



# **Recognizing and Treating Mood Disorders in Long Term Care**

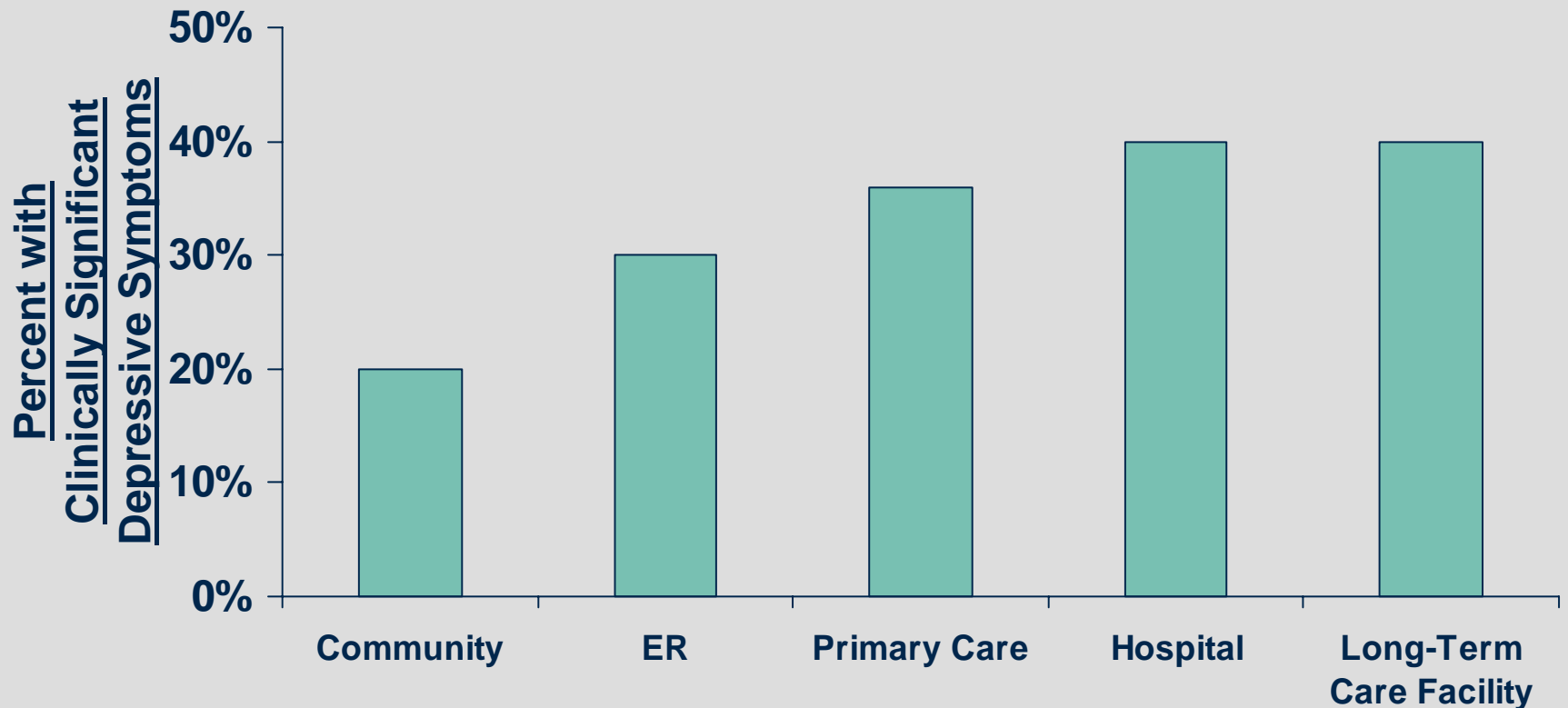
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# Nursing Home Demographics<sup>1</sup>

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- # 5% of the elderly live in nursing homes
  - 20-25% of elderly require nursing home care at some time
  - 22% of adults  $\geq$  85 years old
- # Number of nursing home residents will double after 2020 and triple by 2040
- # Prevalence of psychiatric disorders in nursing homes is 41-87%, but only 10% of mental health service needs are met

