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

*Administration on Aging. Statistics on the Aging Population, Rockville, MD; US Department of Health and Human Services; 2003; U.S. Bureau of the Census.

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).
**Jeste, DV, Consensus statement on the upcoming crisis in geriatric mental health, Arch. Gen. Psychiatry 1999: 56(9): 848-53.
** * Olfson M, Outpatient mental health care in non-hospital settings. Am. J Psychiatry 1996; 153(10): 1353-6.
* ** * Kaplan MS, et al, Managing depressed and suicidal geriatric patients. Gerontologist 1999; 39(4): 417-25.

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)

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]

1. NIH Consensus Development Panel on Depression in Late Life. *JAMA.* 1992;268:1018–1024.
2. Fernandez F et al. *J Clin Psychiatry*. 1995;56(suppl 2):20–29.

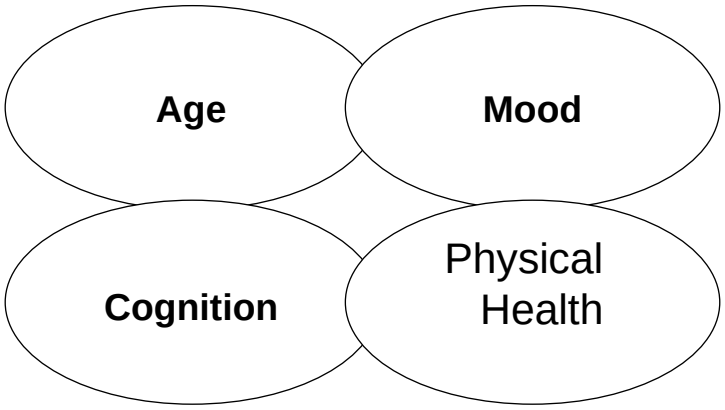
Adverse Life Events & Aging

Multiple Losses

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

Mood, Cognition and Health in Late Life

Complex Interactions



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

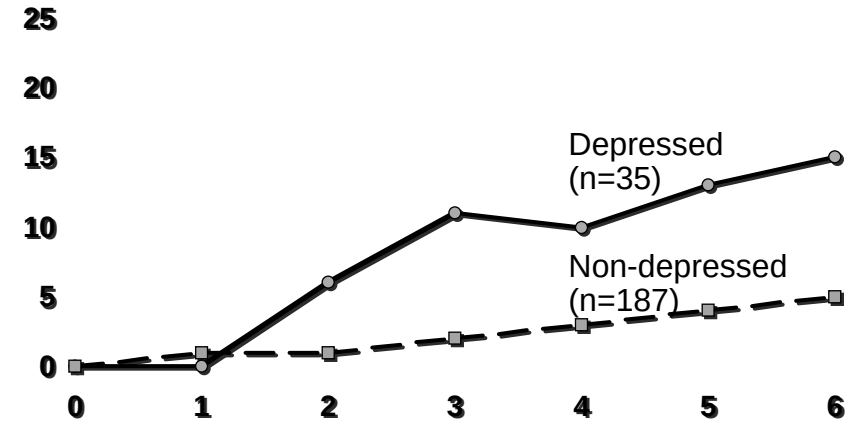
• Stroke	22–50%
• Cancer	18–39%
• Myocardial infarct	15–19%
• Rheumatoid arthritis	13%
• Parkinson's disease	10–37%
• Diabetes	5–11%

Cohen-Cole, 1993

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

Morris PLP, et al. 1993

Cumulative Mortality for Depressed and Nondepressed Patients 6 Months After An MI

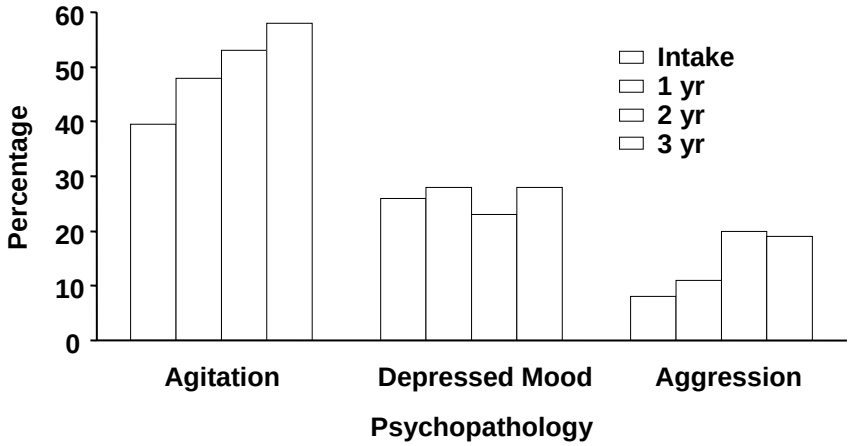


Frasure-Smith et al., 1993

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)

