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What Would You Do in This Case of MDD?

Real Examples From Your Community

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The Scope and Impact of MDD

- Depression is the leading cause of disability worldwide
- MDD lifetime prevalence: ~11%
- Depression affects multiple aspects of people's lives
  - Cognition
  - Fatigue
  - Mood
  - Sexual function
  - Sleep

Not every disability is visible

WHO website.

DSM-5 Diagnostic Criteria for MDD

A. At least 5 of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; 1 of the symptoms is either 1 or 2 below
   1. Depressed mood most of the day, nearly every day, as indicated by either subjective report or observation made by others
   2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day
   3. Significant weight loss when not dieting or weight gain or decrease or increase in appetite nearly every day
   4. Insomnia or hypersomnia nearly every day
   5. Psychomotor agitation or retardation nearly every day
   6. Fatigue or loss of energy nearly every day
   7. Feelings of worthlessness or excessive or inappropriate guilt
   8. Diminished ability to think or concentrate, or indecisiveness, nearly every day
   9. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide
B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
C. The episode is not attributable to the physiological effects of a substance or to another medical condition
D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders

DSM-5. 2013:160-168.

HEDIS® Measures

- Primarily process measures
- Standardized and audited data collection nationwide for commercial, Medicaid, and Medicare managed care plans via
  - Administrative and claims data
  - Medical record review
- Contains 70 measures across 8 measurement domains
- CMS uses HEDIS to oversee the performance of Medicare managed care organizations
- Current indicators address
  - Preventative services
  - Chronic disease management
  - Behavioral health care
  - Appropriate use of services

NCQA website.

National Healthcare Quality and Disparities Report

- AHRQ analyzes 179 HEDIS measures and produces annual report
  - Allows comparisons across plans nationwide
  - Latest 2015 Report
    - Quality is improving
    - Gaps exist
    - Improvement is possible

AHRQ. *2015 National Healthcare Quality and Disparities Report and 5th Anniversary Update on the National Quality Strategy*.

Depression Care Quality Measures

- Use of the PHQ-9 to monitor depression symptoms for adolescents and adults
  - The percentage of members age ≥12 with a diagnosis of depression who had an outpatient encounter with a PHQ-9 score present in their record in the same assessment period as the encounter (first implemented in HEDIS 2016)
- Depression Remission or Response for Adolescents and Adults
  - The percentage of members age ≥12 with a diagnosis of depression and an elevated PHQ-9 score, who had evidence of response or remission within 4 to 8 months after the initial elevated PHQ-9 score (first implemented in HEDIS 2017)
- Depression Screening and Follow-Up
  - The percentage of members age ≥12 who were screened for clinical depression using a standardized tool and, if screened positive, who received follow-up care (will be implemented in HEDIS 2018)

NCQA website.

Case 1 Sam: Social History

- 32-year-old roughneck
- Laid off almost 3 years ago
- Increasingly despondent about his unsuccessful job search
- Previously active and engaged with wife and 2 toddlers
- Now withdrawn from family and friends
- Stopped exercising or engaging in healthy activities
- No set sleep pattern
- Has recently gained 35 pounds
- Body mass index: 31 kg/m^2
- Smokes 1 pack of cigarettes/d
- Consumes 5-6 cups coffee/d
- Consumes 3-4 beers each evening and night
- Smokes marijuana 2-3×/wk
- Denies other illicit or prescription drug use

Case 1 Sam: Diagnosis and Care by Family Physician

- Visits family physician at wife's insistence
- Physician screens for depression
  - MDQ
    - Score: 1
    - Unlikely to fall within the bipolar spectrum
  - PHQ-9
    - Score: 18
    - Moderately severe depression

Depression Rating Scales

- Validated tools should be used
- Rating scales should be used in as many patients as possible
- Purpose of using scales
  - Improves the identification of depression
  - Is the only reliable way to obtain an objective measure
  - Can serve to monitor safety and effectiveness of treatment
- The scale must be easy to use
- Rating scales should be used
  - During initial evaluation
  - At treatment initiation
  - When medication changes are implemented
  - When the patient reports a change in symptoms

Siu AL, et al. *JAMA*. 2016;315:380-387.

