Late Life Depression

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Geriatric Statistics: U.S. Bureau of the Census:

- Life expectancy: 1950 = 68 years; 1991 = 79 years for women/72 years for men*
- In the year 2000 = 12.4% of the U.S. population - 35 million Americans - were 65 years or older*
- By 2030 = percentage increases to 20% -1 in 5 people will be older than 65; 2025 in Florida – 1 in 4 people
- People age 85 and older: are the fastest growing segment of our population – from 4 M today to 20 M by 2050;* constitute 10% of those 65 years and older; there are 39 men for every 100 women 85 years old or older


Geriatric Statistics: Mental Health

- 20% of the US population over the age of 65 has a mental illness**
- As the population ages, the number of people with mental illness will double to 15 million by 2030
- Number of people over age 65 years with mental illness will equal the number of people with mental illness in ALL other age groups*
- Older adults are less likely to seek mental health: only 4% of non-institutionalized US population seek mental health treatment***
- Older adults are more likely to be identified, diagnosed and receive treatment from their primary care physician****

*Bartels SJ (in press).
# Psychiatric Disorders in the elderly

Mood D/O (Depressive D/O and Bipolar D/O)*  
Adjustment D/O*  
Anxiety D/O*  
Somatoform/Factitious/Dissociative D/O  
Impulse Control D/O  
Paraphilias/Sexual and Gender Identity D/O  
Eating D/O  
Sleep D/O*  
Delirium, Dementia, Amnestic and other Cognitive D/O*  
Alcohol and Substance Related D/O*  
Schizophrenia and other Psychotic D/O  
(such as Delusional D/O)

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# Late Life Stressors  
that place older adults at risk of mental health disorders

- Chronic physical health condition(s)  
- Death of a loved one  
- Caregiving  
- Social isolation/lack or loss of social support  
- Significant loss of independence  
- History of mental health problems
Diagnostic Considerations in the Elderly Population

- Perception and stigma of psychiatric illness\(^1\)
- Variable clinical presentation\(^2\)
- Concomitant drug therapy\(^2\)
- Comorbid medical conditions\(^2\)
- Co-existing neurologic/psychiatric disorders\(^2\)

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Adverse Life Events & Aging

Multiple Losses

- Jobs
- Money
- Homes
- Friends
- Abilities
- Health
- Hopes and dreams
- Bereavement

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Mood, Cognition and Health in Late Life

Complex Interactions

Age  Mood

Cognition  Physical Health

Categories of Medical Problems Among 205 Elderly Inpatients With Major Depression (Mean Age 71)

- Circulatory system 69
- Digestive system 61
- Endocrine, nutritional, metabolic 45
- Musculoskeletal & connective tissue 45
- Ill-defined conditions 25
- Genitourinary 24
- Mean number of medical problems = 5

Zubenko et al., 1994
Prevalence of Depression in Medical Illness

- Stroke 22–50%
- Cancer 18–39%
- Myocardial infarct 15–19%
- Rheumatoid arthritis 13%
- Parkinson’s disease 10–37%
- Diabetes 5–11%

*Cohen-Cole, 1993*

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Depression and Mortality 10 Years After a Stroke (N=91)

*Morris PLP, et al. 1993*
Depression and Cognitive Disorder

- Depression can cause cognitive impairment
  - usually mild and of recent onset
- 20–40% with Alzheimer’s disease exhibit depressive symptoms or syndromes
  - often an early symptom
  - depression impairs quality of life, leads to excess functional disability, and increases likelihood of placement in long-term care facility
  - responds to treatment
- Similar rates of depression have been reported in patients with subcortical dementias (e.g., Parkinson’s disease)

Frasure-Smith et al., 1993
Prevalence (%) of AD-Related Disorders During 3-Year Follow-Up

Adapted from: Devanand et al 1997

Depression vs. Alzheimer’s Disease

**Depression with Alzheimer’s Disease**
- Cognitive deficits minimized
- Memory, executive dysfunction
- “Indirect” depressive symptoms (e.g., agitation, insomnia)
- Language, motor skills
- Aphasia, apraxia

**Cognitive Disturbances**
- Cognitive deficits exaggerated
- Impaired motivation
- Mood complaints
- Intact
Emphasis on Somatic and Cognitive Symptoms

