Community Wellness through Depression Recovery

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Disclosures

• **Julie A. Dopheide, PharmD, BCPP, FASHP**, declares receiving honoraria as an advisory board member for Alkermes.

• **Kelly N. Gable, PharmD, BCPP** declares no financial conflicts of interest associated with this presentation.

• **No off-label indications for pharmacotherapy will be discussed**
Learning Objectives

1. Describe the patient’s perspective of the experience of major depression and suicidality.
2. Discuss etiology, course, and health outcomes associated with major depression.
3. Employ effective communication skills to destigmatize depressive symptoms, screen for depression and suicide, and engage patients in treatment to achieve recovery.
4. Differentiate drug and nondrug treatment options for depression based on effectiveness, tolerability, safety, and convenience.
5. Formulate an appropriate treatment plan aimed at recovery in a given case scenario of a patient with depression, co-occurring diagnoses, and medications.
CPE Information

• Target Audience:
• ACPE#:
• Activity Type:

(APhA will complete this information.)
CPE Information

- Target Audience: Pharmacists and Pharmacy Technicians
- ACPE#: 0202-0000-19-071-L01-P/T
- Activity Type: Application-based

(APhA will complete this information.)
1. A patient presents with several symptoms of depression, including low mood, insomnia, anhedonia, and vacillating thoughts of suicide. What defining features must be present for a diagnosis of depression?

   A. \( \geq 4 \) symptoms for at least 1 week
   B. \( \geq 5 \) symptoms for at least 2 weeks
   C. \( \geq 5 \) symptoms for at least 4 weeks
   D. 10 symptoms for at least 2 weeks
2. A patient taking amlodipine, benazepril, lansoprazole and quetiapine for over 6 months presents with depressive symptoms. Which medication might contribute?

A. Amlodipine
B. Benazepril
C. Lansoprazole
D. Quetiapine
3. What is an example of a frequently used depression screening tool?
   A. The Healthy Living Questionnaire
   B. Patient Health Questionnaire-9
   C. Life Event Checklist
   D. Generalized Anxiety Disorder-7
Assessment Question: Complimentary Treatments

4. Which complementary treatment has the strongest evidence base for improving symptoms of depression as monotherapy?
   A. St. John’s Wort
   B. Omega-3 fatty acids
   C. Cholecalciferol
   D. S-adenosylmethionine
5. A 50 year old patient with severe depression (PHQ-9 is 22), PTSD and alcohol use disorder did not respond to 2 months of sertraline 200mg/day or escitalopram 30mg daily. The patient is partially responsive to 6 weeks of venlafaxine XR 300mg/day (PHQ-9 is now 17). Genetic polymorphisms, hypothyroidism and low Vit D have been ruled out. Select the most appropriate treatment intervention:
A. Brexanolone infusion
B. Esketamine nasal spray
C. Add St. John’s Wort or Adjunctive Omega-3 fatty acids
D. Discuss adding trauma-focused cognitive-behavioral therapy (CBT)
Depression: Impact, Prevalence, Etiology

Julie Dopheide, PharmD, BCPP, FASHP
Depression Impacts All Elements of Disease and Wellness

Dec 7, 2018: CDC reports decrease in life expectancy: 78 years, 7 months (based on death certificates 2017)
  2016: 78 years, 9 months
  2015: up from prior years
10 leading causes of death: heart disease, diabetes, dementia, cancer, drug overdose, suicides

Depression increases early death by worsening outcomes of all these......
Depression Is a Leading Cause of Poor Health Globally

• Depression is #1 cause of disability worldwide in 2017, according to the World Health Organization (WHO)
  • 18% spike in depression from 2005-2015
• U.S. Preventive Health Services Task Force recommends that all persons ≥12 years old should be screened for depression
  • Systems should be in place to ensure accurate diagnosis and treatment of depression
• Return on Investment (ROI) 4:1

What is the prevalence and course of major depression?

