Behavioral Health: Patients with Severe Depression and Suicidality

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Learning Objectives

Assess the severity of depression in a patient presenting for care.
Develop a treatment plan for severe depression.
Assess suicidality in a patient presenting for care.
Develop a treatment plan for suicidality.

Table of contents

01

Major Depressive Disorder (MDD)

Major Depressive Disorder (MDD)

Also known as

Depression, major depression, major depressive affective disorder, unipolar depression, unipolar disorder, or unipolar mood disorder.

Impaired function, increased illness

Persons with MDD have more pain and physical illness and decreased physical and social functioning.

Disorder versus “feeling down”

MDD is different from everyday “ups and downs” that people naturally experience.

Evaluation of Depression

- Evaluate functional status, PMH, FH, past treatments (as applicable).
- Screening
- Rule out secondary causes
  - Hypothyroidism, anemia, B-12 deficiency, pain, chronic disease, syphilis.
- Evaluate for suicidality or homicidality
- Additional features (psychosis, seasonal pattern, mixed. etc.)

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Screening

Who should be screened?

- **All patients not receiving treatment for depression**
- Previous recommendations
  - All adults at least every 5 years
  - Part of a health maintenance visit (PHQ-9 in waiting room)
  - High risk groups every year
  - History of depression (PMH)
  - Family history of depression or bipolar disorder
  - Chronic illnesses
  - High utilization of services
  - Pregnancy (2016 recommendation)
  - Those with complaints suggestive of depression (insomnia, fatigue, changes in attention or concentration, etc.)

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Contributors

When evaluating a patient for MDD, it is essential to rule out underlying medical causes or drug causes

- Cardiovascular
  - Calcium channel blockers, clonidine, methyldopa
  - Beta blockers (controversial)
- Hormones
  - Oral contraceptives (OCAs), corticosteroids, GnRH agonists
- Other
- Acyclovir, Alcohol, AEDs (phenobarbital, primidone, levetiracetam, topiramate), antipsychotics, barbiturates, interferon, isotretinoin, levodopa, varenicline, benzodiazepines, opioids

Celano CM, et al.. Dialogues Clin Neurosci. 2011;13(1):109-25
DSM-5-TR.

Screening via PHQ-9

Over the last 2 weeks, how often have you been bothered by any of the following?		Not at all	Several days	More than half the days	Nearly every day
a	Little interest or pleasure in doing things?	0	1	2	3
b	Feeling down, depressed, or hopeless?	0	1	2	3
c	Trouble falling or staying asleep, or sleeping too much?	0	1	2	3
d	Feeling tired or having little energy?	0	1	2	3
e	Poor appetite or overeating?	0	1	2	3
f	Feeling bad about yourself—or that you are a failure or have let yourself or your family down?	0	1	2	3
g	Trouble concentrating on things, such as reading the newspaper or watching television?	0	1	2	3
h	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?	0	1	2	3
i	Thoughts that you would be better off dead or of hurting yourself in some way?	0	1	2	3
For office coding: Total Score =_____+_____+_____+_____					

VA/DoD Clinical Practice Guideline 2022.

Diagnostic Criteria Per DSM-5-TR

Must have **5 features** during the same **2-week period** that **impair functioning:**

1. *Depressed mood (can be an irritable mood in children/adolescents)
2. *Loss of interest or pleasure must be present
3. Weight loss or gain
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation
6. Fatigue
7. Feelings of worthlessness, excessive/inappropriate guilt
8. Decreased concentration
9. Thoughts of death or suicide

DSM-5-TR.

Diagnostic Criteria Per DSM-5-TR

- One symptom of either depressed mood or loss of interest or pleasure must be present
- Symptoms must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- Other medical conditions or substance use must not account for symptoms.
- No history of manic or hypomanic episodes (Bipolar disorder)

DSM-5-TR.

02

Severity Assessment

Using the PHQ-9

Over the last 2 weeks, how often have you been bothered by any of the following?		Not at all	Several days	More than half the days	Nearly every day
a	Little interest or pleasure in doing things?	0	1	2	3
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h	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?	0	1	2	3
i	Thoughts that you would be better off dead or of hurting yourself in some way?	0	1	2	3

For office coding: Total Score = 0 + 4 + 6 + 0 **Total = 10**

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Test your knowledge

Based on the PHQ-9 score of 10, how would the patient's major depressive disorder (MDD) severity be classified?

