LATE- LIFE DEPRESSION IN PRIMARY CARE: The Mind Body Interface

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Disclosures

- No relevant relationships to disclose.
Objectives

- By the end of this presentation, participants will be able to:
  - Understand the prevalence and impact of depression
  - Discuss medical co-morbidities that may impact depression
  - Review depressive syndromes and diagnostic challenges
  - Compare/contrast validated screening tools
  - Review evidence-based treatment options
Depression is Common

- Lifetime prevalence of major depressive disorder (MDD) in general population: 15-17% [1]
- Frequently treated by primary care physicians
- Up to 50% undiagnosed/untreated [2]

1. Kessler RC et al
2. Pratt LA et al.
Depression in Older Adults

- Prevalence of MDD in geriatric population: ~4% [1]
- F>M (4.4% vs 2.7%) [2]
- 15-25% with sub-syndromic depression [3]

1. Gonzalez et al
2. Steffens et al
3. Mckinney et al
Depression is Costly

- Depression is 3rd leading cause of global burden of disease
- By 2020, Major Depression will be the second leading cause of disability worldwide [1]
- Total economic burden of MDD estimated to be $210.5 billion per year, representing a 21.5% increase from $173.2 billion per year in 2005.
  - 48%-50% attributed to the workplace, including absenteeism (missed days from work) and presenteeism (reduced productivity while at work)
  - 45%-47% are due to direct medical costs (e.g., outpatient and inpatient medical services, pharmacy costs shared by employers, employees, and society
  - About 5% of the total expenditures are related to suicide[2]

1. World Health Organization.
2. Greenberg PE et al.
Burden of Disease

Days in Bed over Prior Month: Depression vs. Chronic Medical Conditions

- Increased number of medical appointments
- Increased length of hospital stay
- Higher costs of ambulatory care
- Decreased adherence
- Loss of workplace productivity

Wells KB et al.

Saravay SM, et al; Verbosky LA et al; Greden JF, et al
Depression and Adherence

- 3-fold decrease in adherence
  - DM+ depression
  - MI+ depression
  - CAD+ depression/dysthymia

- 4-fold higher health care costs
Depression ↔ Medical Illness

- Bi-directional relationship
  - Depression associated with poorer medical outcomes
  - Medical co-morbidities negatively impact course of depression

McKinney et al
Biologic Factors

Medical illness

- Med-related
- Vascular risk factors
- Depression
- Genetics
- Substance-related
Depression and Medical Illness

2 to 3-fold higher rates of major depression vs. age- and gender-matched primary care patients

Katon et al; Raj et al
Post-MI Depression: Morbidity and Mortality

van Melle et al.

OR 95% CI

<table>
<thead>
<tr>
<th>Event</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>2.38</td>
<td>2-2.59</td>
</tr>
<tr>
<td>Cardiac mortality</td>
<td>2.59</td>
<td></td>
</tr>
<tr>
<td>New CV events</td>
<td>1.95</td>
<td></td>
</tr>
</tbody>
</table>
Depression and Diabetes: Morbidity and Mortality

Microvascular complications [1]
Macrovascular complications [1]
All-cause mortality [2]

- Depression + DM: 11.32
- Depression + DM: 9.3
- Depression + DM: 2.5
- Depression + DM: 2.64
- DM only: 1.37
- DM only: 1.88
- DM only: 1.2

Black et al
Egede et al
HIV Statistics

- 1.1 million Americans living with HIV
- By age, of persons diagnosed with HIV in the United States in 2015:
  - 4% were aged 13-19
  - 37% were aged 20-29
  - 24% were aged 30-39
  - 17% were aged 40-49

HIV in Older Adults

- 17%: age 50+
  - 12% (4,870) age 50-59
  - 5% (1,855) age 60+

cdc.gov  HIV Surveillance Report 2015;26
Epidemiologic Profile

Figure 1.01 shows total incidence (the number of new cases within a specified time period), deaths, and prevalence of HIV/AIDS cases in South Carolina since 1996.