• Less
  – dysphoria
  – guilt
  – suicidal ideation

• More
  – fatigue
  – sleep and appetite changes
  – vague GI complaints, somatic worries
  – memory and concentration problems
  – anxiety and/or irritability
  – apathy and/or withdrawal

Diagnosing Depression in the Old-Old (>80)

• DSM-IV criteria may not be useful
  – deny most mood and somatic symptoms

• PMS (persistent miserable syndrome)
  – loss of interest in usual activities
  – social withdrawal
  – irritability
  – somatization

Salzman, 1995
Course and Outcome of Late Life Depression
One-Year Follow-Up

- Died 14%
- Well, but relapsed 22%
- Never well (chronic) 29%
- Got well & remained well 35%

Insights from Imaging

- Evidence from different imaging techniques (MR and MT)
- Lower MTR were found in elderly patients with late life major depression, in the left hemisphere, when compared to controls.
- Lower MTR in white matter is suggestive of lower myelin content and axonal density.
- Suggests vulnerability to MDD in late life
Consequences of Untreated Depression in the Elderly

- Pervasive despair and suffering
- Loss of personal happiness
- Strained relationships with those who share daily lives
- Increased expenses associated with treatment of physical illness
- Increased mortality

Major Depression Can Be Fatal

- Increases mortality rates of comorbid general medical conditions
- Leading cause of suicide

Suicide

- 15% of severely depressed persons commit suicide
- 8th leading cause of death (>16,000 annually in U.S.)
- Elderly white males at greater risk
- >60% causally related to depression
- 80% consult physician in month before death

Epidemiology of Late Life Depression

Characteristics of Nursing Home Residents

- Majority are:¹
  - 75 years old and over (median age, 83 yrs), women, white
  - With multiple chronic conditions
  - Functionally impaired
- Polypharmacy is common¹
  - 75% of residents receive ≥3 medications
  - 45% of residents receive ≥5 medications
- More than half of the residents receive a psychoactive medication²
- Many medical problems are often underdiagnosed and misdiagnosed¹


Prevalence of Depression in the Elderly by Health/Independence Status

<table>
<thead>
<tr>
<th></th>
<th>Community Residents¹</th>
<th>Primary Care Outpatients²</th>
<th>Nursing Home Residents³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Depression (%)</td>
<td>3%</td>
<td>10%</td>
<td>16–50%</td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td>15%</td>
<td>24%</td>
<td>5–43%</td>
</tr>
</tbody>
</table>


*Men only.
Risk Factors for Depression in Nursing Home Residents

- New admission or change in environment
- Personal/family history of mood disorder
- History of alcohol/substance abuse
- History of psychiatric hospitalization/suicide attempt
- Pervasive loss (family, friend)
- Loss of autonomy, function, or body part
- Concurrent medical illness (dementia, Parkinson’s, stroke)
- Concomitant medications can predispose the elderly to depression

Underdiagnosis and Undertreatment of Depression in the Elderly Nursing Home Setting

• Underdiagnosis
  - Only 14% of the depression diagnoses made, prior to nursing home admission, by psychiatrists were also made by nursing home psychiatrists at admission¹

• Undertreatment
  - Only ~25% depressed patients receive treatment¹
  - When treated
    • Use of nonspecific agents as monotherapy, eg, antipsychotics, anxiolytics²
    • Subtherapeutic antidepressant dosages²
    • Inadequate treatment duration³
Impact of Depression on Nursing Home Staff Time

<table>
<thead>
<tr>
<th>Mean Time (min/day)</th>
<th>Unadjusted</th>
<th>Adjusted for RUG-III†</th>
<th>Adjusted for RUG-III ADL Index‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without Depression</td>
<td>110</td>
<td>120</td>
<td>130</td>
</tr>
<tr>
<td>With Depression</td>
<td>115</td>
<td>130</td>
<td>140</td>
</tr>
</tbody>
</table>

* $P < 0.0001$.
† Resource Utilization Group II.
‡ Resource Utilization Group III Activities of Daily Living Index.