Depression Screening Tools

Standard Screening Tools

- Beck Depression Inventory-II
- Center for Epidemiologic Studies of Depression Scale Revised

Short-Form Screening Tools

- PHQ-9
- Clinically Useful Depression Outcome Scale
- Quick Inventory of Depressive Symptomatology

Scales to Quantify Level of Depression and Response to Treatment

- Hamilton Depression Scale
- Inventory of Depressive Symptomatology
- Montgomery-Åsberg Depression Rating Scale
- Zung Self-Rating Depression Scale

Gelenberg AJ, et al. *Practice Guideline for the Treatment of Patients With Major Depressive Disorder, Third Edition.* 2010.

Scales for Measuring Specific Components of MDD

- AEs of treatment
  - Frequency, Intensity, and Burden of Side Effects Scale[a]
- Cognition
  - Cognitive Impairment in Psychiatry
  - Depressive Cognition Scale
  - Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire
  - MOS Cognitive Functioning Scale
  - Perceived Deficits Questionnaire
  - THINC-it
- Fatigue
  - Fatigue Questionnaire
  - MGH-Cognitive and Physical Functioning Questionnaire
- Sexual function
  - Arizona Sexual Experiences Scale
  - Female Sexual Function Index
  - Sexual Dysfunction Questionnaire
  - Sexual Function and Satisfaction Measures
  - Sexual Function Questionnaire

a. Wisniewski SR, et al. *J Psychiatr Pract*. 2006;12:71-79.

Case 1 Sam: Results of Laboratory Testing

- Hemoglobin: 12.2 g/dL
- Hematocrit: 37%
- Thyroid function
  - TSH: 1.7 mIU/L
  - Total T4: 8.7 µg/dL
  - Total T3: 123 ng/dL
  - Free T4: 1.9 ng/dL
  - Free T3: 0.48 ng/dL
- Lipid panel
  - TC: 212 mmol/L
  - HDL-C: 37 mmol/L
  - LDL-C: 147 mmol/L
  - Triglycerides: 178 mmol/L
- Comprehensive metabolic panel
  - Fasting glucose: 91 mg/dL
  - Calcium: 9.1 mg/dL
  - Albumin: 4.2 g/dL
  - Total protein: 7.2 g/dL
  - BUN: 11.3 mg/dL
  - Creatinine: 1.1 mg/dL
  - Electrolytes
    - Sodium: 142 mEq/L
    - Potassium: 4.2 mEq/L
    - CO_2: 27 mmol/L
    - Chloride: 101 mmol/L
  - ALP: 123 IU/dL
  - ALT: 27 IU/dL
  - AST: 29 IU/dL
  - Direct bilirubin: 0.19 mg/dL

Case 1 Sam: Initial Depression Treatment by Primary Care Physician

- Paroxetine hydrochloride
  - Initial dose: 10 mg q am
  - Titration schedule: 10-mg increase weekly
  - Target dose: 40 mg
- Return visit
  - 3 months
  - PHQ-9 score: 18

The Case for Switching Antidepressants

- Clinically necessary when first drug is poorly tolerated
- Second drug selection is iterative, guided by outcome with first
- Can pick medications with distinctly different mechanisms of action
- Efficacy of second antidepressant clearly established
- Florida Medicaid Guidelines
  - Evaluate adherence
  - Optimize the dose of current medication
  - Switch to a different single agent*

*Agent from the same or different class (eg, SSRI, SNRI, mirtazapine, bupropion, vortioxetine)

McIntyre RS, et al. *J Clin Psychiatry*. 2017;78:703-713.