A. No MDD
B. Mild
C. Moderate
D. Severe

Severity via PHQ-9 Score

Severity Level	PHQ-9 Total Score	Number of Symptoms According to DSM-5	Functional Impairment
Mild	10 – 14	5	Mild
Moderate	15 – 19	6 to 7	Moderate
Severe	≥20	8 to 9	Severe

Additional symptoms that indicate severe depression

- Active suicidal ideation with intent, plan, or attempt
- Active homicidal ideation
- Psychotic symptoms
- Severe anorexia
- Inability to maintain activities of daily living
- Catatonia

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Treatment Options

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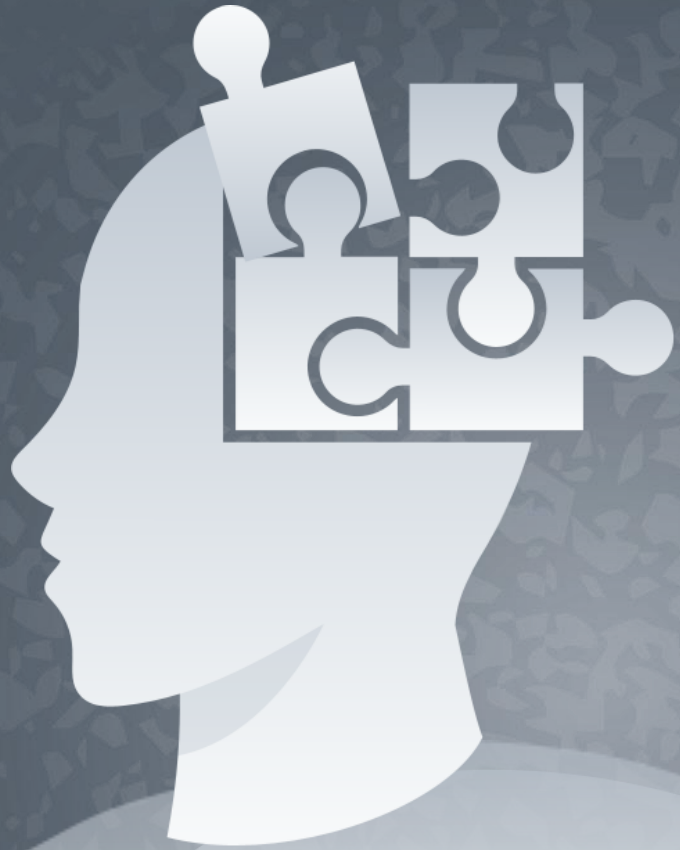

Nonpharmacological treatments

- Evidence Based Psychotherapy
  - Recommended for all patients with severe depression
- Repetitive transcranial magnetic stimulation (rTMS)
  - Nonresponse or partial response to 2/+ pharmacotherapies
- Electroconvulsive Therapy (ECT)
  - In severe MDD with at least one of the following:
    - Catatonia, psychosis, severe suicidality,
    - Need for rapid response
    - History of poor response or intolerable SE to multiple antidepressant agents
    - Risk associated with other treatments are greater those associated with MDD
- All patients should be encouraged to eat well, sleep well, and exercise
  - Light therapy and bibliotherapy may be considered

VA/DoD Clinical Practice Guideline 2022.

Pharmacologic treatments

*Efficacy based on Cipriani A et al. Lancet 2018;391:1357-66

Treatment option	Efficacy (OR)*	Side effects	Cost	Notes
SSRIs	1.52-1.75	Mild	$	Considered most tolerable class
SNRIs	1.49-1.85	Moderate	$$	Helps with pain, +/- energy
Mirtazapine	1.89	Mild	$	Helps with sleep and appetite
Bupropion	-	Moderate	$$	Helps with fatigue
Vortioxetine	1.66	Moderate	$$$	May help with neuropsychological performance
Vilazodone	-	Mild	$$$	“Less” sexual side effects
TCAs	1.49-2.13	High	$	Helps with pain, insomnia
MAOIs	-	High	$-$$	Reserved/last line for TRD

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“Newer” treatments

- NMDA antagonists for augmentation
  - Ketamine
    - Can exacerbate psychosis, BP monitoring required.
  - Esketamine
    - Recommended after non-response to several adequate trials
    - Suicidality
- Gepirone
  - Serotonin 1A receptor agonist
    - Note buspirone is a 5HT1A partial agonist and 5HT2 agonist
  - Modest (2.5 point) improvement on HAM-D
  - May be best suited for those with MDD with anxious features

Partial or non-response

- Switch
  - Different medication
  - Psychotherapy
- Augment
  - Second generation antipsychotic (SGA)
  - Psychotherapy

**consider degree of response and number of failed trials*

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Augmenting Agents

- **Antipsychotics**
  - **Aripiprazole, brexpiprazole, cariprazine, lurasidone, quetiapine, olanzapine, or risperidone**
- Antidepressants with alternative MOA
- Lithium
- Liothyronine
- Buspirone
- Stimulants
- Some mood stabilizers (controversial)

VA/DoD Clinical Practice Guideline 2022.