# Depressive Symptoms in Late Life: Prevalence by Setting



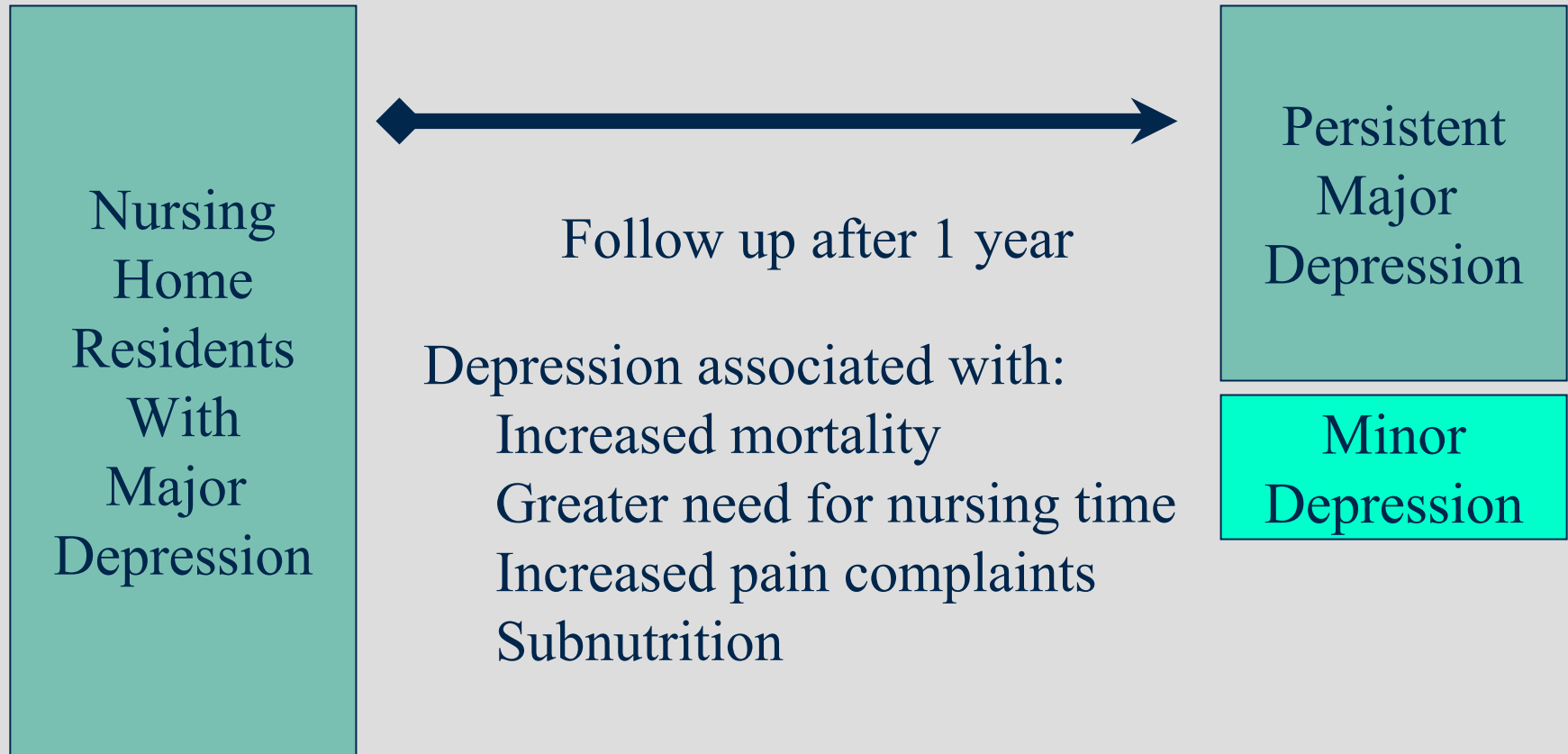
Koenig and Blazer, 1992; Fabacher, 2002; Alexopoulos, 1996; Koenig et al., 1997; Parmelee, 1989.

# Depression in Nursing Homes

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- Depressive sx's in nursing home: 11 – 50% <sup>1</sup>
- Major Depressive Disorder (MDD): 6 – 25% <sup>2</sup>
- MDD in demented residents: 10-33% <sup>3</sup>

# Persistence of Depression



# Inadequate Treatment of Depression in Nursing Homes

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- # 1992 study<sup>1</sup>: Only 10% of depressed nursing home residents received antidepressant medications
  - Neuroleptics/benzodiazepines prescribed more often than antidepressants
- # 2002 study<sup>2</sup>: 55% of depressed nursing home residents received antidepressants, but
  - Dose was below recommended minimum in 32% of these
  - Patients with severe cognitive impairment, black, or  $\geq 85$  years old were more likely to receive no antidepressant