Case 1 Sam: Second Depression Treatment by Primary Care Physician

- Sertraline
  - Initial dose: 50 mg q am
  - Titration schedule: 50-mg increase weekly
  - Target dose: 200 mg
- Return visit
  - 3 months
  - PHQ-9 score: 19
  - Specialist referral for evaluation and management of depression

Case 1 Sam: Initial Psychiatrist Visit

- Nonadherent with treatment because of its effect on his libido
- Columbia Suicide Severity Rating Scale
  - No suicide plan
  - Ready access to guns
  - Occasional thoughts of using gun on himself
- MDD affects not only patient but also family dynamics

Treatment-Resistant Depression

- Persistent depression across 6 months of treatment suggests a low chance of spontaneous remission
- Nonresponse to 2 adequate trials is "entry" definition of treatment-resistant depression
- Use of scales alone increases chance of treatment success
- After 2 SSRI trials, should either switch classes OR use an adjunctive treatment

Risk Factors for Treatment-Resistant Depression

Comorbid conditions

- Anxiety disorder
- Medical conditions

Alcohol or substance abuse

History of

- Suicide attempt
- Psychiatric hospitalization

Early age of onset of depression

Higher body mass index

Personal or family history of

- Depression
- Mood disorder

Rizvi SJ, et al. *Can J Psychiatry.* 2014;59:349-357.

Case 1 Sam: Treatment

- Best chance of success in first 4 weeks of treatment
- No SSRI
  - Dose-limiting AE of sexual dysfunction
  - Previous lack of response to 2 SSRIs
- Switch antidepressant class
  - Choose a drug with minimal effect on sexual function
  - Select drug that has weight-neutral effects
- Drug selected: Bupropion
- Monitor at 2, 4, and 6 wk

Antidepressant	Rate of sexual dysfunction in trials, %
Bupropion[a]	7.0
Citalopram[a]	30.0-72.7
Duloxetine[a]	23.4
Fluoxetine[a]	23-57.7
Fluvoxamine[a]	62.3
Mirtazapine[a]	24.4
Paroxetine[a]	25-70.7
Sertraline[a]	25.0-62.9
Venlafaxine[a]	30-67.3
Vortioxetine[b]	0.6-4.9

a. Reichenpfader U, et al. *Drug Saf*. 2014;37:19-31; b. Jacobsen PL, et al. *CNS Spectr*. 2016;21:367-378.

The Case for Adjunctive Therapy

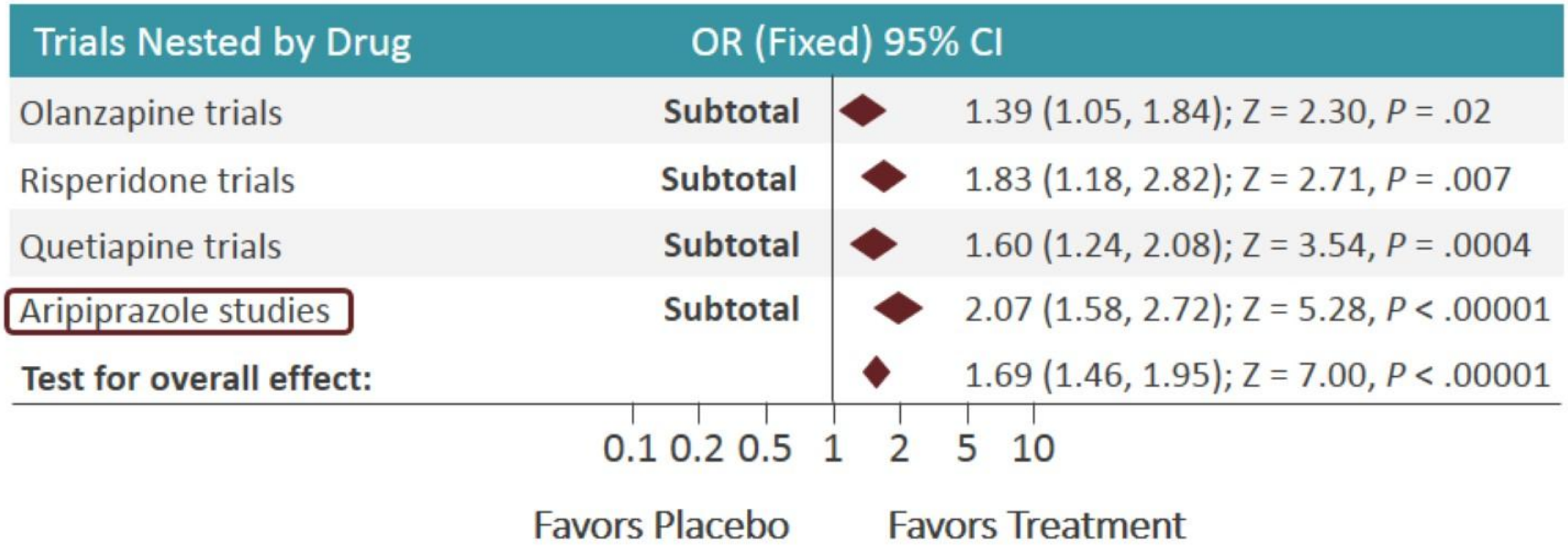
- If suboptimal response (PHQ-9: 10), consider adjunctive therapy
- Builds on partial success of first therapy
- Combine existing antidepressant monotherapy with
  - Evidence-based psychotherapy
    - Cognitive behavioral therapy
    - Interpersonal therapy
  - Aripiprazole* or brexpiprazole*
  - Another antidepressant agent†
- Avoiding washout is a pragmatic benefit for patients
- When effective, benefits may be rapid
- Therapeutic agent can be chosen to target specific symptoms