Test your knowledge

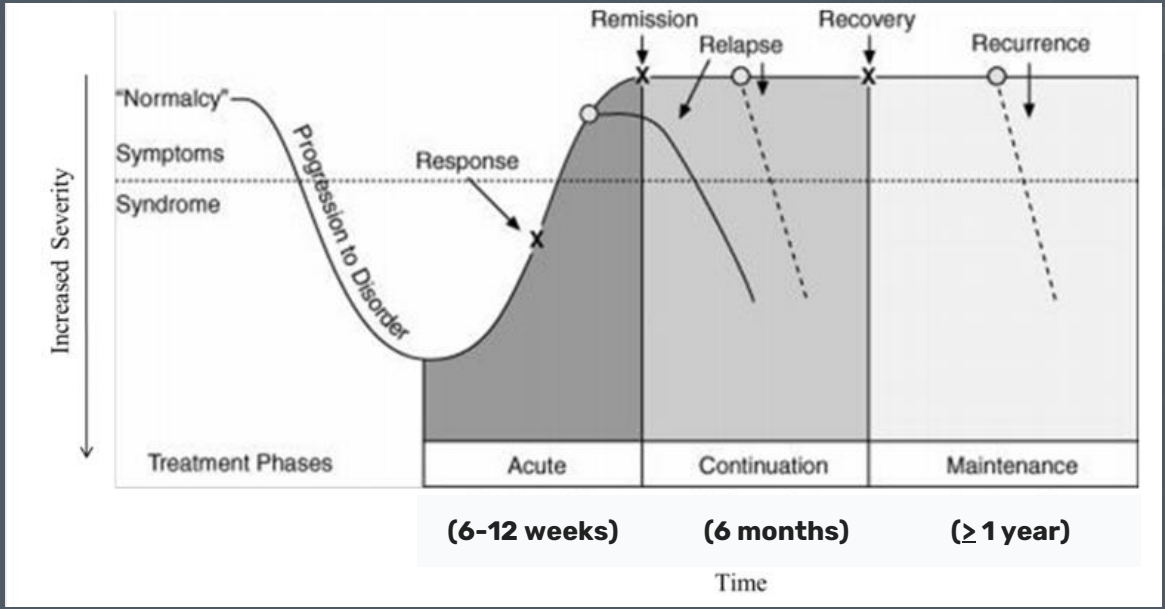
What is an appropriate duration of treatment for severe MDD?

A. 3 months
B. 6 months
C. 9 months
D. Indefinitely

Duration

At least 6 months after remission (Va/DoD 2022)

Remission = a period of 2 or more months with no symptoms; 1-2 symptoms of mild degree



Among patients who achieve response the six-month risk of relapse is ~41% if antidepressants are discontinued

Treatment of Severe Depression

- Psychotherapy should be combined with pharmacotherapy
- When considering medications, efficacy > tolerability
- Consider potent dual mode of action drugs or combinations
  - SNRIs
  - TCAs
  - Vortioxetine
  - MAOIs
- ECT
- Antipsychotic augmentation whether or not psychotic symptoms are present

VA/DoD. Gautam S et al. Indian J Psychiatry. 2017 Jan;59(Suppl 1):S34-S50.

Boyce P et al. Aust Prescr 2021;44:12-15.

Test your knowledge

What limits the use of MAOIs in practice?

A. Side effects
B. Drug interactions
C. Food interactions
D. Administration

Aripiprazole versus Bupropion

Study design

Systematic literature review of 5 RCTs, which evaluated the efficacy and safety of aripiprazole (ARI-A) or bupropion (BUP-A) augmentation and bupropion switching (BUP-S) for patients with TRD or MDD.

Data collection

Including 4480 patients, through April 2023. Outcomes measured were changes in the MADRS, response and remission rates, and serious adverse events.

Ji M, et al. PLoS One. 2024 Apr 26;19(4):e0299020.

Results Aripiprazole versus Bupropion

- **ARI-A** was associated with a significantly **higher response rate** compared with **BUP-A** (RR: 1.15; 95% CI: 1.05, 1.25; P = 0.0007; I2 = 23%).
    - Between ARI-A and BUP-A there was no significant difference in improvement of MADRS (WMD: -2.07; 95% CI: -5.84, 1.70; P = 0.28; I2 = 70%)
- **ARI-A** had a significantly **higher remission rate** compared **BUP-S** (RR: 1.22; 95% CI: 1.00, 1.49; P = 0.05; I2 = 59%)
- BUP-A had a significantly higher remission rate compared with BUP-S (RR: 1.20; 95% CI: 1.06, 1.36; P = 0.0004; I2 = 0%).
- Between ARI-A and BUP-A there was no significant difference in remission rates (RR: 1.05; 95% CI: 0.94, 1.17; P = 0.42; I2 = 33%)
- No significant difference was observed in adverse events and serious adverse events among the three treatment strategies.

Ji M, et al. PLoS One. 2024 Apr 26;19(4):e0299020.