Figure 1.01: South Carolina HIV/AIDS incidence, prevalence, and deaths

Note: number of cases diagnosed in S.C. only; excludes out of state cases returning to S.C.
AIDS prevalence:
- Columbia ranked #11
- Charleston SC #39
- Greenville #55
HIV and Depression

- Depression is the most prevalent psychiatric disorder in HIV patients
- Lifetime rates are estimated between 35-50%
- Depression in HIV patients correlates with poorer outcomes:
  - Lower CD4 counts
  - Higher rates of noncompliance
  - Longer time to HAART initiation
  - Shorter time to AIDS diagnosis

Pyne JM et al
HIV and Depression

- **39%** of HIV infected community dwelling older adults with major depression
- **27%** considered suicide

**Stressors:**
- Less social support
- Less surviving peers
- Fewer family/caregivers
- Higher co-morbid health problems

Heckman et al
Risk Factors for Depression in HIV Patients

- History of mood disorder
- Substance abuse
- Anxiety disorder
- History of suicide attempt
- Family psychiatric history
- Polypharmacy
- Inadequate social support
- Non-disclosure of status
- Multiple losses
- Advancing illness
- Financial stressors
- Treatment failure
Psychiatric Side Effects of HAART

- **Zidovudine**: confusion, agitation, insomnia, mania, depression
- **Efavirenz**: confusion, stupor, agitation, amnesia, hallucinations, insomnia, abnormal or vivid dreams
- **Ritonavir**: anxiety
- **Didanosine**: lethargy, nervousness, anxiety, depression, psychosis
- **Stavudine**: sleep and mood disorders
- **Enfuvirtide**: anxiety, depression
- **Steroids**: mania, depression, psychosis
- **Interferon**: depression, delirium
- **Interleukin-2**: depression, disorientation, confusion and coma
- **Vinblastine**: depression, cognitive impairment
- **Antibiotics**: can often cause delirium, psychosis
DSM-5 Criteria- Major Depressive Episode

Five or more of nine symptoms present for ≥ 2 weeks. Must include symptom 1 or 2.

1. **Depressed mood**
   OR

2. **Anhedonia (loss of interest)**
   +

3. Weight change (loss or gain)
4. Changes in sleep (too much or too little)
5. Decreased energy
6. Decreased concentration
7. Psychomotor agitation or retardation
8. Guilt
9. Suicidal thoughts

- Must cause impairment in function
- Must not be due to medical illness/substance use.

American Psychiatric Association, 2013
DSM-5: Other Variants

- Persistent Depressive Disorder (Dysthymia)
- Premenstrual Dysphoric Disorder
- Recurrent brief depression
- Substance/Medication Induced Depressive Disorder
- Depressive Disorder due to Another Medical Condition
- Unspecified Depressive Disorder

American Psychiatric Association, 2013
Diagnostic Challenges

- Time
- Adherence
- Stigma
- Under-diagnosis / mis-diagnosis
- Treatment resistance
Suspect Depression in Primary Care Settings

- Treatment resistant medical condition
- Persistent “somatic” complaints:
  - Pain
  - Headache
  - Fatigue
  - Insomnia
  - GI symptoms
  - Malaise
- Frequent calls and visits for non-targeted symptoms
- High service utilization
- Frequent medication-related (side) effects
Depression Clues

- Suspect in hospitalized patients:
  - Post CABG, MI, stroke
  - Delayed recovery
  - Treatment non-adherence/ refusal

- Additional indicators:
  - Apathy, withdrawal
  - Irritability, isolation
  - Agitation
  - Delayed rehabilitation
  - Sleep disturbances
Screening Tools

- **Brief tools**
  - Single question regarding “depressed mood”
    - Sensitivity 72%, Specificity 83%
  - Two-item screen- low mood and anhedonia
    - Sensitivity 91%, Specificity 86% [1]

- **PHQ (Patient Health Questionnaire)**
  - Self-report tool (2 or 9 items) derived from PRIME-MD
  - Assessing symptoms and functional impairment
  - Deriving a severity score to help select and monitor treatment: score 5, 10, 15, 20: mild, mod, mod severe, severe

1. Mitchell AJ
2. Lowe B et al.
3. Spitzer et al.
4. Kroenke K et al
Patient Health Questionnaire (PHQ-9); Screening Questions.

<table>
<thead>
<tr>
<th>Over the last two weeks, how often have you been bothered by the following problems?</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Little interest or pleasure in doing things?</strong></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>B. Feeling down, depressed or hopeless?</strong></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>C. Thoughts that you would be better off dead or of hurting yourself?</strong></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

A+B = PHQ-2
score ≥ 3, Sensitivity 82%, Specificity 96% for MDD

Kroenke K et al
Over the last two weeks, how often have you been bothered by the following problems?