- 12-month prevalence is 7 – 10%
- Lifetime prevalence is 13 – 17%
  - Untreated episodes can last 6 months or longer
- 1 episode: 50% chance of recurrence
- 2 episodes: >70% chance of recurrence
- 3 episodes: >90% chance of recurrence
- Medical Comorbidity: 3-5x greater risk of depression

Better Outcomes of Medical Comorbidity when Depression Treated

Vital Statistics’ Centers for Disease Control at CDC.gov
American Psychiatric Association Guidelines for Major Depression 2010
Depression and Suicide Impacts All of Us: We Need to Get Comfortable Talking About It!

45,000 Americans took their lives by suicide in 2016

2,000 were teenagers

~ 50% see health care provider within month prior to suicide

www.cdc.gov/vitalsigns/suicide
Pathophysiology of Major Depression

MDD 30–40% genetic in origin

↓ Brain Derived Neurotrophic factor (BDNF)

Neuroactive steroids:
↓ Allopregnanolone

Corticotropin Releasing factor (CRH)
Antagonists can improve depression

Glutamate Dysregulation

Pro-inflammatory Cytokines

adapted from Maletic Int J of Clin Pract 2007; Hasler World Psych 2010; Meltzer-Brody, Lancet 2018
Risk of Depression Increases When a Patient Takes Medications Known to Cause Depression

Prevalence of U.S. Adults Taking Meds That May Cause Depression 37.2%

N=23,561 – NHANES Data

0 medications known to cause depression
N=17,039

1 medication known to cause depression
N=4,394

2 medications known to cause depression
N=1,418

≥ 3 medications known to cause depression
N=710

PHQ-9 Score >10

4.7

6.9

9.5

15.3


PHQ-9 = Patient Health Questionnaire-9
# What Medications or Substances Cause Depression?

<table>
<thead>
<tr>
<th>Prescription Medications</th>
<th>Substances of Abuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Antihypertensives</td>
<td>Alcohol</td>
</tr>
<tr>
<td>• Proton-pump inhibitors (PPIs)</td>
<td>Methamphetamine crash</td>
</tr>
<tr>
<td>• Glucocorticoids</td>
<td>Cocaine/Crack crash</td>
</tr>
<tr>
<td>• Benzodiazepines</td>
<td>Opioids</td>
</tr>
</tbody>
</table>

Proton-pump Inhibitor (PPI)-Induced Depression

“Brain-Gut Axis dysregulation” caused by alteration of the human gut microbiota

N=2,366 exposed to PPIs – depression
N=9,464 exposed to PPIs – no depression
Matched for age, sex, enrollment period
Retrospective observational study
OR = 2.08, 95% CI =1.61-2.68

Chronic malabsorption of magnesium, vitamin D, and B₁₂ associated with depression

The Patient’s Experience of Depression

Kelly Gable, PharmD, BCPP
The Experience of Depression


Chronic Pain

Appetite Changes

Tearfulness

Poor Focus

Headaches

Sleep Changes

Social Isolation

Interest Lacking

Guilt Hopelessness

Energy Decrease

Excessive Worry

Irritability
Symptoms of Depression: D + SIGECAPS

**Depressed mood** or anhedonia
Sleep (insomnia or hypersomnia)
Interest (loss of)
Guilt or worthlessness
Energy loss
Concentration loss
Appetite changes (weight loss or gain)
Psychomotor agitation or retardation
Suicidal ideation

≥5 symptoms for at least 2 weeks

• Mild, moderate, severe
• With psychotic features (hallucinations, delusions)
• With catatonia
• With melancholic features (elderly patients):
  • Early morning awakening, anhedonia, marked psychomotor agitation/retardation, significant weight loss
• With atypical features (younger patients):
  • Overeating (weight gain), hypersomnia, leaden paralysis
• With seasonal pattern
• With postpartum onset

• Public stigma emerges when pervasive stereotypes lead to prejudice against those who suffer from a mental illness — “people with mental illness are dangerous or unpredictable”
  • “It would be nice if everyone accepted my mental illness, but at the end of the day I don’t want someone blocking my right to work and live independently.”

• > 100 peer-reviewed, empirical articles have been published demonstrating stigma as a barrier to treatment

• Stigma impacts care seeking at personal, provider, and system levels

Lack of Experience and Mental Health Stigma Impact Patient Care

• Overall, pharmacists provide fewer clinical services to those with mental illness
• Random sample of 3,008 community pharmacists in U.S. surveyed
  • 239 (7.95%) surveys returned
• Only 39% of respondents reported adequate knowledge of medication therapy for mental illness
• Ratings for willingness and interest in providing services to persons with mental illness higher than comfort, confidence

Mental illnesses are largely biological disorders; people are not to blame.