Discussion

Limitations

I2 = heterogeneity (higher numbers = higher heterogeneity) which makes results difficult to apply.
Aripiprazole may not be the best antipsychotic medication for everyone.
Bupropion may not be the best antidepressant for everyone.

Conclusions

It is logical to initiate a medication that can produce a faster response when treating severe MDD.
It is still important to ensure the first-line/primary agent is efficacious, and rapid augmentation can cloud this assessment but may be necessary for the benefit of the patient.

04

Suicidality

Background

- May occur in patients experiencing MDD, other psychiatric diagnosis, or individuals with no psychiatric history.
- Suicide is defined as death caused by self-directed injurious behavior with intent to die as a result of the behavior.
- A suicide attempt is a non-fatal, self-directed, potentially injurious behavior with intent to die as a result of the behavior.
    - A suicide attempt might not result in injury.
- Suicidal ideation (SI) - thinking about, considering, or planning suicide.
- As of 2019, the Centers for Disease Control and Prevention listed suicide as the 10th leading cause of death among Americans (47,500 people)
    - 2nd leading cause of death among 10 to 34-year-olds
- All patients diagnosed with MDD should be assessed for suicidal thoughts
- Suicidality can be passive or active, and can fluctuate from moment to moment

Screening

- **Anyone with risk factors:**
  - Chronic major mental illness or personality disorders
  - History of previous suicide attempts or SUD
  - Chronic medical conditions or pain
  - Limited coping skills or ability to identify reasons for living
  - Unstable psychosocial support (housing, relationships, employment)
- **Tools**
  - Question # 9 of the PHQ-9
    - "Do you have thoughts that you would be better off dead or of hurting yourself in some way?"
  - Columbia-Suicide Severity Rating Scale (C-SSRS)
  - Suicide Assessment Five Step Evaluation and Triage (SAFE-T)
- **Cause? (MDD, life stressors, other psychiatric diagnosis)**

VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide. 2019.

Warning signs

- Recognition of warning signs is the key
  - Helps create an opportunity for early assessment and intervention
- Three direct warning signs are particularly indicative of suicide risk:
  - Communicating suicidal thought verbally or in writing
  - Seeking access to lethal means such as firearms or medications; and
  - Demonstrating preparatory behaviors such as putting affairs in order
- Presence of one or more of these warning signs is a strong indication that further assessment is needed
- Indirect warning signs (e.g., agitation, hopelessness, insomnia, shame) are important to assess as well

VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide. 2019.

Severity

- High Acute Risk
  - Plan
  - Means and/or access
  - Recent attempt
  - Inability to maintain safety
  - Acute episode related to psychiatric diagnosis
- C-SSRS screening version can help differentiate low, moderate, or high risk.

VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide. 2019.

05

Interventions

Nonpharmacological

- **Cognitive Behavioral Therapy**
- **Crisis Response Plan**
- **Reduced access to means**
  - Weapons
  - Time alone
  - Specific medications
  - Medication quantities
- **Increased outreach**
- **Case/care management**

VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide. 2019.

Pharmacological

- Medications to target underlying diagnosis
  - Could see multiple agents used
- Therapies with positive evidence for suicidality
  - Ketamine augmentation
    - IV 0.5 mg/kg has moderate evidence for acute symptom improvement of SI within 24 hours of treatment, with a moderate effect size that continues for 1-6 weeks.
    - In a meta-analysis of ketamine trials, 55% of patients after 24 hours and 60% at seven days reported no suicidal ideation.
  - Esketamine (not discussed in GL)
  - Lithium + additional psychotropic
  - Clozapine for schizophrenia or schizoaffective

VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide. 2019.
Fan W, et al. Oncotarget. Jan 10 2017;8(2):2356-2360
Grunebaum MF, et al. Am J Psychiatry. Apr 1 2018;175(4):327-335.
Wilkinson ST, et al. Am J Psychiatry. Feb 1 2018;175(2):150-158.

Test your knowledge

A patient with a history of severe MDD presents for regular follow-up and discloses suicidality with a plan. Current medication include sertraline 200 mg by mouth daily. What is an appropriate intervention?

A. Initiate ketamine
B. Initiate lithium
C. Change sertraline to venlafaxine
D. Initiate CBT

06

Conclusions

Take Home Points

- Severe depression describes the presentation and does not necessarily direct treatment decisions or outcomes.
- Number of symptoms, level of impairment of function, or PHQ-9 score can be used to gauge severity.
  - Modifiers for severity exist (SI, HI, psychosis, etc.)
- Nonpharmacologica interventions for suicide are strong (versus weak for drugs) recommendations.
- Must address and treat underlying problem successfully.
  - This includes treating insomnia.
- Lithium used to be the predominant medication for augmentation of suicidality, but ketamine is now recommended in the most recent guidelines.

Questions?

Thank you for your time and attention!

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