Advances in Diagnosis, Neurobiology, and Treatment of Mood Disorders

June 13 - 14, 2016

Field House Coral Gables
University of Miami
Coral Gables, FL

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CURSO INTERAMERICANO DE ACTUALIZACIÓN EN PSIQUIATRÍA

CME Outfitters

Management of Depression in the Geriatric Patient

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CME Outfitters

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Disclosures

- Dr. Sabbag has no disclosures to report.

Learning Objectives

- Identify clinical signs and symptoms that will lead to the recognition and diagnosis of mood disorders in the elderly
- Integrate evidence-based, best-practice options for the assessment and treatment of depression in the elderly

Audience Response

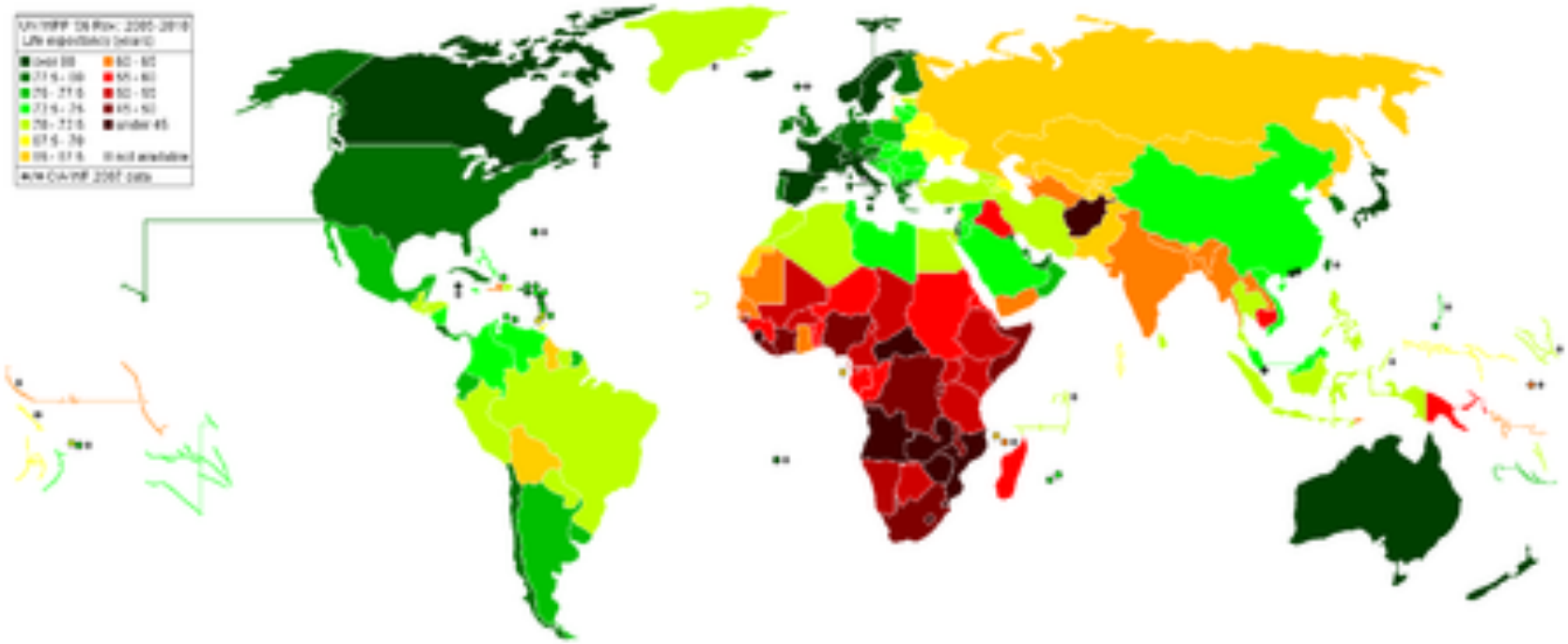
You have been treating a 75 year old female over the past 3 months for depression with 100 mg of sertraline daily. It was the patient's first episode. Currently the patient reports a resolution of all her symptoms and she feels "back to herself." She is complaining of some mild morning nausea that she attributes to the medication, and she would like to discontinue the sertraline.

