

# **Major Neurocognitive Disorder and Geriatric Depression: What's New in 2016?**

**Brent Forester, MD, MSc**

**Chief, Division of Geriatric Psychiatry,  
McLean Hospital**

**Medical Director, Behavioral Health Integration Program,  
Center for Population Health, Partners HealthCare**

**Assistant Professor of Psychiatry,  
Harvard Medical School**

# Disclosures

- Treasurer/Secretary and Member of the Board of Directors of the American Association for Geriatric Psychiatry (2016-17)
- Grants and Research Support Last Three Years:
  - NIMH
  - Rogers Family Foundation
  - Assurex, Eli Lilly, Biogen
- Consulting Last Three Years:
  - Sunovion Pharmaceuticals, Inc.; Eli Lilly

Dr. Forester will discuss unapproved or investigational use of pharmaceutical compounds.

# Outline

- ◆ General Principles of Geriatric Psychopharmacology
- ◆ Geriatric Depression - Management Strategies.
- ◆ Major and Mild Neurocognitive Disorders: Diagnosis, Biomarkers, Treatment and Prevention
- ◆ Management of the Behavioral and Psychological Symptoms of Dementia
- ◆ Risks Associated with Pharmacological Interventions
- ◆ Questions

# Principles of Geriatric Psychopharmacology

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- ◆ 1. Always develop a working diagnosis
- ◆ 2. Addition by subtraction
- ◆ 3. Start Low and Go Slow, BUT GO
- ◆ 4. Behavioral interventions and psychotherapy will augment treatment response

# Geriatric Depression: Overview

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- ◆ Affects 6 million Americans over the age of 65
- ◆ 1 in 6 patients in primary care practice setting
- ◆ **NOT** a normal fact of aging – Beware of Ageism Bias
- ◆ Associated with Functional Disability and Suicide
- ◆ Can alter risk and course of general medical conditions
- ◆ Side effects directly affect compliance
- ◆ A recurrent disorder that can be treated and diagnosed in primary care setting.

# Risk Factors for Late Life Depression

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- ◆ Medical Illness
- ◆ Self-report of poor health and disability
- ◆ Pain; Use of pain medication
- ◆ Cognitive Impairment
- ◆ Substance Abuse
- ◆ Financial difficulties
- ◆ Bereavement
- ◆ Isolation; dissatisfaction with social network

# Depression May Worsen Outcome of Many General Medical Conditions

Patient Population	Increased Morbidity	Increased Mortality
Post-MI <sup>1,2</sup>	✓	✓
CHF <sup>3,4</sup>	✓	✓
Nursing home patients <sup>5</sup>		✓
Post-stroke <sup>6</sup>	✓	

- Depression also may worsen outcomes of cancer, diabetes, AIDS, and other disorders<sup>7</sup>

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# Factors Contributing to Relapsing, Chronic Illness Course in Geriatric Depression

- ◆ Psychosocial factors:
  - Role transitions, bereavement, increasing dependency, interpersonal conflicts: RESPONDS WELL TO Interpersonal therapy (IPT)
- ◆ Progressive depletion of psychosocial and economic resources
- ◆ Chronic sleep disturbances
- ◆ Cerebrovascular Disease
- ◆ Neurodegenerative disorders
- ◆ Limited access to adequate treatment

# Tricyclic Antidepressants

- ◆ Amitriptyline, imipramine, nortriptyline, desipramine.
- ◆ Avoid as first line agents in elderly.
- ◆ Problems: orthostatic hypotension, anticholinergic SEs, cardiac conduction delays.