*FDA approved for adjunctive treatment in MDD.
†Do not combine SSRI and SNRI.

McIntyre RS, et al. *J Clin Psychiatry*. 2017;78:703-713.

Meta-Analysis of Response Rates in Double-Blind, Placebo-Controlled, Atypical Augmentation Trials

Odds Ratios of Response Rates With Atypical Antipsychotic Agents and Placebo



Nelson JC, et al. *Am J Psychiatry*. 2009;166:980-991.

Combining Antidepressants

- Once considered indicative of bad practice, combining antidepressants is now commonly done for TRD
- Bupropion and mirtazapine are preferred as add-on antidepressants
- No antidepressant has FDA approval for this use, and only 1 (mirtazapine) has the support of 2 positive studies
- Most newer combos are safe, but all have caveats

McIntyre RS, et al. *J Clin Psychiatry.* 2017;78:703-713.

Neuromodulation Strategies

- Electroconvulsive therapy
- Transcranial magnetic stimulation
- Vagus nerve stimulation
- Deep brain stimulation

McIntyre RS, et al. *J Clin Psychiatry.* 2017;78:703-713.

Other Nonpharmacologic Treatment of MDD

- Psychosocial interventions[a]
  - Patient psychoeducation
  - Cognitive behavioral therapy
  - Interpersonal therapies
  - Mindfulness-based approaches
- Lifestyle modification[b,c]
  - Exercise[d]
  - Sleep
  - Smoking cessation[e]
  - Weight loss

a. Parikh SV, et al. *Can J Psychiatry.* 2016;61:524-539; b. Ravindran AV, et al. *Can J Psychiatry.* 2016;61:576-587; c. Goracci A, et al. *J Affect Disord.* 2016;196:20-31; d. Knapen J, et al. *Disabil Rehabil.* 2015;37:1490-1495; e. Mathew AR, et al. *Addiction.* 2017;112:401-412.