What do you recommend?

Audience Response

A. Patient is now free of depressive symptoms and through the acute phase of the depressive episode and may now stop the medication.
B. Patient must continue treatment for 6 months to prevent relapse of the depressive episode
C. Patient must continue treatment for 6 months to prevent relapse but she may cut the dose in half to minimize side effects
D. Patient must continue treatment for a minimum of 2 years to prevent a subsequent depressive episode

Life Expectancy Demographics Today



www.worldlifeexpectancy.com

Demographic Transition

- By 2045, average life expectancy in the US will be 80 years
- By 2030, almost 20% of Americans will be 65+
- By 2030, proportion of older Hispanics will nearly double from 5.6% to 10.9%

US Census Bureau, 2010. www.**census**.gov/**2010census**/

Geriatric Specialty Shortages

- Without significant national changes, older Americans will lack access to affordable, quality healthcare[1]
- 1 geriatric psychiatrist for every 10,000 Americans older than 75 (estimated need is 5000, only 1746 board- certified Geriatric Psychiatrists – in 2011)
- Only 65% of psychiatrists currently accept Medicare

1. Institute of Medicine Report. Retooling for an Aging America: Building the Health Care Workforce. 2008.

Prevalence of Geriatric Mental Illness

- More than 2 million of the 34 million Americans 65+ suffer from some form of depression[1]
- Older adults more likely to seek MH care in primary care settings
- Depression and cognitive disorders most commonly seen

MH = mental health

1. National Institutes of Mental Health. NIMH Website: https://www.nimh.nih.gov/health/topics/depression/index.shtml. Updated May 2016.

Scope of Geriatric Depression

- In the community, major depression is rare (1.8%), minor depression is more common (10%) but rates of select depressive symptoms are higher (14%)[1]
- 7-36% in primary care settings[2]
- 25% of hospitalized patients (10-21% major depression)[3]
- 20-47% of long-term care residents[4]
- Primary health care providers for the elderly have difficulty recognizing severe depression, only recognize 40-50% of cases[5]

1. Beekman AT, et al. *Br J Psychiatry*. 1999;174:307-311.; 2. Koenig HG, et al. *Int J Geriatr Psychiatry.* 1998;13(4): 213-224.; 3. Koenig HG, et al. *Am J Psychiatry*. 1997;154(10):1376-1383.; 4. Berkman LF, et al. *Am J Epidemiol.* 1986;124(3):372-388. PMID: 3740038; 5. Mitchell Aj, et al. *J Affect Disord.* 2010;125(1-3):10-17.

Why the Under-Recognition of Geriatric Depression

- Symptoms attributed to chronic medical conditions due to somatic presentations[1]
- Often do not complain of depressed mood or crying spells, only anhedonia[1] or irritability
- Social isolation and withdrawal
- Symptoms not prominent every day
- Depression as “normal” part of aging[2]
- Psychosocial and physical losses divert attention from consideration of depression diagnosis
- Stigma[2]

1. Evans DL, et al. *Biol Psychiatry*. 2005;58(3):175-189.
2. Park M, et al. *Psychiatr Clin North Am*. 2011;34(2):469-487.

Minority Disparities

- Ethnic and racial minorities
  - Less likely than Caucasian elderly to seek specialty MH care
  - More likely to express psychological distress through somatic symptoms
- Barriers: language, stigma, lack of transportation, costs, waits for appointments, cultural distance with provider, mistrust
- Use of complimentary and/or alternative medicine

Minority Health and Mental Health Disparities Program. NIMH Website: http://www.nimh.nih.gov/about/organization/gmh/minority-health-and-mental-health-disparities-program.shtml. Updated May 2016.