People choose to be mentally ill because they are fundamentally weak.
Reducing Stigma While Treating Depression

• Ensure that pharmacies have private counseling areas for more personal discussions surrounding mental health wellness.

• Approach each patient with empathy. Provide patient-centered care, using person-first language. Be mindful of tone and words used.

• Serve as a positive role-model for pharmacy students in training by promoting a stigma-free work environment.
  • Support initiatives such as the National Alliance on Mental Illness (NAMI) StigmaFree campaign (https://www.nami.org/stigmafree).

• Enhance exposure and knowledge: interactions with people with lived experience
  • NAMI “In Our Own Voice”
  • Mental Health First Aid (https://www.mentalhealthfirstaid.org)
  • Perform routine depression screenings
Screening for Depression

• Patient Health Questionnaire-9 (PHQ-9)
• 2 quick questions from Primary Care Evaluation of Mental Disorders (PRIME-MD) can provide a highly sensitive (94%) but not very specific (35%) screening test for depression:
  1. Have you been bothered by little interest or pleasure in doing things?
  2. Have you been feeling down, depressed, or hopeless in the last month?
• With + response to these 2 questions, only 4 follow-up questions—on sleep disturbance, appetite change, low self-esteem, and anhedonia—needed to confirm a diagnosis of depression.

### Patient Health Questionnaire-9

**Over the last 2 weeks, how often have you been bothered by any of the following problems?**

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half of days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Feeling bad about yourself- or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such a reading the newspaper or watching television</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. 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</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

**Scoring:**

- 0-4 = none
- 5-9 = mild
- 10-14 = moderate
- 15-19 = moderately severe
- 20-27 = severe

**“A” Pair up to role-play administering PHQ-9**

<table>
<thead>
<tr>
<th>Patient Identifying information</th>
<th>Current Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>32 year old</td>
<td>Escitalopram 20mg (positive response x 1 year)</td>
</tr>
<tr>
<td>Major Depression without psychosis</td>
<td>Levothyroxine 100mcg daily</td>
</tr>
<tr>
<td>Hypothyroid</td>
<td>Montelukast 10mg daily</td>
</tr>
<tr>
<td>Asthma</td>
<td>Albuterol 2 puffs as needed for SOB</td>
</tr>
<tr>
<td>Mental Status Exam: restless, fidgety, depressed and anxious mood, (+) worries of relationship, insomnia, emotional eating</td>
<td>Supplements: Omega 3 1000mg at bedtime</td>
</tr>
<tr>
<td>No suicidal Thoughts</td>
<td>Vitamin B with C daily</td>
</tr>
<tr>
<td>Presents today with concerns over conflict with girlfriend/boyfriend</td>
<td>Positive response the past 2 months; PHQ-9 &lt; 3</td>
</tr>
<tr>
<td>PHQ-9: 10 today</td>
<td>Past 2 months PHQ-9 only 3</td>
</tr>
</tbody>
</table>
**“B” Pair up to role-play administering PHQ-9**

<table>
<thead>
<tr>
<th>Patient Identifying information</th>
<th>Current Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 year old male/female</td>
<td>Vortioxetine 15mg daily, current</td>
</tr>
<tr>
<td>Major Depression without psychosis</td>
<td>Past trials: sertraline- excessive diarrhea, escitalopram not effective, bupropion-dizziness, insomnia</td>
</tr>
<tr>
<td>CHF, s/p MI, HTN, Dyslipidemia</td>
<td>Atorvastatin 40mg daily</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>ASA 81mg daily</td>
</tr>
<tr>
<td>Sciatica</td>
<td>Carvedilol 25mg bid</td>
</tr>
<tr>
<td>Cocaine use disorder: clean 15 years</td>
<td>Enalapril 5mg bid</td>
</tr>
<tr>
<td>Mental Status Exam: Psychomotor slow</td>
<td>Pantoprazole 20mg daily</td>
</tr>
<tr>
<td>Low energy, slouched posture, walks with cane (+) worries over health, hopeless Depressed mood Sad affect, watery eyes Insomnia, aggravated by pain</td>
<td>Linagliptin 5mg daily Metformin 1000mg bid Glipizide 20mg bid</td>
</tr>
<tr>
<td>PHQ-9: 17 and 21 past 2 visits</td>
<td>Methocarbamol 750mg bid Gabapentin 600 mg bid Nerve block injections</td>
</tr>
<tr>
<td>PHQ-9: 22 today (+) item 9</td>
<td>Goal: recovery from depression, relief from pain</td>
</tr>
</tbody>
</table>
Let’s Discuss