<table>
<thead>
<tr>
<th>Problem</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feeling tired or having little energy?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Poor appetite or overeating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>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>Feeling bad about yourself – or that you are a failure or have let yourself or your family down?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Trouble concentrating on things, such as reading the newspaper or watching television?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>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>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Score ≥ 10, sensitivity 88%, specificity 88% for MDD

Kroenke K et al.
Screening Tools

- **GDS (Geriatric Depression Scale)**
  - Yes/No checklist
  - 30 item (long version)
    - sensitivity 82%; specificity 78% (21 studies)
    - cut off score of 10
  - 15 item (short)
    - sensitivity 84%; specificity 74% (12 studies)
    - score >5 suggestive of depression
  - 4 and 5 item (ultra short)
    - sensitivity 92.5%; specificity 77% (limited data, 3 studies)
    - Cut off score of 2

Mitchell AJ et al.
Suicide and Primary Care Contact

- Rates increase with age (20% of suicide deaths).
- Highest among Americans > 65 years.
- Higher correlation with depression than in younger individuals.
- Many had contact with Primary Care Provider preceding suicide.

<table>
<thead>
<tr>
<th>PCP contact</th>
<th>All ages</th>
<th>Age 55+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact within 1 month</td>
<td>45%</td>
<td>58%</td>
</tr>
<tr>
<td>Contact within 1 year</td>
<td>77%</td>
<td>77%</td>
</tr>
</tbody>
</table>

Luoma et al. 2002
Suicide Assessment

- **Risk Factors**
  - Mood disorder
  - Previous suicide attempt(s)
  - Chronic medical illness- HIV, COPD, CHF, chronic pain
  - Functional impairment – feelings of guilt /burden
  - Family discord
  - Social isolation
  - Impending long term care placement

- **Protective Factors**
  - Spiritual/religious beliefs
  - Cultural attitudes against suicide
  - Social connectedness

Van Orden K et al.
Suicide Warning Signs

IS PATH WARM?

<table>
<thead>
<tr>
<th>Ideation -</th>
<th>Talking about death, threatening or looking for ways to hurt self</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance Abuse -</td>
<td>Increased alcohol or drug use</td>
</tr>
<tr>
<td>Purposelessness -</td>
<td>No reason to live, feeling no sense of purpose</td>
</tr>
<tr>
<td>Anxiety -</td>
<td>Anxious, agitated, sleep disturbance</td>
</tr>
<tr>
<td>Trapped -</td>
<td>Feeling trapped, like there’s no way out</td>
</tr>
<tr>
<td>Hopelessness -</td>
<td>Loss of hope that situation will improve</td>
</tr>
<tr>
<td>Withdrawal -</td>
<td>Withdrawal from family, friends, society</td>
</tr>
<tr>
<td>Anger -</td>
<td>Anger, rage, seeking revenge</td>
</tr>
<tr>
<td>Recklessness -</td>
<td>Engaging in risky behavior</td>
</tr>
<tr>
<td>Mood Changes -</td>
<td>Dramatic changes in mood</td>
</tr>
</tbody>
</table>

1. Rudd et al
Cognition and Depression

- Depression associated with cognitive deficits
  - Reduced processing speed, executive dysfunction
- Dementia syndrome of depression vs co-morbid underlying cognitive disorder
- Late-life depression associated with increased risk of dementia
  - Risk factor vs prodrome?

1. Ellison JM et al
2. Barnes DE et al
Cognitive Assessment Tools

- Folstein MMSE - 19 items, 10 minutes
- SLUMS
- MoCA
  - May better detect mild cognitive impairment than MMSE
- Mini-Cog
  - 3 item recall + clock drawing if recall 1-2/3 items after 5 min
  - 3 minutes to administer
  - Sensitivity and specificity >80%

Brodaty H et al
Treatment
Course of Depression

- Normalcy
- Symptoms
- Syndrome
- Treatment phases
  - Response
  - Remission
  - Recovery
  - Relapse
  - Recurrence
  - Incomplete recovery
  - Chronicity