Diagnostic Criteria for Major Depressive Disorder

DSM-5 criteria

- 5 or more of the following symptoms present for 2 or more weeks:

- **Must have:**
  1. Depressed mood or Anhedonia
  2. Change in weight or appetite
  3. Insomnia or hypersomnia

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. 5th ed. 2013.

Diagnostic Criteria for Major Depressive Disorder

- **Must have (cont'd)**
  4. Psychomotor agitation or retardation
  5. Low energy
  6. Feelings of worthlessness or guilt
  7. Poor concentration
  8. Recurrent suicidal thoughts or attempt

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. 5th ed. 2013.

Bereavement and Major Depressive Disorder

- Grief/Bereavement
  - Is not considered an illness
  - Can trigger a major depressive episode
- *DSM-5* eliminated the bereavement exclusion[1]
  - Symptoms are not better accounted for Bereavement;
    - after the loss of a loved one, symptoms persist for ≥ 2 months or are characterized by marked functional impairment, psychomotor retardation, suicidal ideation, psychotic features or morbid preoccupation with worthlessness.

1. Kendler KS, et al. *Am J Psychiatry*. 2008;165(11):1449-1455.

Bereavement and Major Depressive Disorder

- Most bereaved elderly will not meet full criteria for MDD
- Normal grief reactions exhibit mixed emotions of sadness and enjoyment
- Clinically depressed patients typically have constant feelings of gloom, hopelessness and despair
- Depressed patients also are isolated and do not seek out/respond to the condolences of others

Kendler KS, et al. *Am J Psychiatry*. 2008;165(11):1449-1455.

Consequences of Untreated Depression

- Worldwide, depression is second leading cause of disability adjusted life years (DALY)1
- Poorer adherence
- Increased health services utilization
- Greater mortality due to co-occurring cardiovascular disease2
- Increased risk for suicide

1. Moussavi S, et al. *Lancet.* 2007;370(9590):851-858
2. Alexopoulos G, et al. *Am J Psychiatry*. 1996;153(7):877-885.

DALY is a Measure of Overall Disease Burden, Expressed as the Number of Years Lost Due to Ill-health, Disability or Early Death. #1 is Cardiovascular

Moussavi S, et al. *Lancet.* 2007;370(9590):851-858.

Depression and Dementia

1) **As a symptom of dementia:**

Prevalence of depression (major and minor): 30-50%[1]

Cache County study: 20% of patients with Alzheimer's disease (AD) suffered from depressive symptoms in the past month[2]

2) **As a risk factor of dementia:**

History of depression conferred increased risk to develop Alzheimer's disease (AD)[3] and vascular dementia later in life[4]

3) **As a prodromal event of dementia:**

Depression at baseline predicted subsequent cognitive decline[5,6]

Patients with mild cognitive impairment (MCI) are more likely to suffer from depression than those cognitively normal[7]

4) **As a reaction to cognitive impairment**

1.Olin JT, et al, *Am J Geriatr Psychiatry*. 2002;;10(2):129-141; 2. Lyketsos CG, et al, *JAMA.* 2002;288(12):1475-1483.; 3.Ownby RL, et al. *Arch Gen Psychiatry*. 2006;63(5):530-538.; 4. Diniz BS, et al. *Br J Psychiatry*. 2013;202(5):329-335. PMID: 23637108 ; 5. Wilson RS, et al. Neurology. 2008;71(12):874-875.. 6. Rovner, BW et al, Alzheimers Dement. 2009;5(1):12-17.; 7. Crocco EA, et al. *Curr Psychiatry Rep*. 2005;7(1):32-36.

Pseudodementia or "True" Dementia?

