Depression in Later Life:
Epidemiology, Assessment, and Treatment

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Self-Assessment Question 1:
Which of the following statements is most correct?

A. Major depressive disorder is less prevalent in older than in younger adults.

B. Major depressive disorder in late life is associated with increased morbidity and mortality from medical illnesses and suicide.

C. Major depression is not a normal concomitant of ageing.

D. Numerous published randomized controlled treatment trials are available to help guide the treatment choices for older adults with major depressive disorder.

E. All of the above are true

Self-Assessment Question 2:
Which of the following statements is most correct?

A. White matter hyperintensities are the most replicated neuroimaging abnormality in late life depression.

B. White matter hyperintensities and late-life depression have a direct cause-effect relationship.

C. White matter hyperintensities represent deposition of beta amyloid plaques in the prefrontal white matter.

D. The most common location of white matter hyper intensities in vascular depression is occipital.

E. None of the above

Self-Assessment Question 3:
Which of the following forms of psychotherapy has/have been empirically validated for the treatment of depression in older adults?

A. Cognitive Behavior Therapy

B. Problem Solving Therapy

C. Interpersonal Therapy

D. All of the above

E. None of the above.

Self-Assessment Question 4:
Which of the following statements is most correct?

A. Efficacy of serotonin reuptake inhibitors in treating late life depression is similar to that of TCAs, though TCA side effects may be less tolerable.

B. For nonpsychotic late life depression, the combination of psychotherapy and medication is recommended.

C. Older adults are more vulnerable than younger adults to anticholinergic side effects of antidepressants.

D. Older adults typically take more concurrently prescribed medications than younger adults, necessitating careful attention to drug/drug interaction possibilities when an antidepressant is prescribed.

E. All of the above

Self-Assessment Question 5:
Which of the following statements is not correct?

A. ECT is usually less efficacious than antidepressants in treating late life depression with psychotic features.

B. Intracranial mass lesion, recent CVA, or recent MI can complicate the safe administration of ECT.

C. Informing patient and family about potential memory disturbance associated with ECT will help them understand and tolerate this usually transient aspect of treatment.

D. Demented patients may experience intolerable cognitive worsening during the course of a series of ECT treatments.

E. Unilateral nondominant ECT is associated with fewer cognitive side effects.

Major Teaching Points

- Depression in later life is an important, under-recognized illness with severe consequences in function and mortality
- Psychotherapy, medication, and ECT have each been shown to be effective treatments and enough information is available to individualize treatment approach to a specific patient's needs

Outline

1. Prevalence and significance of depressive symptoms and depressive syndromes in later life
2. Characteristic presentations and assessment process
3. Treatment approaches
   - ❖ Psychotherapy
   - ❖ Medications
   - ❖ ECT
4. Treatment resistance
5. Maintenance treatment issues

The High Prevalence of Depressive Symptoms in Later Life

- Minor depressive disorders are more common than major depressive disorders among older adults
  - Minor depression ~ 8-10%
  - Major depression ~ 3-4% [1]
- Depression is common in primary care settings [2]
  - Depression or depressive sx in 17% to 37%
  - 35% to 50% reporting sx were not diagnosed by PCP
- Depression is highly prevalent and undertreated in LTC settings [3]

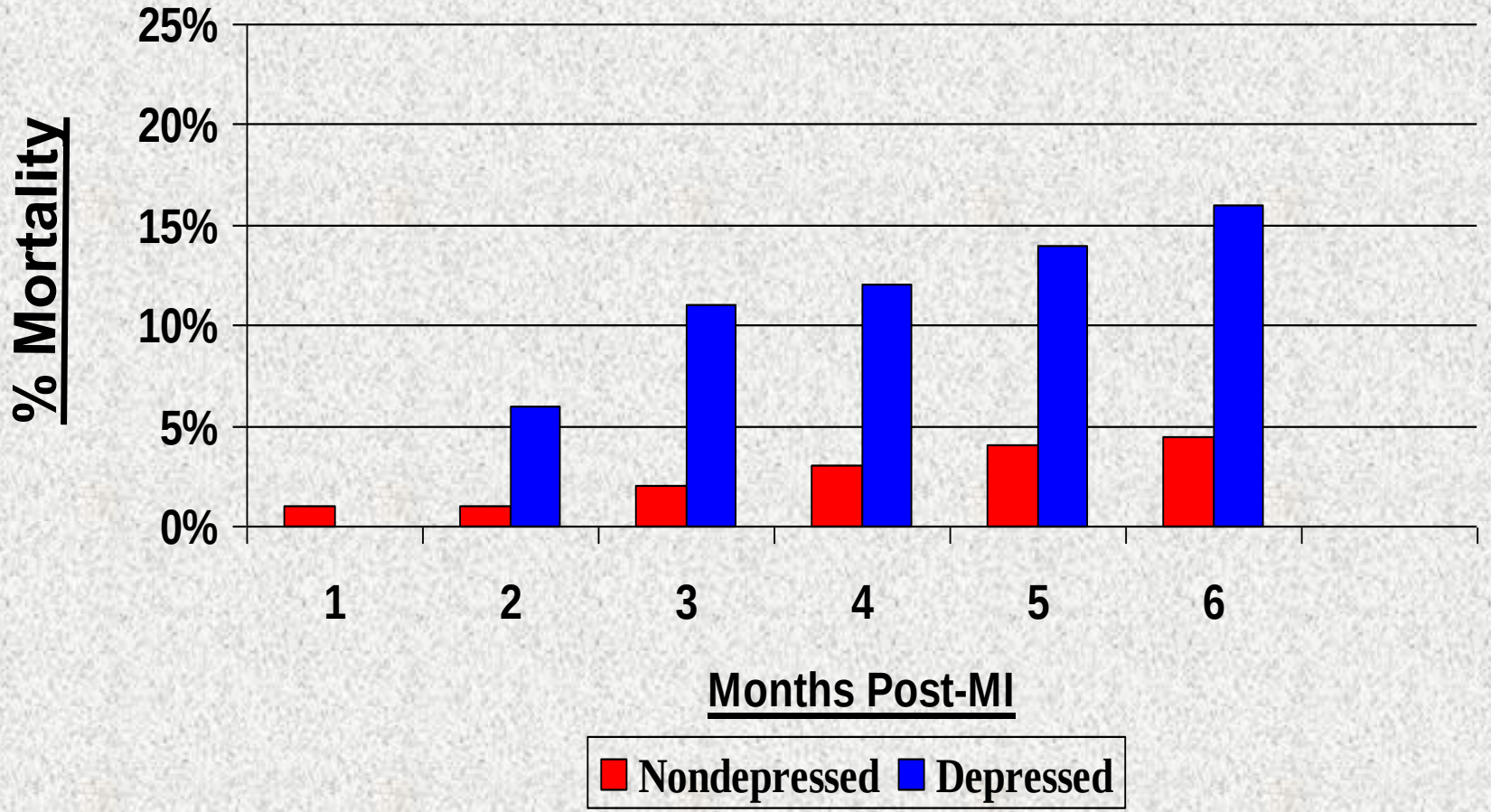
1. Steffens et al. 2000; 2. Garrard JL et al. J Gerontology Medical Sciences. 1998; 3. Brown et al. J Am Geriatr Soc. 2002;50(1):69-76.