# Consequences of Untreated Late Life Depression

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- # Functional decline / Increased disability<sup>1</sup>
- # Increased use of non-mental health services<sup>1</sup>
- # Increased morbidity and mortality rates<sup>2-5</sup>
- # Depression (depressive symptoms, Major Depressive Disorder) are associated with a 1.6 – 3x increase in mortality rate in LTC<sup>5</sup>

1. Beekman et al. 1997; 2. Penninx et al. 1999; 3. Frasure-Smith et al. 1993;  
4. House et al. 2001; 5. Katz and Parmelee 1997

# Depression in LTC Increases Mortality

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- # Mechanisms of increased mortality:
  - Reluctance to seek/accept treatment
  - Life-threatening behavior
  - Direct physiologic mechanisms
- # Specific increases measured in:
  - Suicide
  - MI mortality
  - CVA mortality

The image features a stylized illustration of a classroom. In the background, a whiteboard is visible with a red silhouette of a teacher standing in front of it, holding a pointer and a book. In the foreground, several stylized human figures in light blue and light green are arranged to represent an audience or students. The word "Assessment" is written in a large, bold, dark blue font across the center of the image.

# Assessment

# Non-Major Depressive Syndromes<sup>1</sup>

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- # Adjustment disorder with depressed mood
- # Minor depression
  - Subsyndromal Depression
  - Dysthymic disorder
- # Mood disorder due to a general medical condition, with depressive features
- # Substance induced mood disorder with depressive features
- # Anxiety disorder with depressive features
- # Major Depression in partial remission

# 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/other psych etiology**
- # **Significant distress or impairment**
- # **Not uncomplicated bereavement**

# Diagnostic Criteria: How Sensitive for Late Life MDD?

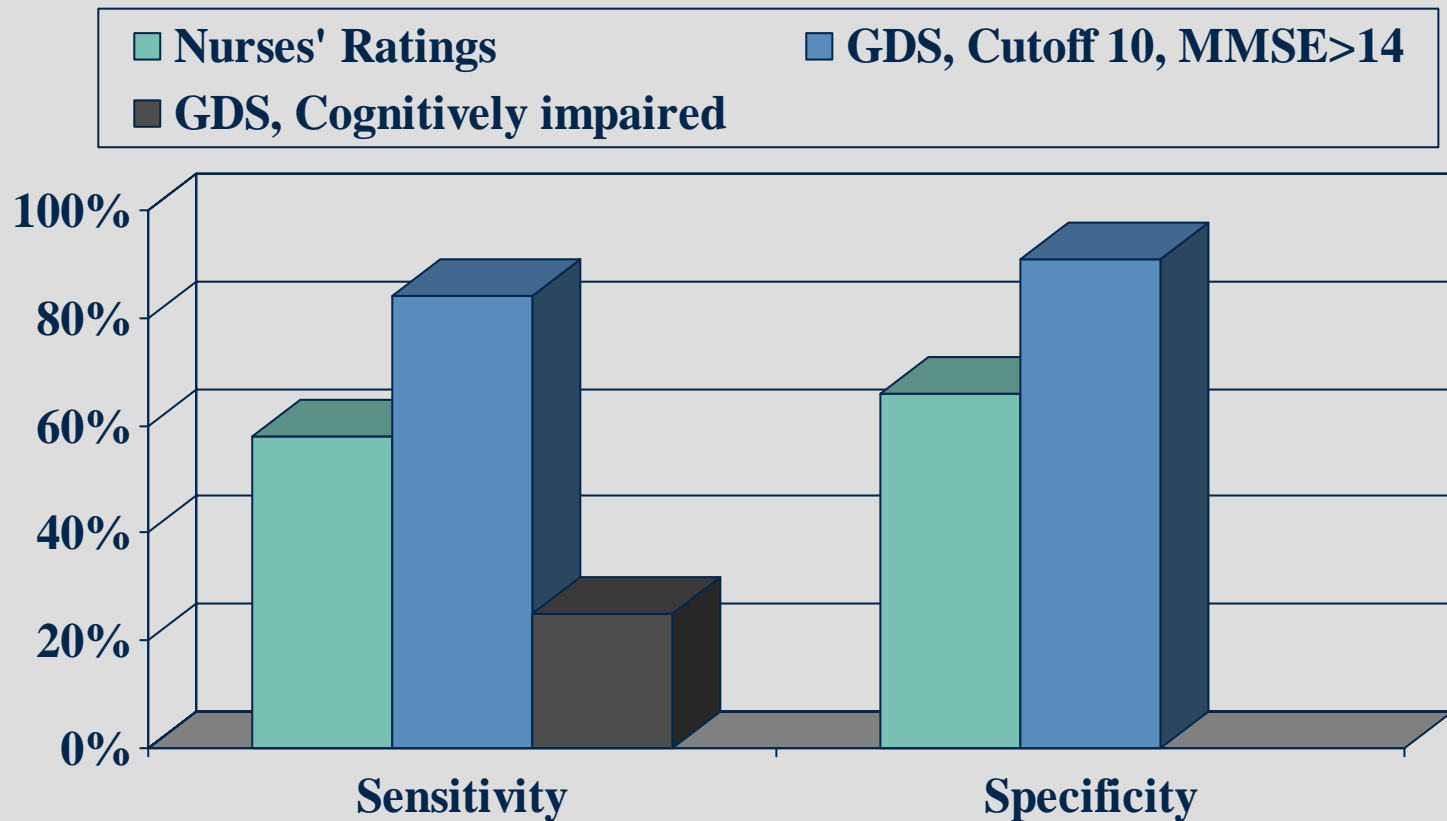
<u>Symptoms</u>	<u>18-44</u>	<u>65 +</u>
<b>Appetite disturbance</b>	<b>27%</b>	<b>16%</b>
<b>Sleep disturbance</b>	<b>25%</b>	<b>19%</b>
<b>Reduced energy level</b>	<b>18%</b>	<b>11%</b>
<b>Feelings of guilt</b>	<b>13%</b>	<b>5%</b>
<b>Concentration problems</b>	<b>16%</b>	<b>8%</b>
<b>Suicidal ideation</b>	<b>31%</b>	<b>22%</b>