• Case A – depression is more situational, recommend therapy/lifestyle modifications, change in antidepressant may not be necessary

• Case B – severe depression with medical complications; need to look at triggering factors such as poorly controlled pain condition

• What barriers to effective depression screening exist in your practice setting?
Depression Treatment: More Options for Recovery

Julie Dopheide, PharmD, BCPP, FASHP
Remission is Key to Recovery

• Treat depression early
• Treat aggressively to achieve remission
  • Optimize antidepressant dose
  • Optimize nonpharmacologic treatments
• Full remission = no sad mood or no lack of interest/pleasure for ≥ 3 weeks
  • < 5 score on PHQ-9; < 7 score on Hamilton Depression Rating Scale
• Partial response = high relapse rate

US Department of Health and Human Services
National Institutes of Health, National Institute of Mental Health 2015.
Depression (NIH Publication No. 15-3561). Bethesda, MD
Treatment Options for Depression

- Psychotherapeutic Interventions
  - Interpersonal Psychotherapy
  - Cognitive Behavioral Therapy

- Pharmacologic Treatment
  - Antidepressants
  - Augmenting Agents
  - Adjunctive Antipsychotics

- Complementary Treatment

- Options for Treatment Resistant Depression

AHRQ: https://effectivehealthcare.ahrq.gov/topics/major-depressive-disorder/clinician/
Lisanby SH. Electroconvulsive therapy for depression NEJM 2007;357
Clinician: Antidepressant or CBT 1\textsuperscript{st} line
\begin{itemize}
  \item CBT as effective as antidepressant in relieving symptoms in adults with mild to severe MDD
  \item Trend toward higher treatment discontinuation with antidepressants but not statistically significant
  \item Switching to a different antidepressant or adding CBT or other augmentation strategy- 2\textsuperscript{nd} step
\end{itemize}

Consumer: Encouraged to Learn About Depression as a Treatable Medical Condition
\begin{itemize}
  \item Explains symptoms of depression and reviews all possible treatment options in plain terms
\end{itemize}

https://effectivehealthcare.ahrq.gov/topics/major-depressive-disorder/clinician/
Cognitive Therapy: helps patients correct false self-beliefs and negative thoughts

Cognitive Behavioral Therapy (CBT): includes a behavioral component such as homework

Interpersonal Therapy (IPT)
  - Focuses on relationships; client/consumer receives reflective feedback, supportive counseling

Psychodynamic therapy: conscious and unconscious feelings and past experiences

Acceptance and Commitment therapy: uses mindfulness techniques, encourages acceptance

Providers Trained in Psychotherapeutic Treatment of Depression

• Licensed Clinical Social Workers (LCSW)
• Masters in Social Work (MSW)
• Psychologist (PsyD)
• Psychologist (PhD)
• Physician (MD, DO)
• Marriage and Family Counselor (MFCC)
Staging of Psychotherapy

Interpersonal Psychotherapy (IPT)

Cognitive Behavioral Therapy (CBT) and IPT

CBT, Well-Being Therapy, Mindfulness Based Cognitive Therapy

Cognitive Behavioral Analysis System of Psychotherapy

Prodromal Phase

Major Depressive Episode

Residual Phase

Chronic Major Depressive Episode

Figure adapted from Guidi et al. The role of staging in planning psychotherapeutic interventions in depression. J Clin Psychiatry 2017
Basic Biochemical Mechanism of Antidepressant

1. Stress, cortisol surge + genetic susceptibility

2. Levels of Camp, brain-derived neurotrophic factor (BDNF) decreases in cell

3. Antidepressants increase neurotransmitter (NT) in synapse (reuptake inhibition, MAOI, 5HT2 antagonism)

4. Over time (2-6 weeks) Camp levels and BDNF increases inside cell, neuronal repair

Bjorkholm C and Monteggia LM. BDNF and antidepressant response Neuropsychopharmacology 2016.
Depression: Phases of Treatment

How effective is the first antidepressant in achieving remission?