Failure to Treat Depression Promotes Adverse Outcomes

- Functional Decline / Increased disability[1]
- Increased use of non-mental health services[1]
- Increased mortality rate
  - Overall[2]: >4x rate of death over 15 months
  - Cardiac[3]: 4x rate of death within 4 mo after MI
  - Suicide[4]: 13% of population and 18% of suicides

1. Beekman et al. 1997; 2. Bruce and Leaf 1989; 3. Romanelli et al. 2000;
4. http://www.cdc.gov/ncipc/wisqars/default.htm

Cumulative Mortality for Depressed and Non-depressed Patients 6 Months After MI



Frasure-Smith et al. 1993

Suicide Rate in Late Life Exceeds That of Other Age Groups

- 9th leading cause of death in US population
  - 12/100,000
- Among the elderly:
  - 19.1/100,000 over age 65
  - 22.9/100,000 ages 75-84
- Depression is the most frequent mental disorder preceding suicide
- Physical illness is the most frequent stressor in suicides over 80 years of age

Major Depressive Episode (DSM IV TR)

- Depressed mood or anhedonia of at least 2 weeks with at least 4 of the following:
  - ↓ interest or pleasure most of the time
  - Significant change in weight when not dieting
  - Insomnia or hypersomnia
  - Psychomotor agitation or retardation
  - Fatigue or loss of energy
  - Feelings of worthlessness, inappropriate guilt
  - ↓ concentration or thinking, indecisiveness
  - Recurrent thoughts of death or suicide
- No medical/substance etiology/mixed episode/other psych
- Significant distress or impairment
- Not uncomplicated bereavement

APA 2000

Geriatric Depression: Can Look Different from Adult Depression

Symptom Domain	Adult Presentation	Geriatric Presentation
Mood	Depressed Anhedonic Suicidal thoughts	Weary, Hopeless, Angry Anxious Thoughts of death
Somatic	↓↑ Sleep ↓↑ Appetite ↓↑ Psychomotor ↓↑ Increased pain	↑ Pain, and Somatic symptoms overlap with effects of medications, comorbid disease
Cognitive	↓ Concentration Indecisiveness	↓ Selective attention ↓ Working memory/retrieval ↓ New learning ↓ Processing speed ↓ Executive function

Gallo et al. 1997; Geiselmann and Bauer 2000; Devanand 1994; Mazure et al. 2002; Lezac 1994; Lavretsky and Kumar 2002

Evaluation of Late Life Mood/Anxiety Disorders:
1. Psychiatric History

- Informant may shed light
- Atypical presentation is typical
- Psychosocial factors can mislead
- Delusions are more common
- Medical comorbidity is relevant
- That includes substance abuse
- Treatment adherence may be poor

Assessment of Late Life Depression: *2. Mental Status Examination*

- Baseline cognitive assessment
- Appearance and self-care
- Variant presentations of mood
  - Withdrawal
  - Weariness
  - Comorbid anxiety
- Mental Content
  - Somatic preoccupations, Pain
  - Complaints re cognitive functioning

Evaluation of Late Life Mood/Anxiety Disorders: Consider Use of Objective Depression Scale

- Why?
  - May facilitate symptom reporting
  - Estimates severity
  - Provides benchmark for treatment evaluation
- What?
  - Geriatric Depression Scale
  - Cornell Scale for Depression in Dementia

GDS 15

1. Are you basically satisfied with your life ?
2. Have you dropped many of your activities and interests ?
3. Do you feel that your life is empty ?
4. Do you often get bored ?
5. Are you in good spirits most of the time ?
6. Are you afraid that something bad is going to happen to you ?
7. Do you feel happy most of the time ?
8. Do you often feel helpless ?
9. Do you prefer to stay at home, rather than going out and doing new things ?
10. Do you feel you have more problems with memory than most?
11. Do you think it is wonderful to be alive now ?
12. Do you feel pretty worthless the way you are now?
13. Do you feel full of energy ?
14. Do you feel that your situation is hopeless ?
15. Do you think that most people are better off than you are ?

GDS is in the Public Domain, can be freely reproduced and used. Score 1 pt for each "Yes" on 2,3,4,6,8,9,10,12,14,15 or "No" on 1,5,7,11,13. A score of 6 or higher suggests need f definitive diagnostic evaluation. (http://www.stanford.edu/~yesavage/GDS.html)

Cornell Scale for Depression in Dementia

Scoring System

A = unable to evaluate 0 = absent 1 = mild or intermittent 2 = severe

Ratings should be based on symptoms and signs occurring during the week prior to interview.

No score should be given in symptoms result from physical disability or illness.

A. Mood-Related Signs

1. Anxiety: anxious expression, ruminations, worrying	a 0 1 2
2. Sadness: sad expression, sad voice, tearfulness	a 0 1 2
3. Lack of reactivity to pleasant events	a 0 1 2
4. Irritability: easily annoyed, short-tempered	a 0 1 2

B. Behavioral Disturbance

5. Agitation: restlessness, handwringing, hairpulling	a 0 1 2
6. Retardation: slow movement, slow speech, slow reactions	a 0 1 2
7. Multiple physical complaints (score 0 if GI symptoms only)	a 0 1 2
8. Loss of interest: less involved in usual activities	a 0 1 2

(score only if change occurred acutely, i.e. in less than 1 month)

Cornell Scale for Depression in Dementia (2)

C. Physical Signs

9. Appetite loss: eating less than usual a 0 1 2
10. Weight loss (score 2 if greater than 5 lb. in 1 month) a 0 1 2
11. Lack of energy: fatigues easily, unable to sustain activities a 0 1 2
(score only if change occurred acutely, i.e., in less than 1 month)

D. Cyclic Functions

12. Diurnal variation of mood: symptoms worse in the morning a 0 1 2
13. Difficulty falling asleep: later than usual for this individual a 0 1 2
14. Multiple awakenings during sleep a 0 1 2
15. Early morning awakening: earlier than usual for this individual a 0 1 2