Severity

Kupfer & Frank
<table>
<thead>
<tr>
<th>Class</th>
<th>Agent</th>
<th>Initial dose (mg/day)</th>
<th>Max. daily dose (mg)</th>
<th>Special dosing considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Gero</td>
</tr>
<tr>
<td>SSRI</td>
<td>Citalopram</td>
<td>20</td>
<td>60</td>
<td>10-20 mg</td>
</tr>
<tr>
<td></td>
<td>Escitalopram</td>
<td>10</td>
<td>40</td>
<td>5-10 mg</td>
</tr>
<tr>
<td></td>
<td>Fluoxetine</td>
<td>20</td>
<td>80</td>
<td>10 mg</td>
</tr>
<tr>
<td></td>
<td>Fluoxetine weekly</td>
<td>90</td>
<td>90</td>
<td>90 mg</td>
</tr>
<tr>
<td></td>
<td>Paroxetine</td>
<td>20</td>
<td>50</td>
<td>10 mg</td>
</tr>
<tr>
<td></td>
<td>Paroxetine CR</td>
<td>25</td>
<td>62.5</td>
<td>12.5 mg</td>
</tr>
<tr>
<td></td>
<td>Sertraline CR</td>
<td>50</td>
<td>200</td>
<td>25-50 mg</td>
</tr>
<tr>
<td>SNRIs</td>
<td>Duloxetine</td>
<td>60</td>
<td>60- 120</td>
<td>20-40 mg</td>
</tr>
<tr>
<td></td>
<td>Venlafaxine</td>
<td>37.5</td>
<td>225-375</td>
<td>25-50 mg</td>
</tr>
<tr>
<td></td>
<td>Venlafaxine XR</td>
<td>75</td>
<td>225</td>
<td>37.5-75 mg</td>
</tr>
<tr>
<td></td>
<td>Desvenlafaxine</td>
<td>50</td>
<td>400</td>
<td>CrCl &lt; 30, adjust dose</td>
</tr>
<tr>
<td>DNRIs</td>
<td>Bupropion IR</td>
<td>100 bid</td>
<td>450</td>
<td>37.5 mg bid</td>
</tr>
<tr>
<td></td>
<td>Bupropion SR</td>
<td>150</td>
<td>400</td>
<td>100 mg</td>
</tr>
<tr>
<td></td>
<td>Bupropion XL</td>
<td>150</td>
<td>450</td>
<td>150 mg</td>
</tr>
<tr>
<td>SARIs</td>
<td>Trazodone</td>
<td>50 tid</td>
<td>600</td>
<td>25-50 mg</td>
</tr>
<tr>
<td>NaSSa</td>
<td>Mirtazapine</td>
<td>15</td>
<td>45</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>TCAs</td>
<td>Nortriptyline</td>
<td>25 (divided)</td>
<td>150</td>
<td>10-25 mg</td>
</tr>
<tr>
<td></td>
<td>Desipramine</td>
<td>75 (divided)</td>
<td>300</td>
<td>10-25 mg</td>
</tr>
<tr>
<td>Category</td>
<td>Drug</td>
<td>Anti M₁</td>
<td>Sedation</td>
<td>A₁ blockade</td>
</tr>
<tr>
<td>----------</td>
<td>--------------</td>
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<td>-------------</td>
</tr>
<tr>
<td>SSRIs</td>
<td>Citalopram</td>
<td>o</td>
<td>o/+</td>
<td>o</td>
</tr>
<tr>
<td></td>
<td>Escitalopram</td>
<td>o</td>
<td>o/+</td>
<td>o</td>
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<tr>
<td></td>
<td>Fluoxetine</td>
<td>o</td>
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<td>o/+</td>
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<td></td>
<td>Venlefaxine</td>
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<td></td>
<td>Desvenlefaxine</td>
<td>o</td>
<td>o</td>
<td>o</td>
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<tr>
<td>NDRI</td>
<td>Bupropion</td>
<td>o</td>
<td>o</td>
<td>o</td>
</tr>
<tr>
<td>NaSSa</td>
<td>Mirtazapine</td>
<td>o</td>
<td>+++</td>
<td>o/+</td>
</tr>
</tbody>
</table>
New Agents

- **2011 - Vilazodone (Viibryd)**
  - SSRI + 5-HT1A partial agonist
  - Dosing: 10 mg x 7 days, 20 mg x 7 days, then 40 mg qday

- **2013 - Levomilnacipran (Fetzima)**
  - Enantiomer of milnacipran (Savella) which is approved for fibromyalgia
  - SNRI
  - Dosing: 20 mg x 2 days then 40 mg qday. Range 40-120 mg/day
New Agents

- 2013- Vortioxetine (Brintellix- now Trintellix)
  - SSRI+ $5HT_{1A}$ agonist, $5HT_{1B}$ partial agonist, antagonist at $5HT_3$, $5HT_{1D}$, $5HT_7$
  - Dosing: starting dose 10 mg qday, increase to 20 mg as tolerated
  - Specifically studied in elderly (5mg dose)
Level 1: Initial treatment: CITALOPRAM

Level 2: Switch to: bupropion SR, Cog Tx, sertraline, venlefaxine ER
Or augment with: bupropion SR, buspirone, Cog tx

Level 2a: (For those on Cog Tx in Level 2)
Switch to: bupropion SR or venlefaxine ER

Level 3: Switch to: mirtazapine or nortriptyline
Or augment with: lithium or triiodothyronine
(only with bupropion SR, sertraline, or venlefaxine ER group)