Case 2 Monique: Social History

- 56-year-old, senior manager accountant
- Never married
- Last serious romantic relationship ended 20+ years ago
- Has concentrated on career
  - Works 60+ hours per week
  - Travels frequently (Monday-Thursday every week)
- Spends free time with brother and his family and sorority sisters
- About 6 months ago
  - Began experiencing
    - Reduced energy
    - Fatigue
    - Apathy
    - Loss of appetite
    - 15-pound unintentional weight loss
  - Withdrew from social activities
  - Stopped exercising
  - Developed sleep-onset insomnia
- In the past month
  - Arrived late at work several times
  - Became lax in her personal grooming

Case 2 Monique: Today's Visit

- Sorority sisters insisted Monique seek help when she missed the fifth Saturday brunch in a row
- After Monique made several errors at work, her boss suggested she "take a break and get herself together"
- Screening for depression and results
  - MDQ: 6
  - PHQ-9: 23
- Diagnosis
  - Severe depression
  - A slight risk for bipolar disorder
  - History negative for hypomania

Case 2 Monique: Family History

- Mother died at age 59 of ovarian cancer
- Father was killed in a motor vehicle crash when Monique was in her first year of college
- Only brother in good health
  - Emeritus economics professor at Georgetown University
  - Married 40 years
  - New grandchild

Case 2 Monique: Chief Concern and Diagnosis

- Impression
  - Bland affect
  - Not spontaneously available
  - Primary difficulty: “Feeling as if her mind is enveloped in cotton bolls," which affects
    - Concentration
    - Cognition
    - Memory
  - Anhedonia
- Diagnosis
  - MDD
  - Cognitive dysfunction

Case 2 Monique: Treatment Plan

- Provide psychoeducation to help her understand her condition and treatment
- Recommend lifestyle changes, primarily resumption of previous exercise regimen
- Provide a list of psychosocial resources

McIntyre RS, et al. *J Clin Psychiatry.* 2017;78:703-713.

Case 2 Monique: Selecting Pharmacologic Therapy

First-Line Antidepressant Agents

Bupropion

Mirtazapine*

SSRIs

SNRIs

Vortioxetine

- Factors affecting agent selection in this patient
  - Cognitive difficulties point to vortioxetine
  - Weight loss and insomnia could favor mirtazapine
- Include adjunctive therapies
  - Cognitive behavioral therapy
  - Wellness plan
  - Exercise
- Pharmacologic selection is a collaborative iterative process between patient and provider

*First-line only for elderly.

McIntyre RS, et al. *J Clin Psychiatry.* 2017;78:703-713.

Following Monique to Recovery

- Collect PHQ-9 at each visit
- Target PHQ-9 scores
  - <10 by weeks 4-6
  - ≤5 by week 12
- Objectively document AEs
- Optimize dose within therapeutic range to obtain best balance of response and AEs
- Provide 6 to 9 months of continuation therapy after adequate response to ensure recovery

Conclusion

- A validated screening tool should be used at every visit in every patient with depression
- AEs of treatment should be formally assessed at every visit
- Treatment should be chosen through shared decision making, taking into consideration
  - Patient values, abilities, and desires
  - Side effect profile of the drug
  - Comorbidities and patient profile
- Patients should be followed closely
- Using scales helps to educate patients and provides a common language for patients and healthcare providers

Abbreviations

AHRQ = Agency for Healthcare Research and Quality
ALP = alkaline phosphatase
APT – alanine amino transferase
AST = aspartate amino transferase
BUN = blood urea nitrogen
CBT = cognitive behavioral therapy
CMS = Centers for Medicare and Medicaid
CO2 = carbon dioxide
C-SSRS = Columbia Suicide Severity Rating Scale
DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
FDA = US Food and Drug Administration

Abbreviations (cont)

HDL-C = high-density lipoprotein cholesterol
HEDIS = Healthcare Effectiveness Data and Information Set
IPT = interpersonal psychotherapy
LDL-C = low-density lipoprotein cholesterol
MDD = major depressive disorder
MDQ = Mood Disorders Questionnaire
MGH = Massachusetts General Hospital
MOS= Medical Outcomes Study
PHQ = Patient Health Questionnaire
qam = every morning
SNRI = serotonin and norepinephrine reuptake inhibitor
SSRI = selective serotonin reuptake inhibitor

Abbreviations (cont)

TC = total cholesterol

TSH = thyroid stimulating hormone