to the regimen only after an adequate trial.

For patients with mild to moderate depression who are treatment resistant and receiving augmentation with pharmacotherapy, many options are available.
- second-generation antipsychotics
- Lithium
- a second antidepressant from a different class
- thyroid hormone
In 1995 Texas implemented a study to determine the effectiveness of use of algorithm-driven disease management in Tx of BPAD, Schizophrenia and MDD.

Texas Medication Algorithm Project

The documented efficacy and long-term benefit of antidepressants in patients with recurrent forms of severe anxiety or depressive disorders support their use in those individuals with these disorders, who experience suicidal thoughts or behavior. In general, it is assumed that antidepressants are beneficial for all symptoms of depression, including suicidality. However, some evidence suggests that Selective Serotonin Reuptake Inhibitors (SSRIs) may cause worsening of suicidal ideas in vulnerable patients. Systematic reviews and pooled analysis of experimental, observational, and epidemiological studies have investigated the use of SSRIs and their association with suicidality. Taking account of the methodological limitations of these studies, the current evidence fails to provide a clear relationship between their use and risk of suicidality in adults. However, in children and adolescents, there appears to be a bit of increased risk of suicidal ideations and attempts, but not of completed suicides. This risk can be anticipated and managed clinically. Clinicians are, therefore, advised to maintain a close follow-up during the initial treatment periods and remain vigilant of this risk. This advisory, however, should not deter clinicians from the use of effective dosages of antidepressants for a sufficient period of time, in every age group of patients, when clinically needed, and if found suitable otherwise.

When to refer
- Treatment refractory depression
- Referral to a mental health specialist should be considered for depressive episodes that are unresponsive to multiple (eg, two to four) next-step treatment trials. In addition, referral is generally indicated for severe major depression characterized by suicidal or homicidal ideation or behavior, psychosis, or catatonia.
- Treatment options: ECT, TMS, neurofeedback

SSRIs and Suicide
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Link to Algorithm
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1764539/figure/i1523-5998-8-5-291-f02/

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Neuromodulatory
- Neurofeedback
- ECT (electroconvulsive therapy)
- TMS (transcranial magnetic stimulation)
Mary has sent her friend who complains of not being able to stop worrying. Can you help....?

- https://uihc.org/transcranial-magnetic-stimulation-tms

Symptoms of Generalized Anxiety Disorder From the DSM-5

- 1. The presence of excessive anxiety and worry about a variety of topics, events, or activities. Worry occurs more often than not for at least 6 months and is clearly excessive. Excessive worry means worrying even when there is nothing wrong or in a manner that is disproportionate to the actual risk. This typically involves spending a high percentage of waking hours worrying about something. The worry may be accompanied by reassurance-seeking from others.
- 2. The worry is experienced as very challenging to control. The worry in both adults and children may shift from one topic to another.
- 3. The anxiety and worry are associated with at least three of the following physical or cognitive symptoms (GAD):
  - Edginess or restlessness
  - Tiring easily; more fatigued than usual
  - Impaired concentration or feeling as though the mind goes blank
  - Irritability (which may or may not be observable to others)
  - Increased muscle aches or soreness
  - Difficulty sleeping (due to trouble falling asleep or staying asleep, restlessness at night, or和完善性 sleep)
  - Many individuals with GAD also experience sweating, diarrhea, nausea
Limits to what medication can do
- Therapy can be helpful alone or in combination with medication
- Quick release medication to alleviate anxiety is a short term measure (less than 2 months) while long term medication is started or adjusted
- Quick release medication should not be used more than ½ the days in a month, or multiple times per day.

SSRIs
- SMS (Serotonin Modulators and Stimulators, Viibryd (vilazodone), Brintellix or Trintellix (vortioxetine))
- SNRIs (desvenlafaxine, duloxetine, venlafaxine)
- NRI (Wellbutrin may cause initial worsening)
- TCAs
  - clomipramine (most serotonergic and may be better with OCD)
Continued

- MAOIs
- Gabapentin, pregabalin
- Buspirone
- Propranolol
- Atenolol
- Guanfacine
- Clonidine
- Prazosin

Quick release

- Hydroxyzine, diphenhydramine
- Seroquel (Thorazine and Haldol used less commonly)
- Trazodone
- Doxepin
- Benzodiazepines
- Buspirone

Non-pharmacological interventions

Supportive psychotherapy

Well, I think you’re wonderful. 
We conducted a meta-analysis of studies in which psychotherapy and antidepressant medication were directly compared in the treatment of depressive and anxiety disorders.