E. Ideational Disturbance

16. Suicide: feels life is not worth living, has suicidal wishes, a 0 1 2
or makes suicide attempt
17. Poor self esteem: self-blame, self-depreciation, feelings of failure a 0 1 2
18. Pessimism: anticipation of the worst a 0 1 2
19. Mood congruent delusions: delusions of poverty, illness, or loss a 0 1 2

Alexopoulos et al. 1988

Evaluation of Late Life Mood/Anxiety Disorders:

Include Cognitive Screen with MSE

- Why?
  - Depression as prodrome
  - Comorbid cognitive symptoms in depression
  - Depression and excess functional impairment
- What?
  - Mini-Mental Status Examination
    - Per-use fee and permission required[1]
  - Montreal Cognitive Assessment (public domain)[2]

1. http://www3.parinc.com/uploads/pdfs/MMSE_Copyright_PermReq.pdf ;
2. www.mocatest.org

Psychiatric Differential Diagnosis

- Bereavement/Adjustment Disorder
- Bipolar Disorder
- Substance Abuse Disorders
- Anxiety Disorders
- Personality Disorder
- Schizophrenia

Confusing Comorbidity: Depression in Demented Patients

- 50% of patients with dementia or other neurological impairments are depressed
  - 17-31% of Alzheimer's patients
  - High rates in Parkinson's and post-stroke
- Detection may require collateral informants
- Treatment is of potential value when mood symptoms are present.

Dementia Syndrome of Depression (DSD) vs. Alzheimer's Disease (AD)

	DSD	AD
Symptom duration	Short	Long
Prior psychiatric history	Usual	Unusual
Patient complaint	Frequent	Variable
Behavior congruent with cognitive deficits	Unusual	Usual
Mood disorder	Autonomous	Reactive
Recognition memory	More intact	Impaired
Effort on tasks	Poor	Good
Prompting effect	Helpful	Less helpful

Adapted from Kaszniak and Christenson, in Storandt and VandenBos, Neuropsychological Assessment of Dementia and Depression in Older Adults: A Clinician's Guide.
Washington, DC, American Psychological Association, 1994.

Assessment of Late Life Depression: *3. Medical History and Physical Examination*

- Essential component of work up
- Medication toxicities
- Cardiopulmonary disorders
- Neurological disorders
- Endocrine/Metabolic disorders
- Nutritional deficiencies
- Sleep disorders
- Infectious disorders
- Neoplasms

Assessment of Late Life Depression: *4. Laboratory Assessment*

- **Hematology**
  - **WBC, differential**
  - **HGB/HCT, MCV**
  - **Platelets**
- **Urine**
  - **Urinalysis**
  - **Culture and sensitivity**
- **Chemistry**
  - **Lytes, BUN, Creatinine**
  - **Liver function tests**
  - **Thyroid function tests**
  - **ESR**
  - **B12 (or methylmalonic acid)**
  - **Folate (or RBC folate)**
  - **Testosterone level (males)**

Assessment of Late Life Depression:
5. Ancillary Studies

- Neuropsychological Testing*
  - Cognitive/memory testing*
  - Assessment of executive functions*
- Neuroimaging Studies*
  - Structural (CT, MRI)*
  - Functional (fMRI, SPECT, PET)*

*Not considered “routine”

Treatment

- Psychotherapy
  - Consensus recommendations
- Pharmacotherapy
  - Acute
  - Continuation
  - Maintenance

Evidence-Based Psychotherapies for Older Adults

- Interpersonal psychotherapy (IPT)
- Cognitive behavior therapy (CBT)
- Problem-solving therapy (PST)
- Brief psychodynamic therapy

Arean PA, Cook BL. *Biol Psychiatry.* 2002;52:293-303.

Age-Related Factors Inhibiting Therapeutic Engagement

- Patient's own perceptions of aging:
  - Time as limited
  - Self as fixed and unchangeable (eg, "old dog . . .")
- Physical limitations
  - Hearing/vision loss
  - Ambulatory/mobility problems
  - Urinary urgency/incontinence
  - Physical discomfort
  - Transportation difficulties
- Cognitive limitations
  - Retention/recall difficulties
- Reimbursement

Antidepressant Treatment of Late Life Depression Is Evidence-Based

- Over 70 Randomized Controlled Trials of pharmacotherapy of geriatric depression
- >25 comparisons of 1 AD to placebo, >50 comparisons of two active antidepressants to each other or to placebo
- Many trials use older antidepressants, optimal rather than typical populations and settings
- Efficacy supported, with limited EBM support for greater side-effect superiority of newer agents

Some Marketed Antidepressants Used for Late Life Depression

- **Tricyclics**
  - Nortriptyline (Pamelor, Aventyl)
- **MAO Inhibitors**
  - Phenelzine (Nardil)
  - Tranylcypromine (Parnate)
  - Selegiline (Emsam)
- **SSRIs**
  - Citalopram (Celexa)
  - Sertraline (Zoloft)
  - Fluoxetine (Prozac)
  - Paroxetine (Paxil)
  - Fluvoxamine (Luvox)
  - Escitalopram (Lexapro)
- **SNRIs**
  - Venlafaxine (Effexor)
  - Duloxetine (Cymbalta)
  - Desvenlafaxine (Pristiq)
- **Others**
  - Bupropion (Wellbutrin)
  - Mirtazapine (Remeron)

Choosing An Optimal Antidepressant:

Overview of Considerations

1. Efficacy
2. Side effects
3. Drug/Drug interactions
4. Cost

Choosing An Optimal Antidepressant: 1. Efficacy

- FDA-indicated antidepressants are effective in treating late-life depression[1]
- Response rate (50% symptom decrease)[2]
  - 50 – 65% in trials with ITT analyses
  - 25 – 30% respond to placebo
  - Number Needed to Treat (NNT): 2.5 to 5
- Remission (≥90% symptom decrease)[2]
  - Typically 30 – 40% with medication vs 15% for placebo
  - NNT: 4 to 7

ITT: Intention to Treat
NNT: Number Needed to Treat

1. Ellison et al. Mood Disorders in Later Life. Informa Health Care 2008; 2. Shanmugham et al. Psychiatr Clin North Am. 2005;28:821-35.