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 Disturbances
Cognitive deficits minimized	Cognitive deficits exaggerated
Memory, executive dysfunction	Impaired motivation
"Indirect" depressive symptoms (e.g., agitation insomnia)	Mood complaints
Language, motor skills	
Aphasia, apraxia	intact

Emphasis on Somatic and Cognitive Symptoms

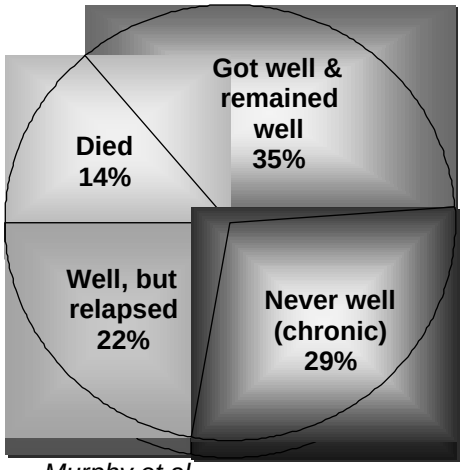
- Less
  - dysphoria
  - guilt
  - suicidal ideation
- More
  - fatigue
  - sleep and appetite changes
  - vague GI complaints, somatic worries
  - memory and concentration problems
  - anxiety and/or irritability
  - apathy and/or withdrawal

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



Poor Outcome
Lack of appropriate treatment
Severe symptoms
Cognitive impairment
Physical illness

Murphy et al., 1991

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

NIH Consensus Development Panel on Depression in Late Life. *JAMA.* 1992;268:1018–1024.

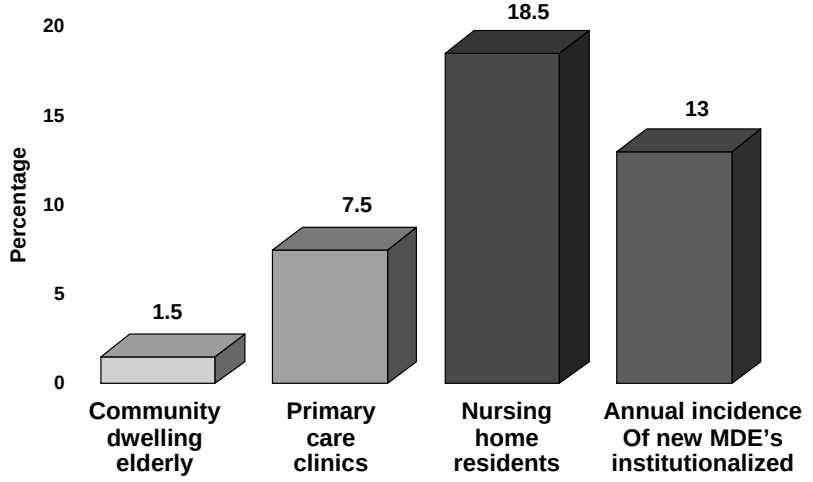
Major Depression Can Be Fatal

- 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



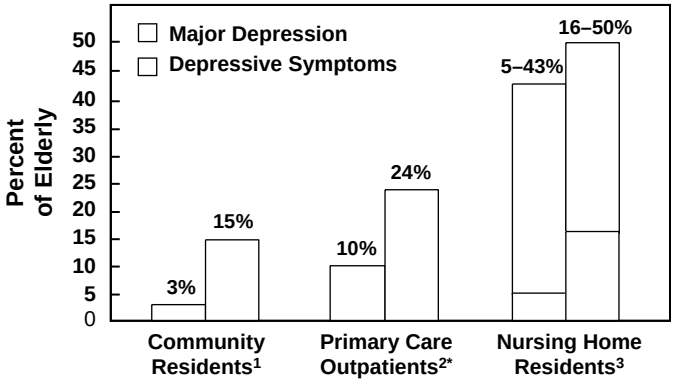
NIH Consensus Development Panel on Depression in Late Life.
***JAMA*. 1992;268:1018–1024.**