# GDS 15

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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 ?

# Recognition of Depression in Nursing Home Residents



Katz and Parmelee 1997

# Provisional Criteria for Depression of Alzheimer's Disease

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## # 3 or more of following in 2 week period

- Depressed mood
- Decreased positive affect/pleasure in usual activities/contacts
  - Meets criteria for DAT
  - Distress or disruption
  - Not delirium, drug, medication, or better accounted for by other conditions
- Social isolation or withdrawal
- Disruption in appetite
- Disruption in sleep
- Psychomotor changes
- Irritability
- Fatigue/loss of energy
- Worthlessness, hopelessness, guilt
- Thoughts of death, SI or behavior

Olin et al. 2002

# “Masked” Depression in Demented LTCF Residents

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- # Delusions (OR 6.8)<sup>1</sup>
- # Verbal/physical aggressive behaviors<sup>2</sup>
- # Disruptive vocalizations<sup>3</sup>
- # Weight loss<sup>4</sup>

1. Bassiony et al. 2002; 2. Menon et al. 2001;
2. 3. Dwyer and Byrne 2000; 4. Morley and Kraenzle 1994

# CSDD: Components

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- # Mood
- # Behavioral disturbances
- # Physical signs
- # Cyclic functions
- # Ideational disturbances
- # Based on Clinician, Patient, and Consensus ratings, score  $\geq 7$  detects depression with sensitivity 90%, specificity 75%

from Alexopoulos et al. 1988

# Psychiatric/Medical History

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- # Use of informant
- # Prior episodes
- # Comorbid disorders, e.g. substance abuse
- # Atypical symptom presentation
- # Psychotic symptoms
- # Psychosocial factors
- # Medical factors

# Organic Differential Diagnosis

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- # Medication toxicities/ Substances
- # Cardiopulmonary disorders
- # Neurological disorders
- # Endocrine/Metabolic disorders
- # Nutritional deficiencies
- # Sleep disorders
- # Infectious disorders
- # Neoplasms
- # Psychosocial/Psychiatric

# Mental Status Examination

- # Appearance and self-care
- # Sensorium/Alertness
- # Speech
- # Baseline cognitive assessment
  - Memory
  - Executive functions
- # Variant presentations of mood disturbance
  - Weariness
  - Withdrawal
  - Anxiety
  - Irritability
- # Mental Content
  - Somatic preoccupations
  - Pain concerns
  - Delusions and/or hallucinations
  - Complaints re cognitive functioning

# Laboratory Assessment of Late Life Depression

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## # 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

## # Additional tests

# Ancillary Studies

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## # Neuropsychological Testing

- Memory
- Executive functions

## # Neuroimaging Studies

- Structural (CT, MRI)
- Functional (fMRI, SPECT, PET)