Choosing An Optimal Antidepressant: 2. Potential Adverse Effects in the Elderly

Medication Property	Possible Clinical Consequences
NE reuptake blockade	Tremors, tachycardia, erectile/ejaculatory dysfunction, elevated blood pressure
Serotonin reuptake blockade	GI symptoms, sexual dysfunction, EPS, bruising/bleeding, bone mass density loss
Dopamine reuptake blockade	Activation, aggravation of psychosis
Histamine H_1 receptor antagonism	CNS depressant potentiation, sedation, weight gain, hypotension
Muscarinic receptor antagonism	Blurred vision, dry mouth, constipation, urinary retention, cognitive dysfunction
NE α_1 receptor antagonism	Potentiation of some antihypertensives, postural hypotension, dizziness, reflex tachycardia

Adapted/modified from http://www.cpgnews.org/DEP/tools.cfm

Antidepressant Treatment is Safe and May Be Medically Beneficial in Cardiac Patients

- SADHART[1] showed that treatment is well-tolerated
  - Sertraline 50-200 mg/d x 24 weeks
  - No change with sertraline vs placebo in:
    - Left ventricular ejection fraction
    - Heart rate, blood pressure, ECG
  - Trend with sertraline vs placebo toward lower incidence of death, recurrent MI, CVA, heart failure, hospitalization for angina
- ENRICHD[2] study found SSRI decreased life threatening outcomes among highly at risk cardiac depressed patients

1. Shapiro et al. Am Heart J. 1999;137:1100-6; 2. Taylor et al. Arch Gen Psychiatry. 2005;62:792-8

Choosing An Optimal Antidepressant: 3. Drug-Drug Interactions

Age exacerbates potential for adverse reactions and interactions at five levels

- **Changes in gastrointestinal absorption**
- **Changes in protein binding**
- **Changes in hepatic metabolism**
- **Changes in renal excretion**
- **Receptor site competition associated with polypharmacy**

Choosing An Antidepressant:

Consider Age-Related Changes in Pharmacokinetics and Pharmacodynamics

- Reduced GI, renal and liver function
- Lower albumin levels
- Increased fat/muscle ratio
- Increased receptor-site sensitivity for many drugs (decreased β-adrenergic)
- Polypharmacy leading to drug-drug and drug-disease interactions

Choosing An Antidepressant: Consider CYP 450 Drug/Drug Interactions

- **Some CYP 2D6 substrates**
  - TCA, fluoxetine, paroxetine, trazodone, venlafaxine
  - selegiline
  - donepezil
  - morphine, dextromethorphan, codeine, meperidine, oxycodone, tramadol
  - encainide, flecainide, lidocaine, mexiletine
  - metoprolol, bisoprolol, propranolol, timolol, labetolol
- **Two CYP1A2 substrates**
  - clozapine
  - warfarin

- **Some CYP 3A4 substrates**
  - alprazolam, midazolam, triazolam, clonazepam
  - carbamazepine, lamotrigine
  - donepezil
  - acetaminophen
  - codeine
  - clarithromycin, erythromycin
  - ketoconazole
  - tamoxifen, vinblastine, doxorubicin
  - amiodarone, quinidine
  - calcium channel blockers
  - lovastatin, simvastatin, atorvastatin, fluvastatin, pravastatin
  - estradiol, cortisol, prednisone, testosterone
  - omeprazole

Zubenko and Sunderland 2000; Cadieux 1999

Choosing An Optimal Antidepressant: 4. Cost

- Affordability affects adherence
- Medicare Part D “donut hole” imposes costs
- Stick with generically available antidepressants when possible
- Not available generically:
  - Lexapro (escitalopram)
  - Emsam (selegiline)
  - Cymbalta (duloxetine)
  - Pristiq (desvenlafaxine)

Antidepressant Choices: Tricyclic Antidepressants (TCAs)

- **Advantages: proven efficacy, availability of blood levels for selected agents, low cost**
- **Disadvantages: sedation, cardiovascular effects, autonomic side effects (hypotension), toxicity.**
- **Examples: nortriptyline 10 to 150 mg daily (guide treatment by plasma level of 50 – 10 ng/ml); desipramine 10 to 150 mg daily**

Antidepressant Choices: Serotonin Reuptake Inhibitors (SRIs)

- **SSRIs and SNRIs**
- **Advantages: Effective with minimal toxicity, avoidance of autonomic side effects, less sedation, ease of administration**
- **Disadvantages: Overstimulation/insomnia, G.I. symptoms, sexual side effects, hyponatremia, drug interactions, cost**
- **Examples: citalopram 10 to 40 mg/day; fluoxetine 10 to 60 mg/day; sertraline 25 to 200 m/day; paroxetine 10 to 50 mg/day; venlafaxine XR 37.5 to 225 mg/d; duloxetine 20-90 mg/d**

Antidepressant Choices: Ungrouped Agents

- **Mirtazapine (start: 15 mg/day) may cause sedation and increased appetite.**
- **Bupropion (start: 37.5 mg BID or bupropion SR 100 mg q d) may increase risk for seizures at higher doses, is not approved for treating anxiety disorders, and is contraindicated with comorbid eating disorder.**
- **Nefazodone: not typically used as primary therapeutic agent because of concerns about rare but serious hepatotoxicity.**
- **Trazodone: rarely used as primary therapeutic agent because of limited potency and significant side effects (sedation, hypotension, priapism) but can be used as an hypnotic in conjunction with SSRI.**

Antidepressant Choices: Monoamine Oxidase (MAO) Inhibitors

- **Advantages: MAO levels increase with age, low cardiac effects, effectiveness for atypical depression.**
- **Disadvantages: Dietary restriction, potential hypertensive crisis, orthostatic hypotension, drug interactions.**
- **Examples: phenelzine 15 mg bid to tid, tranylcypromine 10 mg bid to tid, selegiline transdermal 6 to 12 mg/d**

Treatment Resistant Depression and the "ABCD" Evaluation

- **A**dequacy of prior treatment
  - Duration of treatment
  - Dosage of medication
- **B**ehavioral/Environmental factors
  - Personality disorder
  - Psychosocial stressors
- **C**ompliance/Adherence
  - Patient education
  - Treatment intolerance
- **D**iagnosis
  - Missed medical diagnosis or adverse medication effect
  - Missed psychiatric diagnosis

In Treatment Resistant Patients: To Switch or To Augment?