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 common[1]
  - 75% of residents receive ≥3 medications
  - 45% of residents receive ≥5 medications
- More than half of the residents receive a psychoactive medication[2]
- Many medical problems are often underdiagnosed and misdiagnosed[1]

1. Nagle BA et al. Geriatrics. In: DiPiro J et al, eds. *Pharmacotherapy: A Pathophysiologic Approach*. 3rd ed. Stamford, Conn: Appleton & Lange; 1997:87–100.
2. Beers M et al. *JAMA*. 1988;260:3016–3020.

Prevalence of Depression in the Elderly by Health/Independence Status



1. NIH Consensus Development Panel on Depression in Late Life. *JAMA*. 1992;268:1018–1026.
2. Borson S et al. *J Am Geriatr Soc*. 1986;34:341–347.
3. Abrams RC et al. *Clin Geriatr Med*. 1992;8:309–322.
***Men only.**

Risk Factors for Depression in Nursing Home Residents

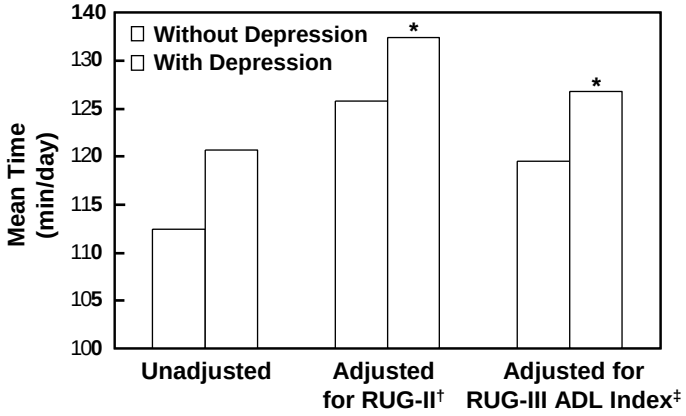
- New admission or change in environment
- Personal/family history of mood disorder
- History of alcohol/substance abuse
- History of psychiatric hospitalization/suicide attempt
- Pervasive loss (family, friend)
- Loss of autonomy, function, or body part
- Concurrent medical illness (dementia, Parkinson's,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

***AMDA Clinical Practice Guideline: Depression*. May 1996.**

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 admission[1]
- Undertreatment
  - Only ~25% depressed patients receive treatment[1]
  - When treated
    - Use of nonspecific agents as monotherapy, eg, antipsychotics, anxiolytics[2]
    - Subtherapeutic antidepressant dosages[2]
    - Inadequate treatment duration[3]

Impact of Depression on Nursing Home Staff Time



* *P* < 0.0001.
† Resource Utilization Group II.
‡ Resource Utilization Group III Activities of Daily Living Index.
Fries BE et al. *MedCare.* 1993;31:898–920.

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

Component	Age Effect	Consequence
Absorption	**↓ gastric pH** **↓ motility**	**↓ absorption (probably minimal effect)**
Distribution	**↑ fat/lean body ratio**	**↑ volume of distribution** **↑ half-life**
Metabolism	**↓ hepatic blood flow** **↓ activity of some catabolic enzymes**	**↓ breakdown** **↑ plasma levels & half-life**
Excretion	**↓ GFR**	**↓ clearance** **↑ accumulation**

Pharmacodynamics
(Effects of Drug on Patient)
and Aging

Increased Sensitivity To:

- Sedation
- Cardiovascular effects
- Anticholinergic effects

Polypharmacy in the Elderly
Facts and Figures

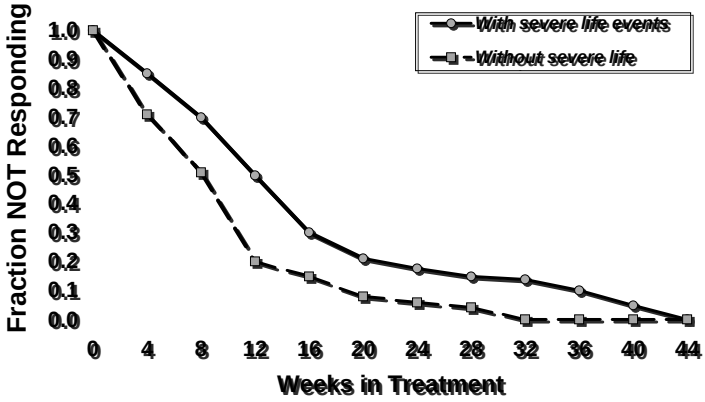
- Average 13 prescriptions/year[1]
- 6–8 different medications daily[2]
- Greater use nonprescription drugs[3]
- 33% nursing home residents receive >8 different drugs daily[4]

[1]Lamy, 1976
[2]Salzman, 1995
[3]Helling et al., 1985
[4]Lamy et al., 1992

Noncompliance in the Elderly

- 40–70% overall noncompliance[1]
- 10% take drugs prescribed for others[2]
- 20% take drugs not currently prescribed[2]
- 40% stop drugs too soon[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, tranylcypramine, isocarboxizide)
- TCAs
  - Tertiary amines (amitriptyline, clomipramine, doxepine, imipramine, trimipramine)
  - Secondary amine (amoxepine, desipramine, maprotyline, nortripyline, protriptyline)
- SSRIs (citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)
- Others
  - NDRI (bupropion - SR)
  - SNRI (venlafaxine - XR)
  - HT_2 antagonist/SNRI (nefazodone, trazodone)
  - $\propto_2/HT_2/HT_3$ antagonist (mirtazapine)
  - NRI (reboxetine)

Selective Serotonin Reuptake Inhibitors (SSRIs)

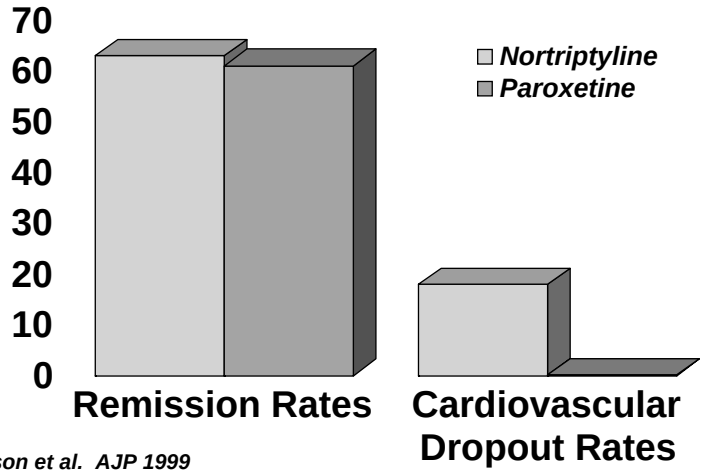
Medication	Target Dose (mg/day)	Range (mg/day)**
Citalopram (Celexa®)	**20**	**10–50**
Fluoxetine (Prozac®)*	**20**	**10–80**
Fluvoxamine (Luvox®)	**200**	**50–300**
Paroxetine (Paxil®)	**20**	**10–50**
Sertraline (Zoloft®)	**100**	**25–200**

*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**

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



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

	5HT Uptake	NA Uptake	DA Uptake	5HT Selectivity
Citalopram	**++++++++**	**0**	**0**	**+++++++++**
Fluoxetine	**++++**	**++**	**+**	**++**
Fluvoxamine	**++++++**	**+**	**0**	**++++**
Paroxetine	**++++++++++**	**++++**	**+**	**++++++**
Sertraline	**++++++++++**	**+++**	**+++**	**++++++++**

Hyttel, 1994

SSRI Withdrawal

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

Bupropion SR (NDRI)

- The good
  - effective
  - tolerable
  - no sexual side effects
  - ADD?
  - safe
  - no ↓ REM
  - bipolar?
  - 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 ($\propto_2$/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

Phase	Goal	Duration
Acute	**Remission**	**Weeks**
Continuance	**Recovery** **Prevent relapse**	**Months**
Maintenance	**Prevent recurrence**	**Years**

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