- Originally defined by Kiloh (1961) as elderly patients who present with symptoms that mimic dementia, typically due to depression, and are reversible.
- May be an early manifestation of a neurodegenerative disorder:
  - > 40% patients with reversible pseudodementia develop "true" dementia in less than 3 years[1]
  - Over 70% of pseudodementia patients converted to "true" dementia within 5-7 years versus 18% of cognitive normal depressed elderly[2]
  - Depressed elderly patients had persistent cognitive impairment in memory and executive function 3 months after resolution of all depressive symptoms[3]

1. Alexopoulos GS, et al. *Am J Psychiatry*. 1993;150(11):1693.; 2. Saez-Fonseca JA, et al. *J Affect Disord*. 2007;101(1-3):123-129.; 3. Marcos T, et al. *J Affect Disord*. 1994;32(2):133-137.

Audience Response

Part of evaluating depression in the elderly is to rule out suicidal thoughts or intent.

Which of the following is **NOT** a major risk factor for completed suicide?

A. Male gender
B. Medical comorbidity with frequent visits to PCP
C. Poor adherence to medical treatment
D. Widowed or divorced status
E. Poor concentration, anhedonia and insomnia

Suicide

- Suicide Rates[1]
  - Females aged 45-54 (9 per 100,000)
  - Adults aged 75 years and older (16.3 per 100,000)
  - Males aged 75 and older (36 per 100,000)
- 40% of elderly suicide completers saw their primary care physician during the week prior
- Elderly white men are disproportionately most likely to complete suicide

1.Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. Web-based Injury Statistics Query and Reporting System (WISQARS) [online]. (2010). [cited 2012 Oct 19] Available from www.cdc.gov/injury/wisqars/index.html.

Risk Factors for Suicide

- Male
  - Age >45
- Depression predominantly with poor concentration, insomnia, complete anhedonia, irrational thoughts/psychosis
- Severe anxiety

(continued)

Risk Factors for Suicide

- Alcohol or drug use
- Organized Plan
- Previous attempt
- Lack of social support
- Separated, divorced or widowed
- Multiple comorbid medical illnesses with frequent PCP visits

Aziz R, Steffens DC. *Psychiatr Clin North Am*. 2013;36(4):497-516.

SAD PERSONS Scale

- **S**: Male sex
- **A**: Older age
- **D**: Depression
  - **P**: Previous attempt
  - **E**: Ethanol abuse
  - **R**: Rational thinking loss
  - **S**: Social supports lacking
  - **O**: Organized plan
  - **N**: No spouse
  - **S**: Sickness

Risk Score:

0–4	Low
5–6	Medium
7–10	High

Patterson WM, et al. *Psychosomatics*. 1983;24(4):343-345, 348-349.

Comorbid Anxiety

- Often the most prominent presenting symptom along with insomnia
- Decreased response rate to antidepressants
- Longer time to response and remission
- Generalized anxiety and panic symptoms may accompany depression in the elderly
- The somatic focus of anxiety may be mistakenly ascribed to medical diagnoses

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-5. 5th ed. 2013.

Treatment of Geriatric Depression: The Acute Phase

- Goal is remission
- Lasts about 3 months
- Treatment regimen must be carefully monitored
- First line antidepressant treatment is SSRIs for both efficacy and safety
- Start at ½ usual adult dosage

Lebowitz BD, et al. *JAMA* 1997; 278:1186.

Treatment of Geriatric Depression: The Acute Phase

- Special attention when:
  - Suicidal ideation
  - Complex medical comorbidity
  - Severe depression with psychotic features
  - Neglect/lack of social support
  - Alcohol and drug abuse
  - Treatment resistance

Lebowitz BD, et al. *JAMA* 1997; 278:1186.