Adapted from Gartlehner G et al. Nonpharmacological Versus Pharmacological Treatments for Adult Patients With Major Depressive Disorder. Comparative Effectiveness Review. No. 161; December 2015.
Comparative Efficacy and Acceptability of 21 Different Antidepressants

Antidepressants Overall Comparable in Efficacy; Tolerability Differences Guide Treatment

Antidepressant Selection

- **SSRIs** – 1st line all MDD types, all ages, effective for comorbid anxiety
- **Bupropion** – NE/DA low to no sexual side effects
- **Venlafaxine** - 5HT/NE, anxiety, nausea, ↑ blood pressure
- **Duloxetine** – 5HT/NE, effective for pain syndromes including neuropathy, liver enzymes
- **Mirtazapine** – unique mechanism, 5HT/NE, no nausea/sexual side effects, sedation, weight gain, ↑ triglycerides

http://www.effectivehealthcare.ahrq.gov/reports/final.cfm

SSRI- Selective Serotonin Re-Uptake Inhibitor
NE- Norepinephrine
DA- Dopamine
5-HT- Serotonin
If a patient is not responsive to a trial of antidepressant, could genotyping assist?

Impact of CYP2C19 Genotype on Escitalopram Exposure and Therapeutic Failure: A Retrospective Study Based on 2,087 Patients

Marin M. Jukić, Ph.D., Tore Haslemo, Ph.D., Espen Molden, Ph.D., Magnus Ingelman-Sundberg, Ph.D.

Objective: The antidepressant escitalopram is predominantly metabolized by the polymorphic CYP2C19 enzyme. The authors investigated the effect of CYP2C19 genotype on exposure and therapeutic failure of escitalopram in a large patient population.

Method: A total of 4,228 escitalopram serum concentration measurements from 2,087 CYP2C19-genotyped patients 10–30 hours after drug intake were collected retrospectively from the drug monitoring database at Diakonhjemmet Hospital in Oslo. The patients were divided into subgroups based on CYP2C19 genotype then monitored longitudinally.

Results: Compared with the CYP2C19*1/*1 group, escitalopram serum concentrations were significantly increased 3.3-fold in the CYP2C19Null/Null group, 1.6-fold in the CYP2C19*Null/*1 group, and 1.4-fold in the CYP2C19Null/*17 group, whereas escitalopram serum concentrations were significantly decreased by 10% in the CYP2C19*1/*17 group and 20% in the CYP1C19*1/*17 group. In comparison to the CYP2C19*1/*1 group, switches from escitalopram to another antidepressant within 1 year were 3.3, 1.6, and 3.0 times more frequent among the CYP2C19Null/Null, CYP2C19*1/*17, and CYP1C19*1/*17 groups, respectively.

Jukic MM et al. Am J Psych 2017
Rosenblat J Clin Psych 2017
Augmentation Strategies

- Add bupropion or buspirone
  - Bupropion more effective for most
- Add liothyronine (T3) or levothyroxine (T4)
- Add lithium with goal level of 0.6-1.0 mEq/L
- Add second generation antipsychotic
- Combination antidepressants: CO-MED Trial showed no additional benefit/worse tolerability
  - Escitalopram-bupropion
  - Mirtazapine-venlafaxine

Second Generation Antipsychotics

- Not appropriate as monotherapy for MDD
  - Studied primarily as adjuncts to SSRIs
- Aripiprazole (Abilify): 2 to 5mg daily; max:15mg/d
  - Akathisia, nausea, pseudoparkinsonism
- Brexpiprazole (Rexulti): 0.5 – 1mg; max:6mg/day
  - Akathisia, nausea, pseudoparkinsonism, weight gain
- Quetiapine XR (Seroquel XR): 50 – 300mg daily
  - Sedation, weight gain, dry mouth, constipation
- Olanzapine combined with fluoxetine (Symbyax)
  - 5mg of olanzapine with 20mg of fluoxetine