# White Matter Hyperintensities

- # Bright spots seen on T2 weighted images
- # Location of WMH in depression: **basal ganglia**<sup>1,2</sup> and **frontal deep white matter**<sup>2-4</sup>
- # Most replicated neuroimaging abnormality in late life depression -- correlated with CVRFs and with small vessel arteriosclerosis
- # WMH more common in late-onset than early-onset depression<sup>3</sup>
- # In depressed patients, WMH associated with impaired<sup>5-7</sup>:
  - Memory
  - Mental speed
  - Executive functioning

# Depression Executive Dysfunction Syndrome (DEDS)

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- # Executive dysfunction in late life depression is associated with:
  - Loss of interest in activities
  - Psychomotor retardation
  - Mild vegetative syndrome
  - Delayed or poor response to antidepressants
  - More residual symptoms
  - Higher rates of relapse and recurrence

# Is DEDS Treated Differently?

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- # 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<sup>1,2</sup>
- # D<sub>3</sub> agonists, modafinil, other novel agents may be of interest



# Treatment of Depression in LTC

# Psychotherapies for Older Adults

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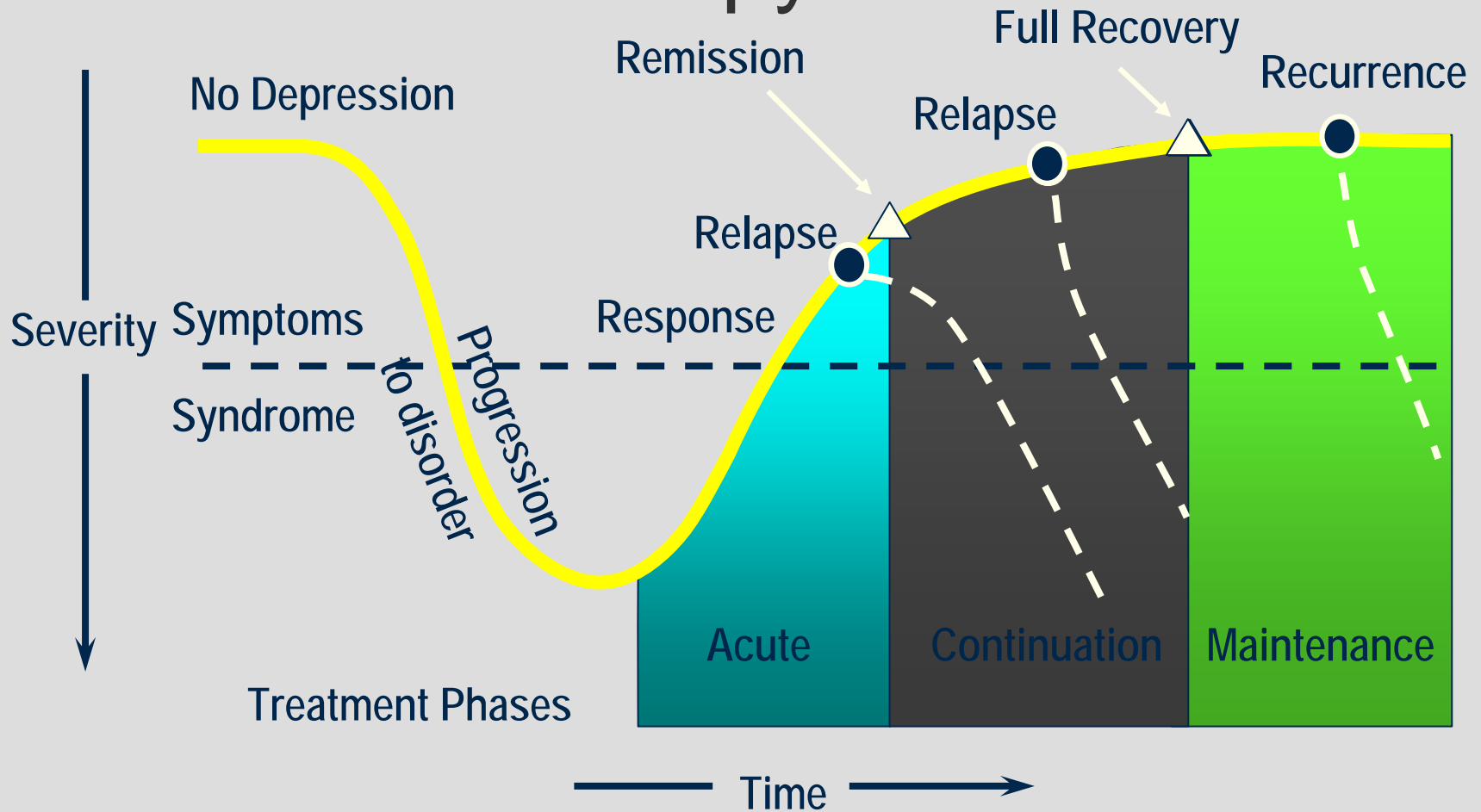
- # Interpersonal psychotherapy (IPT)
- # Cognitive behavior therapy (CBT)
- # Problem solving therapy(PST)
- # Brief psychodynamic therapy
- # Social Skills Training
- # Individualized Music Therapy
- # For Depression+AD patients:
  - IMT; Pleasant Events Schedule
  - Simulated Presence Therapy