Level 4: Switch to: tranylcypromine or mirtazapine combined with venlefaxine ER

Rush et al, AJP 2000
STAR*D TRD Data

- STAR*D:
  - Stage 1: 48.6% response, 36.8% remission rates
  - Stage 2: 27.3% response, 27.0% remission rates (switch data)
  - Stage 2: 32% response; 39% remission rates (combination with bupropion)
  - Stage 3: 16.8% response, 13.7% remission
  - Stage 4: 16.3% response, 13.0% remission

Rush AJ et al
PHARMACOLOGIC ALGORITHM
Initiate agent based on cost, tolerability (sertraline or citalopram)

If response is inadequate, switch or augment SSRI, OR switch class based on symptom profile (or side effect)

<table>
<thead>
<tr>
<th>Apathy, retardation</th>
<th>Insomnia, anxiety, anorexia</th>
<th>Pain</th>
<th>Atypical, melancholic, anxious</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion or Fluoxetine</td>
<td>Mirtazapine or Paroxetine</td>
<td>Duloxetine</td>
<td>venlafaxine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>If inadequate response…</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Atypical</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MAOI</td>
</tr>
</tbody>
</table>

Kastenschmidt EK, Kennedy GJ
## Clinician Response Defined by Initial PHQ-9 Score

<table>
<thead>
<tr>
<th>PHQ-9 Score</th>
<th>Diagnosis/ Severity</th>
<th>Clinician Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>5-9</td>
<td>Minimal symptoms</td>
<td>Support, educate to call if worse; return in 1 month</td>
</tr>
<tr>
<td>10-14</td>
<td>Minor depression</td>
<td>Support, watchful waiting; re-eval in 4-8 weeks</td>
</tr>
<tr>
<td></td>
<td>Dysthymia</td>
<td>ADT/ psychotherapy</td>
</tr>
<tr>
<td></td>
<td>MDD (mild)</td>
<td>ADT/psychotherapy; monthly visits</td>
</tr>
<tr>
<td>15-19</td>
<td>MDD (moderate)</td>
<td>ADT/ psychotherapy; visits or phone contact q 2-4 weeks</td>
</tr>
<tr>
<td>≥20</td>
<td>MDD (severe)</td>
<td>Immediate initiation of ADT and, if severe impairment or poor response to therapy, expedited referral to mental health for psychotherapy and/or collaborative management</td>
</tr>
</tbody>
</table>
Clinic Response Defined by Subsequent Score on the PHQ-9 after 4-6 Weeks of Antidepressant Treatment at Recommended Dose.

<table>
<thead>
<tr>
<th>PHQ-9 Score or Change</th>
<th>Outcome</th>
<th>Clinician Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drop of 1 point OR No decrease OR increase</td>
<td>Non-response</td>
<td>Increase dose: Augmentation; Switch; Informal or formal psychiatric consultation; Add psychotherapy IN PATIENT ADMISSION</td>
</tr>
<tr>
<td>2-4 points decrease</td>
<td>Partial response</td>
<td>Increase ADT dose/ augmentation</td>
</tr>
<tr>
<td>5 or more point decrease</td>
<td>Response</td>
<td>Maintain medication Follow up in 4 weeks</td>
</tr>
<tr>
<td>PHQ-9 ≤ 4-5</td>
<td>Remission</td>
<td>Maintain medication Follow up in 4 weeks</td>
</tr>
</tbody>
</table>

Adapted from Oxman TE. Re-Engineering Systems for Primary Care Treatment of Depression; The Respect Depression Care Process supervising psychiatrist manual. Trustees of Dartmouth College, 2003
Psychotherapy modalities

- Interpersonal psychotherapy
- Cognitive behavioral therapy
- Problem-solving therapy
- Behavioral therapy
- Brief focused psychodynamic therapy
- Family therapy
- Psycho-education
Psychotherapy as Monotherapy

- Consider for:
  - (Out)-patients with mild to moderate depression.
  - Patients who cannot/ will not take medication.
  - Patients with predominant psychosocial stressors.
  - Patients with dysthymia or personality disorders.
  - Patients without psychotic features or suicidal ideation.
Mental Health Referral

- Unclear diagnosis
- Evidence of psychotic features
- History of bipolar symptoms (mania, hypomania)
- Concomitant substance use
- Signs of comorbid psychiatric conditions
- Need for psychosocial interventions
- Treatment resistance
- Patient preference
HAVE ANY QUESTIONS

DO YOU?
References


References


20. www. cdc.gov


References