American Psychiatric Association Guideline for Major Depression 2010
Electroconvulsive Therapy

- Highly effective, particularly in MDD with psychosis
  - 55-75% achieve remission in 6-12 treatments
- Need two psychiatrists to document need, safety
- Patient/Guardian consent
- Adverse effects: headache, short-term memory loss
- High relapse rate

Lisanby S. Electroconvulsive therapy 2007
Esketamine Intranasal – Adjunct to Antidepressant for Treatment Refractory MDD

NMDA receptor Antagonist

Rapid onset

Adverse effects:
Increased BP, HR
Dissociative symptoms

Brexanolone: Gamma-amino butyric acid (GABA)$_A$ allosteric modulator for post-partum depression

60 mg or 90 mg infusion
Given over 60 hours to
Women < 6 months post-partum

**Complementary Therapeutics for Depression: Adjunctive**

**Supplement**
- SAM-e *(monotherapy)*
- Methylfolate
- Omega-3 fatty acid
- Vitamin D
- St. John’s Wort  
  - not recommended
- Vitamin C

**Intervention**
- Exercise
- Yoga
- Acupuncture
- Meditation
- Mindfulness
- Tai-Chi

APA Practice Guideline on Management of Depression 2010
S-adenosyl methionine (SAMe)-monotherapy

- Methyl group donor for biological reactions including methylation, methyltransferase
- Usual dose: 800 – 1600mg/day
- 1980’s: (+) 4-8 wk trials primarily in women; more effective than placebo; useful adjunct
- 2014 RCT n=189 -MDD showed 1600-3200mg/d as effective as escitalopram 10-20mg
- ADRs: nausea, stomach upset, switch to mania risk in persons with bipolar disorder
- Expert panel recommends for Parkinson’s, HIV, pain

https://nccih.nih.gov/health/supplements/SAMe
Sarris J Adjunctive Nutraceuticals for Depression Am J Psych 2016
Evidence for Folic Acid or Methylfolate as An Adjunct to Antidepressant

L-methylfolate is a cofactor in the production of monoamines: 5HT, NE, DA
Up to 70% have genetic variant preventing conversion of dietary folate to active L-methylfolate
  Methylenetetrahydrofolate reductase (MTHFR) variant
L-methylfolate is FDA approved as adjunct to antidepressant for managing major depression
Dose 7.5 to 15mg daily
Well-tolerated; pruritus or rash reported-uncommon
Not recommended in cancer patients; can accelerate cancer growth (i.e. prostate cancer)

Sarris J Adjunctive Nutraceuticals for Depression Am J Psych 2016
Shelton Primary Care Companion for CNS disorders 2013
Omega-3 Evidence Moderate/Strong at Adjunct to Antidepressant

- Eicosapentaenoic acid (EPA): fatty acid found in the flesh of cold water fish (e.g., mackerel, herring, tuna) EPA more therapeutic than DHA; most products contain 3:2 ratio EPA/DHA where (i.e. 1000mg = 180 EPA/120 DHA) >60%
- Dose: 200-2200 mg of EPA showed benefit in RCTs; need >60% EPA in product
- Best as adjunct to antidepressant
- Bedtime dosing can cut down on “fishy burps”

Adapted from Sarris J et al. Am J Psych 2016
Sublette ME et al. Meta Analysis of EPA trials in Depression J Clin Psych 2011
Cholecalciferol (Vitamin D)

• Established association between low Vit D levels and depression
  • < 20 ng/mL Deficient
  • 20 - 30 ng/mL Insufficient
  • 31 - 50 ng/mL Sufficient
  • > 75 ng/mL Possible adverse events
• If < 20ng/ml, supplement w/ 50,000 IU weekly x 8 weeks
• If 20-30ng/ml, give 1,000 - 2,000 IU daily
• 1500 IU Vit D effective adjunct to fluoxetine according to RCT n=44 patients with mean Vit D of 23+/- 4 ng/ml in both groups

Maddock J et al. Vit D and Common Mental Disorders Clinical Nutrition 2013
Exercise facilitates transcriptional cofactors that increase production of kynurenine aminotransferases (KATs) in skeletal muscle. KATs cause Kynurenine to become Kynurenic acid: cannot cross blood brain barrier.