Switch

- Simpler, less costly
- Avoids drug-drug interactions
- Reduces side effects
- Introduces “different mechanism”
- Implementation is slower
- Outpatient setting

Augmentation

- More complex and costly
- Risks drug-drug interactions
- Risks side effect increase
- Avoids loss of partial response effect
- Implementation is faster
- Inpatient setting

Antidepressant "Augmenters"

Augmenter	Evidence in Adults	Evidence in Late Life Depression
Lithium carbonate	**+**	**Mixed results**
Triiodothyronine	**+**	**No specific study**
Atypical antipsychotic	**+**	**+ Open trials: aripiprazole, risperidone**
Modafinil	**+/-**	**+/- case reports**
Testosterone	**+ Hypogonadal men**	**+ ? Hypogonadal men**
Buspirone	**+/-**	**No specific study**
Estrogen	**+ Peri/postmenopausal women??**	**+ Peri/postmenopausal women**
Lamotrigine	**?**	**?**

+ signifies presence of credible evidence base for use

Augmenters: Atypical Antipsychotics

- Small, mostly open label, studies support atypicals as SRI augmenters in depressed nongeriatric nonpsychotic adults[1]
  - Risperidone: 0.5 to 1 mg/d
  - Olanzapine: 1 RCT at 5-20 mg/d
  - Ziprasidone: 20-80 mg bid
  - Aripiprazole: 5-10 mg/d
  - Quetiapine: Anecdotal support for augmentation
  - Clozapine: Anecdotal support for augmentation
- In elderly, 1 open trial each: aripiprazole[2], risperidone

1. Papakostas GI 2005; 2. Rutherford et al. 2007

Prescribe Atypicals with Caution in Elderly Patients

- FDA warnings re use in psychosis/dementia geriatric patients
  - CVA risk
  - Overall mortality risk
- Concerns re metabolic effects
  - Weight gain
  - Glucose
  - Lipids
- Safety and risk-management considerations

Augmenters: Testosterone

- Low total testosterone level predicts higher incidence of depressive illness among older men (enhanced with comorbid medical morbidity).[1]
- One RCT found testosterone +SSRI = placebo + SSRI in older hypogonadal men[2], while others have supported testosterone coadministration[3] including in SSRI-resistant hypogonadal[4] or eugonadal[5] men
- Prescreen: Contraindicated with prostate cancer, may cause hepatotoxicity and other adverse effects.

1. Shores et al. 2005; 2. Seidman et al 2001; 3. Pope HG Jr et al .2003; 4. Seidman and Rabkin 1998; 5. Seidman et al. 2005

Antidepressant "Co-Prescribing"

Augmenter	Evidence in Adults	Evidence in Late Life Depression
TCA + SSRI/SNRI	+	+ Nortriptyline/paroxetine[1]
SSRI/SNRI + bupropion	+	+ Bupropion/paroxetine[1]
SSRI/SNRI + mirtazapine	+	No specific study
Stimulant	+	+/- Methylphenidate, (dextroamphetamine)

1. Dew et al. 2007; 2. Orr and Taylor 2007

+ signifies presence of credible evidence base for use

Hormone Treatments for Late-Life Mood and Cognitive Disorders

- Several hormones may influence mood and cognition in late life
- Estrogen, historically used as an antidepressant augmenter, was supported by limited evidence but is used infrequently to treat depression following the WHI and other studies raising concern about the safety of estrogen treatment.
- Testosterone has been used to treat depression in men with low testosterone levels absent risk factors (e.g. prostatic hypertrophy, cancer, or elevated PSA).

Delusional Depression: An Important Source of Treatment Resistance in Late Life Depression

- More prevalent among older than younger depressives
- Associated with:
  - Hypochondriacal and nihilistic delusions
  - Worse response to antidepressant monotherapy
  - Longer hospitalizations
  - High relapse rate
  - Delusional relapses

*

Treatment of Late Life Delusional Depression

- ECT may be more rapidly effective
- No RCTs guide choice of agent (antipsychotic or antidepressant) in treatment of geriatric psychotic depression
- Antipsychotic adjunctive treatment shown important in younger adults
  - Expert consensus: APD + AD is first line treatment for geriatric psychotic major depression[1]
  - Atypicals vs typicals? Two positive delusional depression treatment studies support use of olanzapine in younger adults – no evidence base in older adults.

1. Alexopoulos et al: J Clin Psychiatry 2004;65 Suppl 2:5-99

Electroconvulsive Therapy

- Underused modality, especially suitable with:
  - Antidepressant intolerance or non-response
  - Prior positive response to ECT
  - Delusions
  - Catatonia
  - Mania
  - Emergency
- High response rates documented[1]

1. Seiner and Henry 2003

ECT and Medical Status Concerns

- **Rarely contraindicated in appropriate setting**
- **Cardiac:** Recent MI, unstable angina, arrhythmias, severe valvular diseases, CHF, hypertension
- **Pulmonary**: COPD, asthma, infections
- **Gastrointestinal**: Aspiration or laryngospasm risk factors
- **Musculoskeletal:** Stress to bones, joints, vertebrae during treatment or in subsequent falls
- **Neurologic**: Intracranial lesions "substantially increase" risk[1]

1. Seiner and Henry 2003

ECT and Memory Loss

- A major concern of patients and families
- ECT may improve depression-impaired cognition but exacerbate impaired cognition of dementia
- Preparation:
  - Education of patient/family
  - Pre-screen to establish baseline
  - Monitor of memory throughout treatment course
  - Decrease treatment frequency when pronounced
  - Treat unilaterally when possible

1. Seiner and Henry 2003

Vascular Depression

- **Observations:**[1]
  - **High rate of depression with HT, DM, CAD**
  - **High rate of depression following CVA**
  - **Prevalence of silent CVA & white matter hyperintensities in late-onset depression**
  - **Lower prevalence of family history for mood disorders in post-CVA depression**