# Age-Related Factors Inhibiting Therapeutic Engagement

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

# Depression: Course of Pharmacotherapy



from Kupfer, 1991

# Comparison of Medications by Mechanism/Receptor Binding

# TCA	→	NE/5HT reuptake inhibitors
# MAOI/RIMA	→	MAO inhibition
# SRI		
■ SSRIs	→	5HT reuptake inhibition
■ Venlafaxine	→	SNRI
■ Nefazodone	→	SARI
# Reboxetine	→	NRI
# Bupropion	→	NDRI
# Mirtazapine	→	SANPA

# Antidepressant Receptor Binding Profiles

	NE RI	5HT RI	$\alpha_2$ NE	$\alpha_1$ NE	ACh	H1	5HT <sub>2a</sub>	5HT <sub>3</sub>
<b>Amitriptyline</b>	+/-	+	+/-	+	+	+	+	-
<b>Nortriptyline</b>	+	+/-	-	+	+	+	-	-
<b>Imipramine</b>	+	+	-	+	+	+	-	-
<b>Desipramine</b>	+	-	-	+	+	-	-	-
<b>Paroxetine</b>	-	+	-	-	+	-	-	-
<b>Other SSRIs</b>	-	+	-	-	-	-	-	-
<b>Bupropion</b>	+	-	-	-	-	-	-	-
<b>Venlafaxine</b>	+	+	-	-	-	-	-	-
<b>Nefazodone</b>	-	+	-	+	-	-	+	-
<b>Mirtazapine</b>	-	-	+	-	+	+	+	+

# SSRI Tolerability > TCA Tolerability

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- # 11 RCT comparisons of antidepressants in elderly subjects suitable for metaanalysis of side effects
- # “Classical” TCAs had increased withdrawal rate (24.4%) vs SSRIs (18%)
- # TCA side effects: dry mouth, constipation, drowsiness, dizziness, lethargy
- # SSRI side effects: Nausea/vomiting, sleep disturbance

# Pharmacodynamic/Pharmacokinetic Considerations in Choosing an Antidepressant

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- # Enhanced vulnerability to anticholinergic side effects in elderly
- # Diminished hepatic drug metabolism leads to higher peak plasma levels
- # Diminished renal secretion results in higher plasma levels, extended elimination half-lives
- # Greater number of co-administered drugs increases risk of CYP450 interactions

# Some CYP450 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

# Antidepressant Choice Based on Pharmacokinetic and Pharmacodynamic Differences

	TCA			SRI						Others		
	Ami	Des	Nor	Flx	Ser	Pax	Flv	Cit, Esc	Nef	Ven	Bup	Mir
Anticholinergic effects	XX	X	X			X						X
Other unwanted neurotransmitter effects	XX	X	X						X			X
Narrow therapeutic range	X	X	X									
Very Short T <sub>1/2</sub>						X				X		
Long T <sub>1/2</sub> +/- active metabolites			X	X							X	
CYP450 interactions	X	X	X	X	x	X	X		X		x	

Ami=amitriptyline, Des=desipramine;Nor=nortriptyline;Flx=fluoxetine; Ser=sertraline;Pax=paroxetine; Flv=fluvoxamine;Cit=citalopram;Nef=nefazodone;Ven=venlafaxine;Bup=bupropion;Mir=mirtazapine

# Depression & AD: Positive Drug Trials (3 of 8 published RCTs)

- # In 6 wk RCT, n=726 inpatients with cognitive impairment (mostly AD) and depression by DSMIII & HAMD, HAMD improved with **moclobemide** dosed up to 400 mg/d max<sup>1</sup>
- # In 6 wk RCT, n=149 inpatients and outpatients with AD and depression by DSMIII & HAMD, **citalopram** 30 mg/d max showed HAMD effect vs placebo<sup>2</sup>
- # In 12 wk RCT, n=22 outpatients with DSMIV AD & Depression, **sertraline** 150 mg/d max showed CSDD but not HAMD effect vs placebo<sup>3</sup>