IDO: indolamine dioxygenase
TDO: tryptophan dioxygenase

Adapted from Harkin A. Muscling in on Depression NEJM 2014;371:24:2333-2334
Pedersen BK, Exercise as Medicine, Scandinavian J Sports Medicine 2015
Optimize Treatment for Each Patient

- Patient A
  - Situational Worsening of Depression
  - PHQ- Moderate
  - Change in Antidepressant?

- Patient B
  - Failed trials of Antidepressants
  - Investigate causes Adherence?
  - PHQ-9 Severe Depression
  - Recommendations?
How to Talk About Suicide

Kelly Gable, PharmD, BCPP

SIUE – Southern Illinois University at Edwardsville
www.activeminds.org
The Spectrum of Suicidal Thinking

• **Suicide ideation**: thoughts of engaging in behavior intended to end one’s life
• **Suicide plan**: the formulation of a specific method through which one intends to die
• **Suicide attempt**: engagement in potentially self-injurious behavior in which there is at least some intent to die
• **Nonsuicidal self-injury (e.g., self-cutting)**: self-injury in which a person has no intent to die
Suicide Warning Signs

- **Talking About Dying:** any mention of dying, disappearing, jumping, shooting oneself, or other types of self harm.
- **Change in Personality:** sad, withdrawn, irritable, anxious, tired, indecisive, or apathetic.
- **Change in Behavior:** difficulty concentrating on school, work, routine tasks.
- **Change in Sleep Patterns:** insomnia, often with early waking or oversleeping, nightmares.
- **Change in Eating Habits:** loss of appetite and weight, overeating.
- **Narrowed Thinking:** black/white, all/nothing, hopelessness.
Suicide: Risk Factors

- Family history of suicide
- Witnessing family violence
- Child abuse or neglect
- Lack of social support
- Sense of isolation
- Recent or serious loss

- Access to lethal means (e.g., firearms, pills)
- Stigma associated with asking for help
- Barriers to accessing services
- Cultural and religious beliefs

- Male gender
- Mental health disorders (particularly mood disorders)
  - Previous suicide attempt
  - Alcohol and other substance use disorders
  - Chronic pain conditions
  - Hopelessness, helplessness

Suicide Prevention Resource Center (SPRC):
https://www.sprc.org/about-suicide/risk-protective-factors
Suicide: Protective Factors

- Family and community connectedness
- Access to effective clinical care for mental health disorders
- Support from ongoing medical & mental health care relationships
- Marriage and young children in the home
- Meaningful ways of coping with stress
- Awareness of religious/moral/social opposition
- Involvement with a hobby or organization
- Positive worldview

Suicide Prevention Resource Center (SPRC):
https://www.sprc.org/about-suicide/risk-protective-factors
Suicide Assessment: Let’s Practice...

• Have you ever felt that life was not worth living?
• Is death something you’ve thought about recently?
• How often do you think about death?
• How likely do you think it is that you will act on these thoughts?
• Have you made a specific plan to harm or kill yourself?
• Do you have any weapons available to you?
• What things in your life make you want to go on living?
• Who is part of your support system?

It’s ok to stumble.
An imperfect response is better than no response, or not asking at all

Statements to avoid:
• “You can’t really mean that.”
• “But you have so much to live for.”
• “Suicide is a selfish act.”
#BeThe1To – Be the 1 to.com
National Suicide Prevention Campaign

**5 Steps to Save a Life**

1. **Ask:** “Are you thinking of killing yourself?”
2. **Be There:** Listen to their reasons
3. **Follow-Up:** Stay connected to the person
4. **Connect:** Help them find support
5. **Keep Them Safe:** Ask if they thought about how

SAMHSA.org http://www.bethe1to.com/resources/
Suicide Risk Assessment

Low:
- some ideation; no plan
  • Provide suicide prevention community resources & with permission, notify provider

Moderate:
- ideation; vague plan
  • Provide suicide prevention community resources & ensure immediate follow-up with provider. Notify provider of your conversation.