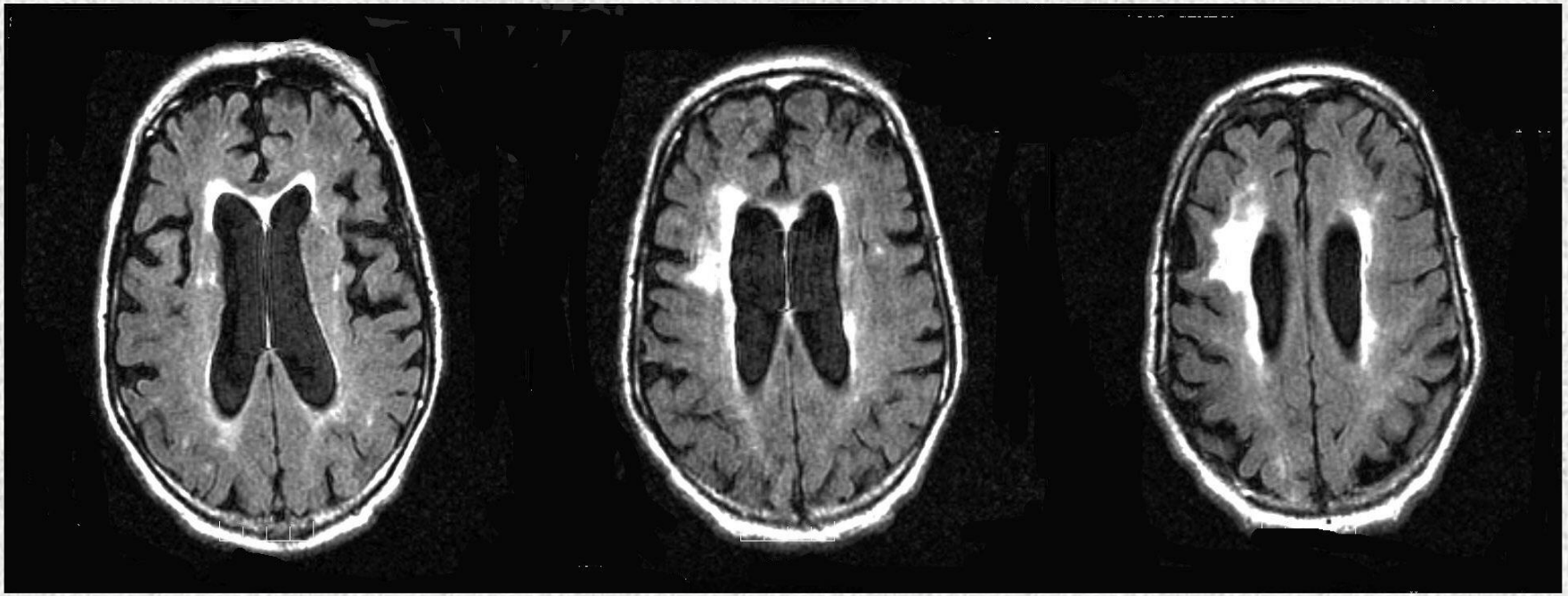
1. Alexopoulos 1997

Vascular Depression: Definition of Syndrome

- **Defined by:**
  - First onset of depression at or after 60 years of age
  - Presence of HT and/or TIA or surgery for vascular disease
- **Associated with:**
  - reduced depressive ideation
  - Increased psychomotor retardation
  - Cognitive dysfunction
    - Impaired fluency/naming
    - Lack of insight
    - Executive dysfunction
- **MRI findings: Left frontal and left putamen deep white matter hyperintensities[2]**

1. Alexopoulos 1997;
2. Greenwald et al. 1998

T2 Hyperintensities on MRI



Courtesy of Martin Goldstein MD

Depression with Executive Dysfunction Syndrome (DEDS)

- Executive dysfunction (by impaired IP on DRS) but not memory impairment predicted:
  - Delayed antidepressant response[1]
  - Greater risk of relapse, recurrence and symptom fluctuation following response[2]
- White matter hyperintensities predicted executive dysfunction[3,4] and poorer treatment response[4] (but not in all studies[5])

1. Kalayam et al. 1999; 2. Alexopoulos et al. 2000; 3. Boone et al. 1992; 4. Hickie et al. 1995; 5. Salloway et al. 2002

Are Vascular Depression and DEDS Treated Differently from Standard Major Depressive Disorder?

- Current approach is “treatment as usual”
- Attention to cerebrovascular risk factors is urged
- Hypothetical microvascular damage to frontostriatal (CSPTC) pathways suggests that glutamatergic, GABA-ergic, dopaminergic, cholinergic, and enkephalin pathways may be of importance[1,2]
- Preliminary data suggest that D_3 agonists, modafinil, nimodipine[3] or other novel agents may be of some interest

1. Alexopoulos et al. 2000; 2. Alexopoulos GS 2001; 3. Taragano et al. 2005

Post-Stroke depression

- CVA: 600,000 per year in US
- At 3-6 months s/p CVA, 9-34% show MDD
- Depression associated with:
  - Left anterior lesions
  - Left basal ganglia lesions
  - Lesions closer to frontal pole
- Minor depression is also common
- Assessment complicated by neurological symptoms
- Treatment
  - No antidepressant clearly superior (Flx, Nor studied)
  - ECT
  - ?Role for stimulants

Whyte and Mulsant 2002

Depression and Dementia

- Depression is common in LTC settings
  - In AD, 19%[1]
  - May be more prevalent in VaD[2]
  - Common feature of several other dementing disorders
- Can predispose to NonCognitive Behavioral Symptoms (NCBS)
- Diagnostic criteria: More lenient than in nondemented patients

1. Wragg and Jeste. Am J Psychiatry 1989;146:577-87; 2. Newman SC J Affect Disord 1999;52:169-76.

Also Note "Masked" Depression in Demented LTCF Residents

- Unrecognized depression may present with disguised symptoms:
  - Delusions[1]
  - Verbal/physical aggressive behaviors[2]
  - Suicidal or self-destructive behaviors
  - Disruptive vocalizations[3]
  - Weight loss[4]

1. Bassiony et al. Int J Geriatr Psychiatry. 2002;17:549-56; 2. Menon et al. Int J Geriatr Psychiatry 2001;16:139-46; 3. Dwyer and Byrne Int Psychogeriatr. 2000;12:463-71; 4. Morley and Kraenzle J Am Geriatr So 1994;42:583-5.

Provisional Criteria for Depression of Alzheimers Disease

- 3 or more of following in 2 week period
  - Depressed mood
  - Decreased positive affect/pleasure in usual activities/contacts
  - Social isolation or withdrawal
  - Disruption in appetite
  - Disruption in sleep
  - Psychomotor changes
  - Irritability
  - Fatigue/loss of energy
  - Worthlessness, hopelessnesss, guilt
  - Thoughts of death, SI or behavior

- Meets criteria for DAT
- Distress or disruption
- Not delirium, drug,
- medication, or better
- accounted for by
- other conditions

Olin et al. Am J Geriatr Psychiatry 2002;10:125-8.

Depression and Dementia

- Several antidepressants studied, including
  - Citalopram[1]
  - Sertraline[2]
  - Clomipramine[3]
  - Moclobemide[4]
- Side effect assessment can be more difficult
- Monitor efficacy / tolerability – and discontinue if ineffective

1. Nyth et al. Acta Psychiatr Scand 1992;86:138-45; 2. Lyketsos et al. Am J Psychiatry. 2000;157:1686-9;
3. Petracca et al. J Neuropsychiatry Clin Neurosci. 1996;8:270-5; 4. Roth et al. Br J Psychiatry 1996;168:149-57.

Anxiety Symptoms Are Highly Prevalent in Late Life

- 10-20% of adults over 65 show clinically significant new or recurring anxiety symptoms[1]
- Symptom picture may confusingly emphasize agitation rather than worry; physical/cognitive rather than affective symptoms, such as sweating, restlessness, pacing, palpitations, poor concentration, fatigue, dizziness, dry mouth, GI symptoms, tremor, aches, pains
- Anxiety even more prevalent among the medically ill elderly

[1]Himmelfarb, Murrell. J Psychol. 1984;159-167.