Pharmacological Treatment of Geriatric Depression

SSRI's and SNRI's have the best safety profile

First-line SSRI's: Escitalopram, citalopram, sertraline, vortioxetine

- QTc prolongation in patients over 60 taking citalopram
- Paroxetine not recommended due to anticholinergic effects
- Fluoxetine not recommended due to long half-life and potent inhibition of multiple CYP450 isoenzymes
- Vortioxetine demonstrated efficacy and tolerability in elderly (64-88 years, n=300) depressed patients at 5mg vs. placebo[1]

SNRI's: Venlafaxine, duloxetine, desvenlafaxine

1. Katona C, et al. *Int Clin Psychopharmacol.* 2012;27(4):215-223.

Pharmacological Treatment of Geriatric Depression

- SSRI Adverse effects: GI distress, insomnia, sexual side effects, somnolence, headache
- Less common, but seen more in geriatric patients: Abnormal GI bleeding, SIADH, hyponatremia
- SNRI's have similar adverse reactions
  - Additionally, may have transient hypertension

SIADH = Syndrome of inappropriate antidiuretic hormone secretion

Katona C, et al. *Int Clin Psychopharmacol*. 2012;27(4):215-223.

Pharmacological Treatment of Geriatric Depression

Most clinical trials comparing SSRI's and SNRI's to placebo, demonstrated high placebo response rates and often no superiority in the drug[1]

- 55-81% will fail to remit especially those with late-life onset
- May be due to:
  - Under-dosing antidepressants: start low and go slow, but do not under-dose
  - Neurodegenerative disease/dementia may lead to depression with different mechanisms of action: acetyl-cholinesterase inhibitors/NMDA antagonist

1. Alexopoulos GS. *J Clin Psychiatry*. 2011;72(1):e04.

Treatment of Anxiety in Geriatric Patients

- SSRIs and SNRIs are the safest
- Sedative hypnotics such as benzodiazepines can be very efficacious in the short term, but must be used with extreme caution in the elderly
- They may contribute to worsening depression, cognitive changes, higher rates of falls/injuries
- Should choose short acting agents with nonactive metabolites (lorazepam, oxazepam, temazepam)

Alexopoulos GS. *J Clin Psychiatry*. 2011;72(1):e04.

Pharmacological Treatment

- Augmentation:
  - Mirtazapine
  - Bupropion XL
  - Lithium* - best evidence, but adverse effects can be substantial
  - Stimulants
  - Lamotrigine*
  - SGAs – aripiprazole, olanzapine-fluoxetine, brexpiprazole
- Treatment resistance:
  - Neurostimulation ECT/VNS/rTMS

Alexopoulos GS. *J Clin Psychiatry*. 2011;72(1):e04.

*FDA approved for bipolar disorder

Augmentation with Aripiprazole

- With venlafaxine vs. venlafaxine alone[1,2]
- 5-10mg dosing
- Effective in improving depressive symptoms in older patients, 50-67 years, with MDD who have had an inadequate response to standard antidepressant medication.[2]
- Weight gain, increase in dreaming, tremor, EPS with akathisia and parkinsonism
- Risk of death in cognitively impaired[3]

1. Lenze, et al. *Dial Clin Neuroscience*, 2008; 2008;10(4):419-430.
2. Steffens D, et al. *Int J Geriatr Psychiatry*. 2011 Jun;26(6):564-572.
3. Schneider LS, et al. *JAMA.* 2005;294(15):1934-1943.

Treatment of Geriatric Depression: The Maintenance Phase

- Goal is to maintain treatment to prevent recurrence of another depressive episode
- The more episodes of depression, the higher the likelihood of recurrence
- In adults, the chance of recurrence is > 90% after 3 or more episodes

Reynolds CF, et al. *N Engl J Med*. 2006;354(11):1130-1138.

Treatment of Geriatric Depression: The Maintenance Phase

- Depression tends to reoccur in the elderly
  - Rates of recurrence of 50-90% over a period of 2-3 years
- Studies indicate that preventing the recurrence of depression in geriatric patients require continued treatment with antidepressants for at least 2 years[1]
- Continuous maintenance treatment for at least 2 years is recommended in patients +65y/o, despite the number of previous episodes

1. Reynolds CF, et al. *N Engl J Med*. 2006;354(11):1130-1138.

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What do you recommend?

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Thank you!