The overall effect size indicating the difference between psychotherapy and pharmacotherapy after treatment in all disorders was $g=0.02$ (95% CI: -0.07 to 0.10), which was not statistically significant.

Pharmacotherapy was significantly more efficacious than psychotherapy in dysthymia ($g=0.30$), and psychotherapy was significantly more efficacious than pharmacotherapy in obsessive-compulsive disorder ($g=0.64$).

Pharmacotherapy was significantly more efficacious than non-directive counseling ($g=0.33$)

Psychotherapy was significantly more efficacious than pharmacotherapy with tricyclic antidepressants ($g=0.21$).
Exercise

- Research also suggests that the benefits of exercise involvement may be long lasting. Depressed adults who took part in a fitness program displayed significantly greater improvements in depression, anxiety, and self-concept than those in a control group after 12 weeks of training (BDI reduction of 5.1 [fitness program] vs. 0.9 [control], p < .001). The exercise participants also maintained many of these gains through the 12-month follow-up period.

Efficacy of exercise

- The mechanisms underlying the antidepressant effects of exercise remain in debate; however, the efficacy of exercise in decreasing symptoms of depression has been well established.
- Data regarding the positive mood effects of exercise involvement, independent of fitness gains, suggest that the focus should be on frequency of exercise rather than duration or intensity until the behavior has been well established.
- The addition of self-monitoring techniques may increase awareness of the proximal benefits of exercise involvement, which is generally reinforcing to the patient.
In a German study published in 2005, 24 women who described themselves as “emotionally distressed” took two 90-minute yoga classes a week for three months. Women in a control group maintained their normal activities and were asked not to begin an exercise or stress-reduction program during the study period.

Though not formally diagnosed with depression, all participants had experienced emotional distress for at least 45 days of the previous 90 days. They were also one standard deviation above the population norm in scores for perceived stress (measured using the Cohen Perceived Stress Scale), anxiety (measured using the Spielberger State-Trait Anxiety Inventory), and depression (scored with the Profile of Mood States and the Center for Epidemiological Studies Depression Scale, or CES-D).

At the end of three months, women in the yoga group reported improvements in perceived stress, depression, anxiety, energy, fatigue, and well-being. Depression scores improved by 50%, anxiety scores by 30%, and overall well-being scores by 65%. Initial complaints of headaches, back pain, and poor sleep quality also resolved much more often in the yoga group than in the control group.

GABA: “The Anti-Anxiety Molecule”
GABA is an inhibitory molecule that slows down the firing of neurons and creates a sense of calmness.

You can increase GABA naturally by practicing yoga, meditation or “The Relaxation Response.”

Benzodiazepines (Such as Valium and Xanax) are sedatives that work as anti-anxiety medication by increasing GABA. These drugs have many side effects and risks of dependency but unfortunately are still widely prescribed.

1st RCT of dietary counseling for tx of depression
Australia 67 patients, dietary counseling v. supportive therapy.
Effect size of 1.16. Similar to effect size of amphetamine salts in ADHD, larger than antidepressants
Modified Mediterranean diet (ModiMedDiet)
It does not restrict calories, but encourages more vegetables, fruits, nuts, beans, whole grains, fish, lean meats, and healthy oils; and less fried, fast, or processed foods and simple sugars.
http://www.psychiatrictimes.com/bipolar-disorder/can-diet-treat-depression
Significant improvement in depression scores: Greater reduction in depression ratings was observed across the duration of the study for the GeneSight® guided group, showing 70% greater improvement in depressive symptoms compared to TAU at 8 weeks.

Higher response rates: When clinicians used the GeneSight report to guide treatment, patients were 2.1 times more likely to respond to their medications compared to treatment without GeneSight.

Higher physician and patient satisfaction: Almost three times as many physicians in the GeneSight guided group perceived their patients to be very highly satisfied with their care compared to the unguided group. Physician reporting of confidence in choice of medication and treatment and satisfaction with care was also substantially higher in the GeneSight guided group.

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- The Prescriber’s Guide, Stahl, S.
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Works cited

I had no way wanting the rest—or now making my own problems seem insignificant.”