Anxiety Symptoms are Commonly Associated with:

- Medications / Drugs of abuse
  - Stimulants or sympathomimetics
  - Withdrawal of CNS depressants
  - Thyroid hormones
  - Nicotine
  - Antidepressants
  - Antipsychotics
  - Corticosteroids
- Conditions
  - Post-CVA
  - Coronary artery disease
  - IBS
  - Endocrine
  - Dementia
  - Depression

Differentiating Anxiety from Depression

- Difficult, because they share disturbances of sleep, appetite, and cognitive functioning[1]
- Initial insomnia, fear, loss of confidence more typical of anxiety[2]
- Anxiety is often associated with depression in the elderly[3]

1. Colenda and Smith: AJGP 1993;1:327-338; 2 Salzman C: Conclusion. In: Salzman C, Liebowitz BD, eds: Anxiety in the Elderly: Treatment and Research 1991; 3. Fernandez et al. J Clin Psychiatry. 1995;56(suppl 2):20-29

Depression with Anxiety: Treatment Recommendations

- The claim for superiority of sedating antidepressants with anxious, insomniac depressed patients has limited evidence base.
- These antidepressants are FDA-Indicated for GAD:
  - Paroxetine
  - Venlafaxine
  - Escitalopram
- Other useful agents may include sertraline, citalopram, mirtazapine, tricyclic antidepressant, buspirone as adjunct
- Avoid chronic benzodiazepines when possible

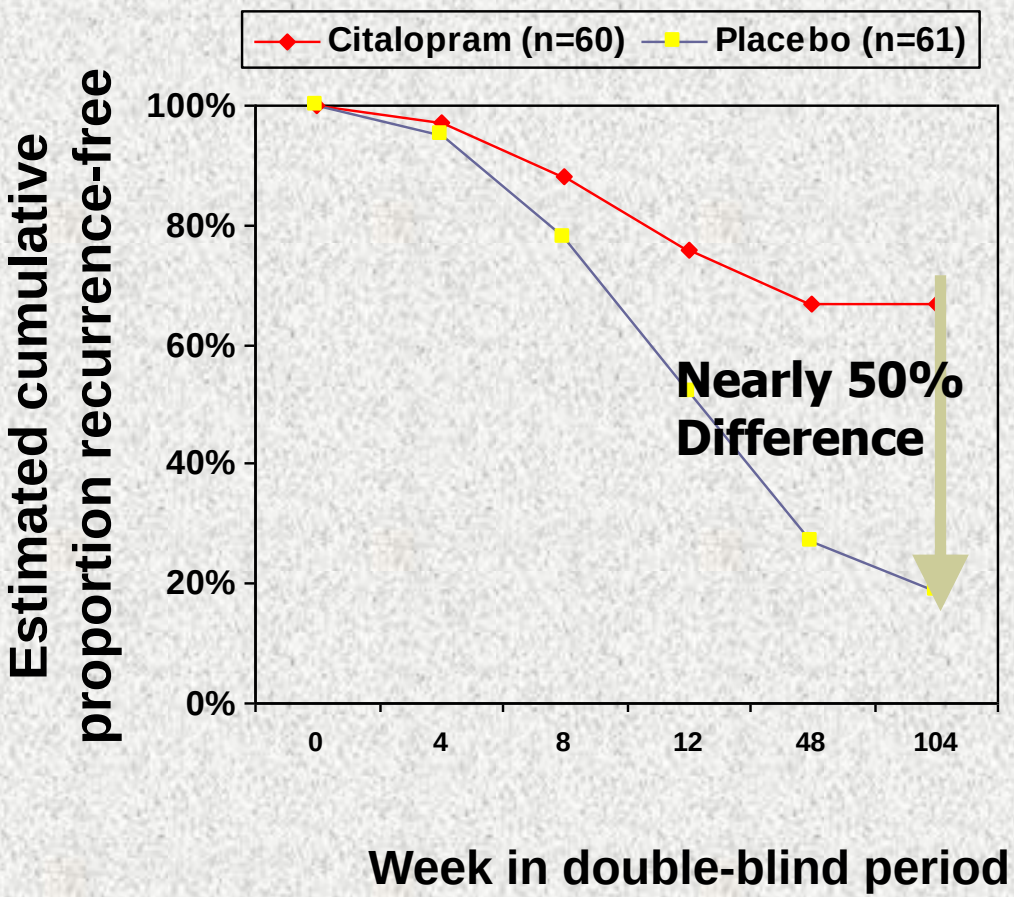
Maintenance Treatment: What do Experts Recommend?

- 1 episode: Continue for 1 year
- 2 episodes: Continue for 1-3 years
- 3 episodes Continue for >3 years

Alexopoulos GS, Katz IR, Reynolds CF III, et al. Postgrad Med Special Report. 2001 (October):1-86.

Citalopram Prevents Depression Recurrence in Elderly

- N=121 outpatients ≥ 65 yr
- 20-40 mg citalopram vs placebo for up to 104 weeks after 2 periods of open-label treatment (up to 24 weeks total) to establish and continue remission
- No treatment-related serious AEs



Klysner R, et al. *Br J Psychiatry.* 2002;181:29-35.

Recurrence after Recovery from Geriatric Depression

- Up to 15 years observational follow up (n=380)
- Recurrence in
  - 85% of those who had recovered
  - 58% of those who had remained well at least 5 years
- Risk factors (not in subgroup with 5 years recovery)
  - more prior episodes
  - longer depressive episode before intake
  - **Low levels of antidepressant treatment**
  - never marrying
  - female

Mueller et al 2000

Adherence 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]