Pharmacologic Complications in the Elderly

• Pharmacokinetics
• Pharmacodynamics
• End-organ physiological change
• Medical illnesses
• Cognitive decline
• Polypharmacy
• Compliance
• Life adversity
Pharmacokinetics (Effects of Drug on Patient) and Aging

<table>
<thead>
<tr>
<th>Component</th>
<th>Age Effect</th>
<th>Consequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absorption</td>
<td>↓ gastric pH, ↓ motility</td>
<td>↓ absorption (probably minimal effect)</td>
</tr>
<tr>
<td>Distribution</td>
<td>↑ fat/lean body ratio</td>
<td>↑ volume of distribution ↑ half-life</td>
</tr>
<tr>
<td>Metabolism</td>
<td>↓ hepatic blood flow, ↓ activity of some catabolic enzymes</td>
<td>↓ breakdown ↑ plasma levels &amp; half-life</td>
</tr>
<tr>
<td>Excretion</td>
<td>↓ GFR</td>
<td>↓ clearance ↑ accumulation</td>
</tr>
</tbody>
</table>

Pharmacodynamics (Effects of Drug on Patient) and Aging

Increased Sensitivity To:

- Sedation
- Cardiovascular effects
- Anticholinergic effects
Polypharmacy in the Elderly
Facts and Figures

• Average 13 prescriptions/year\textsuperscript{1}
• 6–8 different medications daily\textsuperscript{2}
• Greater use nonprescription drugs\textsuperscript{3}
• 33% nursing home residents receive >8 different drugs daily\textsuperscript{4}

\textsuperscript{1}Lamy, 1976
\textsuperscript{2}Salzman, 1995
\textsuperscript{3}Helling et al., 1985
\textsuperscript{4}Lamy et al., 1992

Noncompliance in the Elderly

• 40–70% overall noncompliance\textsuperscript{1}
• 10% take drugs prescribed for others\textsuperscript{2}
• 20% take drugs not currently prescribed\textsuperscript{2}
• 40% stop drugs too soon\textsuperscript{3}
Effect of Severe Life Event on Time to Response in Elderly Depressed Patients

Adopted from Karp et al., 1993

Principles of Pharmacologic Treatment

- Use medications with minimal anticholinergic, cardiovascular, and orthostatic effects
- Begin with low doses
- Monitor closely for compliance and side effects
- Increase dose slowly and carefully
Antidepressant Choices

- MAOIs (phenelzine, tranylcypromine, isocarboxizide)
- TCAs
  - Tertiary amines (amitriptyline, clomipramine, doxepine, imipramine, trimipramine)
  - Secondary amine (amoxepine, desipramine, maprotyline, nortriptyline, protriptyline)
- SSRIs (citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)
- Others
  - NDRI (bupropion - SR)
  - SNRI (venlafaxine - XR)
  - HT₂ antagonist/SNRI (nefazodone, trazodone)
  - α₂/HT₂/HT₃ antagonist (mirtazapine)
  - NRI (reboxetine)

### Selective Serotonin Reuptake Inhibitors (SSRIs)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Target Dose (mg/day)</th>
<th>Range (mg/day)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram (Celexa®)</td>
<td>20</td>
<td>10–50</td>
</tr>
<tr>
<td>Fluoxetine (Prozac®)*</td>
<td>20</td>
<td>10–80</td>
</tr>
<tr>
<td>Fluvoxamine (Luvox®)</td>
<td>200</td>
<td>50–300</td>
</tr>
<tr>
<td>Paroxetine (Paxil®)</td>
<td>20</td>
<td>10–50</td>
</tr>
<tr>
<td>Sertraline (Zoloft®)</td>
<td>100</td>
<td>25–200</td>
</tr>
</tbody>
</table>

*First antidepressant approved for elderly
**May be even lower in frail, old, or medically compromised
Selective Serotonin Reuptake Inhibitors (SSRIs)

- **The good**
  - effective
  - safe
  - tolerable
  - simple
  - anxiety disorders

- **The bad**
  - activation
  - GI
  - headaches
  - sexual
  - enzyme inhibition
  - withdrawal
    - CYP P450, 1A2, 2C9,2C19, 2D6, 3A4

- **The ugly**
  - serotonin syndrome

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**Nortriptyline vs Paroxetine in Patients with MDE and Ischemic Heart Disease**

![Graph showing remission rates and cardiovascular dropout rates for Nortriptyline and Paroxetine.](Nelson et al. AJP 1999)
## SSRIs
Are They All Alike?