# Where Do MAOIs Fit In?

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- # Compelling evidence for efficacy of moclobemide
- # Some evidence for phenelzine
- # Side effect concerns
- # Drug/Food and Drug/Drug interactions

# Stimulants for Geriatric Depression

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- # Use remains controversial
- # Effect is often rapid
- # May be justified with:
  - apathy/psychomotor retardation
  - concurrent medical illness
  - intolerance of antidepressants
  - need for rapid response
- # Effect can be lasting

*Wallace et al 1995; Kaplitz 1975; Katon and Raskin 1980, Pickett et al. 1990; Askinazi et al. 1986*

# Electroconvulsive Therapy

- # Underused modality, especially suitable with:
  - Antidepressant intolerance or non-response
  - Prior positive response to ECT
  - Delusions
  - Catatonia
  - Bipolar states
  - Emergency
- # High response rates documented<sup>1-5</sup>
  - Associated with shorter time to remission
  - Paucity of large studies on safety and efficacy
- # Generally safe, but often a last-resort option

1. Seiner S, Henry ME. Chapter 10: Electroconvulsive therapy for the treatment of late life depression. In: Ellison JM, Verma SK, eds. *Depression in Later Life*. New York, NY: Marcel Dekker, Inc.;2003; 2. Bosworth HB, et al. *Am J Geriatr Psychiatry*. 2002;10(5):551-9; 3. Philibert RA, et al. *J Clin Psychiatry*. 1995;56(9):390-4; 4. Stoudemire A, et al. *Gen Hosp Psychiatry*. 1998;20(3): 170-4; 5. Cattan RA, et al. *J Am Geriatr Soc*. 1990;38(7):753-8.

# ECT and Medical Status Concerns

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- # **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<sup>1</sup>

# ECT and Memory Loss

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- # A major concern of patients and families
- # ECT may improve depression-impaired cognition but exacerbate impaired cognition of dementia
- # Preparation should include:
  - Psychoeducation of patient/family
  - Pre-screening of memory to establish baseline
  - Monitoring of memory throughout treatment course
  - Decreased treatment frequency when memory disturbance is pronounced
  - Use of unilateral treatment when reasonable

# Should “Vascular Depression” Be Treated Differently?

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- # Nortriptyline resistance (relapse/recurrence)<sup>1</sup>
  - was correlated with executive dysfunction
  - was NOT correlated with memory dysfunction or age
- # Does this reflect damage to CSPTC pathways?
- # Integrity of dopaminergic, cholinergic, and enkephalin neurotransmission in these pathways may be a differential therapeutic target. <sup>1</sup>

# Durations of Medication Trials: What do Experts Recommend?

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## # Duration of trial<sup>1</sup>:

- No response to high dose: 3.4 – 6.1 weeks
- Partial response to high dose: 4.1 – 7.5 weeks

## # In actual trials:

- Most symptoms did not improve significantly before the 4<sup>th</sup> week (phenelzine vs nortriptyline comparison)<sup>2</sup>
- In 40% of responders to nortriptyline, improvement was delayed up to 10 weeks<sup>3</sup>

# To Switch or To Augment?

- **Switch:** preferred to augmentation?
  - Simpler
  - Less costly
  - Avoids potential drug-drug interactions
  - Side effects fewer/more easily attributable
  - With side effect intolerance, may switch within class
  - Choice of “different mechanism” has been proposed
- **Augmentation**
  - Builds on current improvement in partial responders
  - Extends potentially successful current trial
  - Prevents discontinuation-related treatment delays
  - Evidence more convincing for  $\text{Li}_2\text{CO}_3$ <sup>13</sup> or T3<sup>14</sup>
  - Synergistic neurotransmitter effect is hypothesized

# SSRI-Nonresponse: What do Experts Recommend?

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- # When patient is SSRI-nonresponsive, SWITCH to:
  - Venlafaxine XR
  - Bupropion SR
  - Nortriptyline
  - Mirtazapine

# What Augmentors Do The Experts Recommend?

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- # When patient is partially SSRI-responsive, augment with:
  - Bupropion SR
  - Lithium carbonate
  - Nortriptyline
  - Mirtazapine
  - Desipramine
  - Stimulant
  - T3