1. Ostrum et al. 1988; 2. Lamy et al. 1992; 3. Jackson et al. 1984

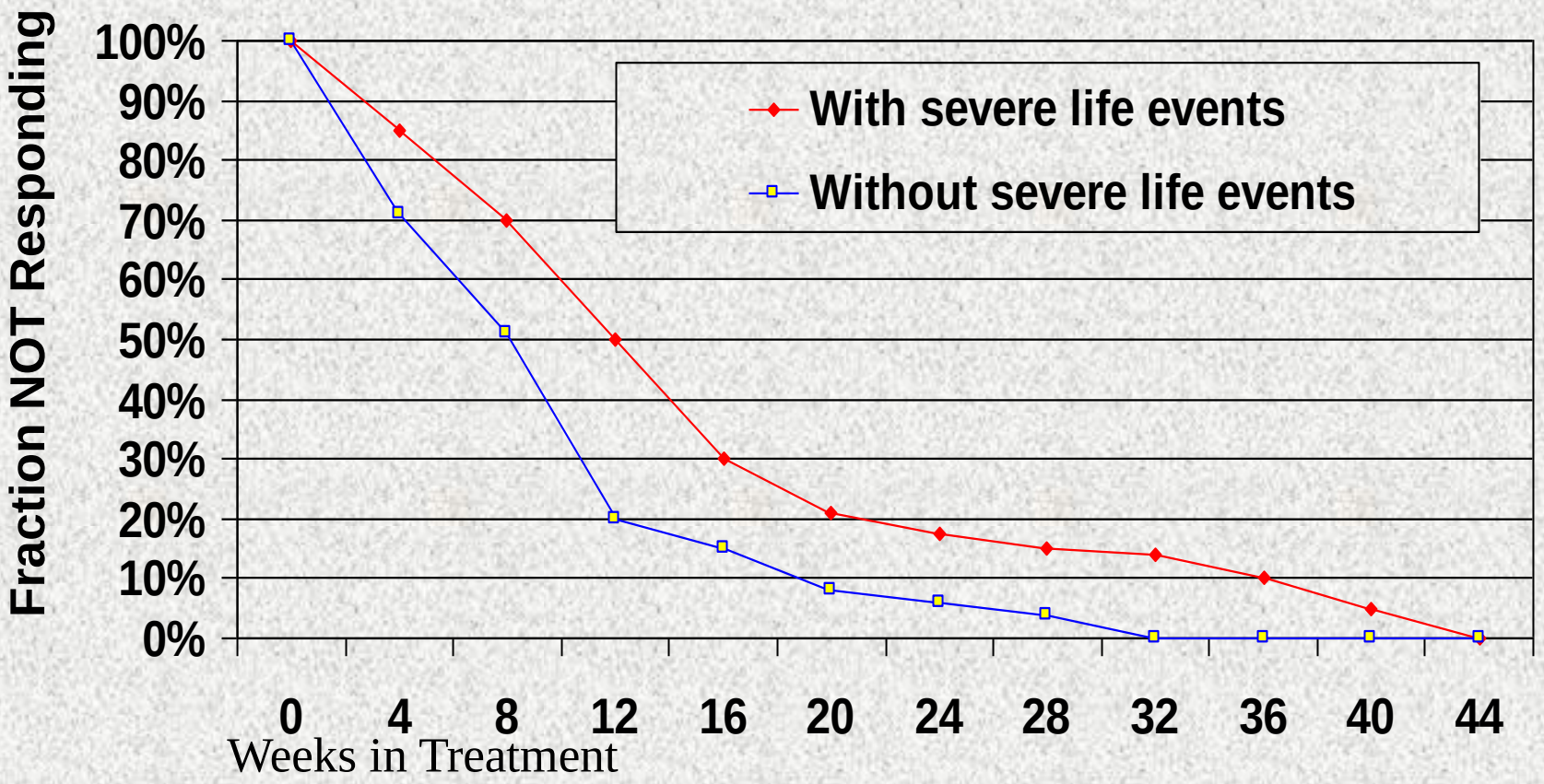
Suggestions to Improve Adherence for Treatment of Geriatric Depression/Anxiety

- Assess for cognitive impairment
- Assume adherence will be a problem
- Ask about non-adherence
- Encourage patient to monitor self-adherence
- Include family members/other supportive individuals as monitors/helpers
- Explore patient's conception of illness/treatment
- Provide clear, easy-to-understand info (repeat frequently, oral/written)
- Maintain appropriately frequent patient contact
- Accept limited adherence in some patients but maintain dialog

Wetherell JL, Unutzer J. *CNS Spectr.* 2003;8(12 suppl 3):48-59.

Importance of Recognizing Significant Psychosocial Factors:

Effect of Severe Life Event on Time to Response in Elderly Depressed Patients



Adapted from Karp et al. 1993

Summary of General Principles of Pharmacotherapy in Late Life Depression

- Differential diagnosis and comprehensive treatment planning
- Consider psychosocial and medical factors
- Psychotherapy may be important treatment ingredient
- Individualized consideration of treatment agents' properties
- Begin with low doses
- Monitor closely for response, side effects, and compliance
- Increase dose slowly and carefully
- Avoid underdosing and premature discontinuation

Self-Assessment Question 1: Which of the following is most correct?

A. Major depressive disorder is less prevalent in older than in younger adults.

B. Major depressive disorder in late life is associated with increased morbidity and mortality from medical illnesses and suicide.

C. Major depression is not a normal concomitant of ageing.

D. Numerous published randomized controlled treatment trials are available to help guide the treatment choices for older adults with major depressive disorder.

E. All of the above are true

Self-Assessment Question 2: Which of the following is most correct?

A. White matter hyperintensities are the most replicated neuroimaging abnormality in late life depression.

B. White matter hyperintensities and late-life depression have a direct cause-effect relationship.

C. White matter hyperintensities represent deposition of beta amyloid plaques in the prefrontal white matter.

D. The most common location of white matter hyper intensities in vascular depression is occipital.

E. None of the above

Self-Assessment Question 3:
Which of the following forms of psychotherapy has/have been empirically validated for the treatment of depression in older adults?

A. Cognitive Behavior Therapy

B. Problem Solving Therapy

C. Interpersonal Therapy

D. All of the above

E. None of the above.

Self-Assessment Question 4: Which of the following is most correct?

A. Efficacy of serotonin reuptake inhibitors in treating late life depression is similar to that of TCAs, though TCA side effects may be less tolerable.

B. For nonpsychotic late life depression, the combination of psychotherapy and medication is recommended.

C. Older adults are more vulnerable than younger adults to anticholinergic side effects of antidepressants.

D. Older adults typically take more concurrently prescribed medications than younger adults, necessitating careful attention to drug/drug interaction possibilities when an antidepressant is prescribed.

E. All of the above

Self-Assessment Question 5: Which of the following is not correct?

A. ECT is usually less efficacious than antidepressants in treating late life depression with psychotic features.

B. Intracranial mass lesion, recent CVA, or recent MI can complicate the safe administration of ECT.

C. Informing patient and family about potential memory disturbance associated with ECT will help them understand and tolerate this usually transient aspect of treatment.

D. Demented patients may experience intolerable cognitive worsening during the course of a series of ECT treatments.

E. Unilateral nondominant ECT is associated with fewer cognitive side effects.

Self-Assessment Question Answers

1. E
2. A
3. D
4. E
5. A

Suggested Further Reading

- Ellison JM, Kyomen H, Verma SK (eds): Mood Disorders in Later Life. Informa HealthCare, 2008.
- Lebowitz BD, Pearson JL, Schneider LS, et al. Diagnosis and treatment of depression in late life. Consensus statement update. JAMA. 278:1186-90, 1997.