- **Citalopram**  most selective
- **Fluoxetine**  longest acting
- **Fluvoxamine**  shortest acting
- **Paroxetine**  most noradrenergic  most sedating(?)
- **Sertraline**  most dopaminergic

## Serotonin Syndrome

- Myoclonus, hyperreflexia, tremor
- Confusion, agitation, hypomania
- Fever, sweating, shivering
- Diarrhea
Treatment of Serotonin Syndrome

- Preventive
- Stop offending drugs
- Supportive care
- Propranolol, methysergide, cyproheptadine, clonazepam

SSRIs
There Is A Difference

<table>
<thead>
<tr>
<th></th>
<th>5HT Uptake</th>
<th>NA Uptake</th>
<th>DA Uptake</th>
<th>5HT Selectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>++++++++</td>
<td>0</td>
<td>0</td>
<td>++++++++</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>+++++</td>
<td>+</td>
<td>0</td>
<td>+++</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>++++++++</td>
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<td>Sertraline</td>
<td>++++++++</td>
<td>+++</td>
<td>+++</td>
<td>++++++++</td>
</tr>
</tbody>
</table>

_Hyttel, 1994_
SSRI Withdrawal

• Dizziness
• Lethargy
• Paresthesia
• Nausea
• Vivid dreams
• Irritability
• Lowered mood

Bupropion SR (NDRI)

• The good
  – effective
  – tolerable
  – no ↓ REM
  – no sexual side effects
  – bipolar?
  – ADD?
  – smoking?

• The bad
  – activation
  – GI
  – headache

• The ugly
  – seizures
    • IR prep
    • much lower with SR
### Venlafaxine XR (SNRI)

- **The good**
  - broad spectrum of efficacy (including melancholia, GAD)
  - dose-related tolerability and safety
  - refractory – dual action
- **The bad**
  - nausea – dizziness
  - activation – sedation
  - sweating – tremor
  - sexual – blood pressure
  - withdrawal
- **The ugly**
  - serotonin syndrome

### Mirtazapine ($\alpha_2$/HT$_2$/HT$_3$ Antagonist)

- **The good**
  - antidepressant
  - anti-anxiety
  - once-daily dosing
- **The bad**
  - somnolence (decreases at 45–60 mg doses)
  - increased appetite and weight gain
  - dizziness
  - dry mouth
  - constipation
- **The ugly**
  - agranulocytosis or neutropenia (3/2, 796 pts)
Psychostimulants

• The good
  – mobilize medically ill
  – neutralize hypotensive effects
  – augment treatment in partial responders

• The bad
  – probably not antidepressant
  – activation
  – increased heart rate and BP
  – ? tolerance

• The ugly
  – dependence
  – withdrawal depression
  – psychosis

Electroconvulsive Therapy (ECT)

• The good
  – most effective for melancholia
  – psychotic or refractory depression
  – Can be life saving

• The bad
  – confusion and memory problems
  – recurrence
  – reactions to anesthetics
  – occasional mild transient cardiac arrhythmia
Phases of Treatment

<table>
<thead>
<tr>
<th>Phase</th>
<th>Goal</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>Remission</td>
<td>Weeks</td>
</tr>
<tr>
<td>Continuance</td>
<td>Recovery</td>
<td>Months</td>
</tr>
<tr>
<td></td>
<td>Prevent relapse</td>
<td></td>
</tr>
<tr>
<td>Maintenance</td>
<td>Prevent recurrence</td>
<td>Years</td>
</tr>
</tbody>
</table>

Pearls

- May take longer to respond
  - Especially late onset, associated with vascular, neurologic, or general medical problems, adverse life events

- May require long-term preventive/maintenance treatment
  - Especially if recurrent, late onset, severe, associated with vascular or neurologic disorders, or residual symptoms
Summary

• Late life depression is a serious illness, often misdiagnosed and undertreated, and responds to standard modalities

• Use a comprehensive approach that takes advantage of effective, safe, and tolerable treatments