# Augmentation with Atypical Antipsychotics

- # Two small studies available in younger adults
  - Risperidone open study, n=8, small doses, increased antidepressant response<sup>1</sup>
  - Olanzapine controlled trial, n=28 fluoxetine-treated patients randomized to olanzapine vs placebo, showed possible superiority over fluoxetine alone<sup>2</sup>
- # Limited support (36%) for addition of atypical antipsychotic to antidepressant in geriatric depression after 2 failed antidepressant trials<sup>3</sup>

1. Ostroff and Nelson 1999; 2. Shelton et al. 2001; 3. Alexopoulos et al: J Clin Psychiatry 2004;65 Suppl 2:5-99

# Poor Adherence Interferes with Treatment of Late Life Depression

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- # Nonadherence to pharmacologic treatment regimens (in general) reaches 60% in older adults.<sup>1</sup>
  - Factors associated with nonadherence:
    - AEs, complicated dosing regimens, cognitive impairment, stigma and insufficient info about mental illness/treatment, lack of family support, cost, poor doctor-patient alliance
  - Premature discontinuation of antidepressant is associated with an increased risk of relapse.

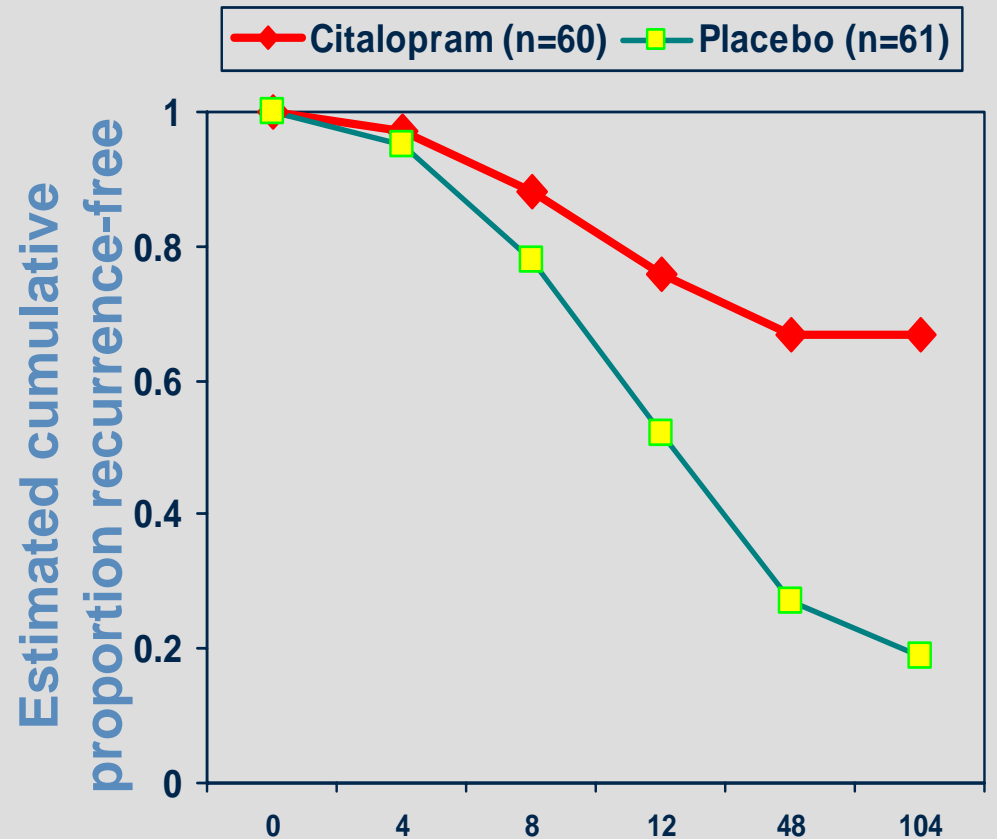
# Maintenance Treatment: What do Experts Recommend?

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

# Citalopram Prevents Depression Recurrence in Elderly

- N=121 outpatients  $\geq$  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



Week in double-blind period

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

# Mood Disorders in Long Term Care: Conclusions

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- # Depressive syndromes are very common and bipolar disorder also requires recognition
- # Mood disorders should not be considered a consequence of ageing or institutionalization
- # Careful differential diagnosis/assessment required
- # Psychotherapy, medications, ECT can be useful with careful dosing and close monitoring
- # Further studies are needed in this area

# For Further Questions

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