High:
- ideation; specific plan established
  • Stay with patient to keep them safe & link them to acute care. Phone 911; request the help of a Crisis Intervention Trained (CIT) officer.

https://suicidepreventionlifeline.org/
A Complicated Case of Depression
JM is a 30 year-old female with a diagnosis of depression and PTSD. She was exposed to childhood trauma and describes her first depressive episode occurring at the age of 12 years-old. She reports experiencing anhedonia, social isolation, panic when she leaves the house, and rates her mood as a “3 out of 10.” She was prescribed paroxetine in her 20s but had trouble remembering to take it regularly and eventually just stopped taking it.

Social History: married with no children. Consumes 2 to 3 glasses of wine daily for the past 3 months. Does not smoke cigarettes. Denies illicit drug use. Works as an administrative assistant for a law firm.

What other information do you need to move forward with treatment?
A Complicated Case of Depression

• Review D-SIGECAPS
• Assess for thoughts of suicide
• Select an antidepressant / initial dosing
• Discuss the influence of alcohol / substances
• Treatment to remission and recovery
A Complicated Case of Depression

- Labs: unremarkable with exception of low vitamin D (15 ng/ml)
- Other diagnoses: hypothyroidism, fibromyalgia, alcohol use disorder, history of suicide attempt x 1 via overdose
- Current medications:
  - Gabapentin 600 mg BID
  - Levothyroxine 100 mcg/day
- Does this information impact your treatment selection?
The patient is initiated on venlafaxine XR and titrated to 225 mg/day over the course of 2 months. They are also initiated on vitamin D 50,000 IU weekly x 8 weeks. After 6 months of treatment, the patient continues to describe daily insomnia, poor appetite, and anxiety. She rates her overall mood as a “6 out of 10.”

Discuss adjunctive and alternative treatment options for depression.
Options for Discussion

- Mirtazapine
- Quetiapine
- Aripiprazole
- Lithium
- Added Psychotherapy
Take Home Points

• Direct communication with PHQ-9 screening and asking about suicide can destigmatize depression and suicidality.

• Connecting patients expressing suicidal ideation with help on the spot is recommended.

• Antidepressants and CBT are comparable in efficacy for depression; ECT and intranasal esketamine are options for treatment refractory cases.

• SAMe may be effective as monotherapy, other complementary treatments are adjunct to antidepressants and lifestyle interventions.

• For a given patient, it may take multiple antidepressant trials, psychotherapy and combinations of medications and lifestyle interventions to achieve depression remission.
1. A patient presents with several symptoms of depression, including low mood, insomnia, anhedonia, and vacillating thoughts of suicide. What defining features must be present for a diagnosis of depression?

A. ≥ 4 symptoms for at least 1 week
B. ≥ 5 symptoms for at least 2 weeks
C. ≥ 5 symptoms for at least 4 weeks
D. 10 symptoms for at least 2 weeks
Assessment Question: Drug-induced depression

2. A patient taking amlodipine, benazepril, lansoprazole and quetiapine for over 6 months presents with depressive symptoms. Which medication might contribute?
   A. Amlodipine
   B. Benazepril
   C. Lansoprazole
   D. Quetiapine
3. What is an example of a frequently used depression screening tool?
   A. The Healthy Living Questionnaire
   B. Patient Health Questionnaire-9
   C. Life Event Checklist
   D. Generalized Anxiety Disorder-7
4. Which complementary treatment has the strongest evidence base for improving symptoms of depression as monotherapy?

A. St. John’s Wort
B. Omega-3 fatty acids
C. Cholecalciferol
D. S-adenosylmethionine
5. A 50 year old patient with severe depression (PHQ-9 is 22), PTSD and alcohol use disorder did not respond to 2 months of sertraline 200mg/day or escitalopram 30mg daily. The patient is partially responsive to 6 weeks of venlafaxine XR 300mg/day (PHQ-9 is now 17). Genetic polymorphisms, hypothyroidism and low Vit D have been ruled out. Select the most appropriate treatment intervention:
A. Brexanolone infusion
B. Esketamine nasal spray
C. Add St. John’s Wort or Adjunctive Omega-3 fatty acids
D. Discuss adding trauma-focused cognitive-behavioral therapy (CBT)