# SSRIs

- ◆ **Fluoxetine (Prozac)**
- ◆ **Sertraline (Zoloft)**
- ◆ **Paroxetine (Paxil)**
- ◆ **Citalopram (Celexa); Escitalopram (Lexapro)**
- ◆ **Fluvoxamine (Luvox)**
  - \***First line treatments for late life depression.**
  - \***Downside: can be activating initially.**
  - \***Instant relief of anxiety unlikely.**
  - \***2011 FDA citalopram warning: dose-dependent QT prolongation > 20 mg/day elderly**

# SNRIs (serotonin-norepinephrine reuptake inhibitors)

## Duloxetine (Cymbalta)

- **DBPCT in patients 65+ demonstrates improved cognition and mood, well tolerated<sup>1</sup>**
- **Dose: 60 mg/day**
- **Adverse event discontinuation rates = to placebo.**

## Venlafaxine (Effexor)

- **At higher doses (150 mg +) acts on both NE/Serotonin**
- **Downside: follow BP especially at higher doses.**
- **Few drug-drug interactions.**

# NaSSA

## (Noradrenergic and specific serotonergic antidepressant)

- Mirtazapine
  - Rapid improvement in sleep (antihistamine effect), anxiety (Blocks 5HT<sub>2</sub> post synaptic receptor).
  - Few GI (5HT<sub>3</sub> post synaptic blockade) and sexual side effects (5HT<sub>2</sub> Blockade).
  - Common side effects: weight gain, sedation.
  - Antidepressant effect still takes 4-6 weeks and is more effective at higher doses (30-45 mg).
  - Mirtazapine (30 mg) plus fluoxetine (20 mg), venlafaxine (225 mg) or bupropion (150 mg) achieved greater remission rates (46-58%) after 6 weeks vs. fluoxetine monotherapy (20 mg) (25%). Mean age mid-40s.
    - Among those who responded, double blind discontinuation of one agent led to relapse in 40% of cases<sup>1</sup>

# Stimulants for Geriatric Depression

- ◆ 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

# Depression/Executive Dysfunction Syndrome: Different Approach to Treatment?

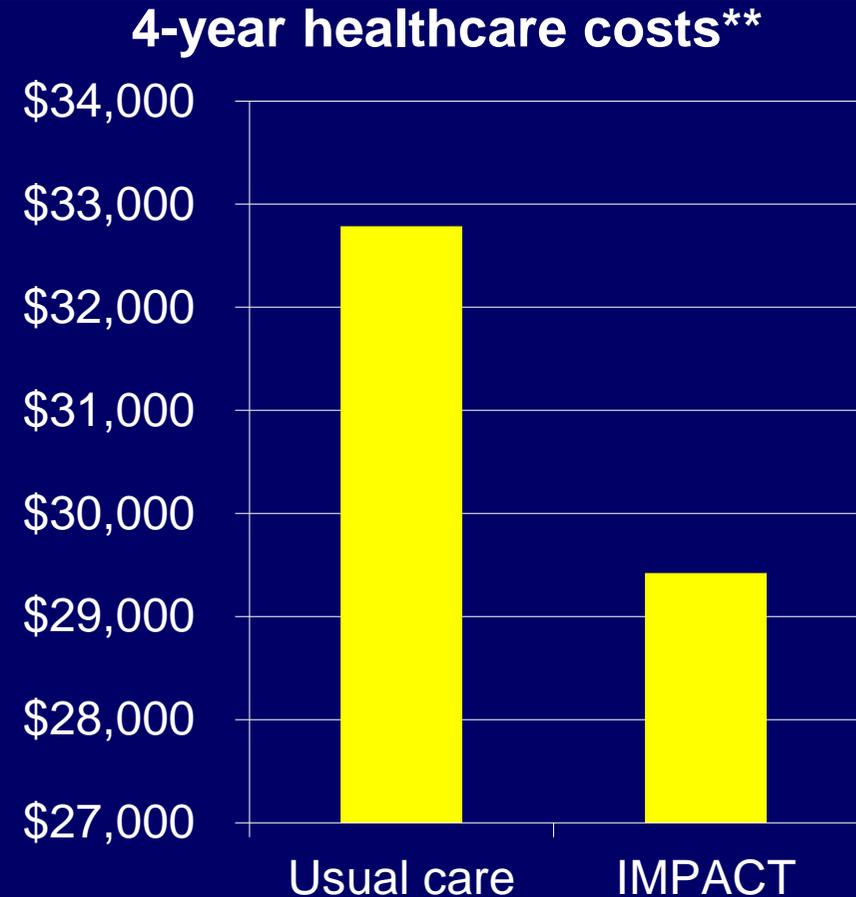
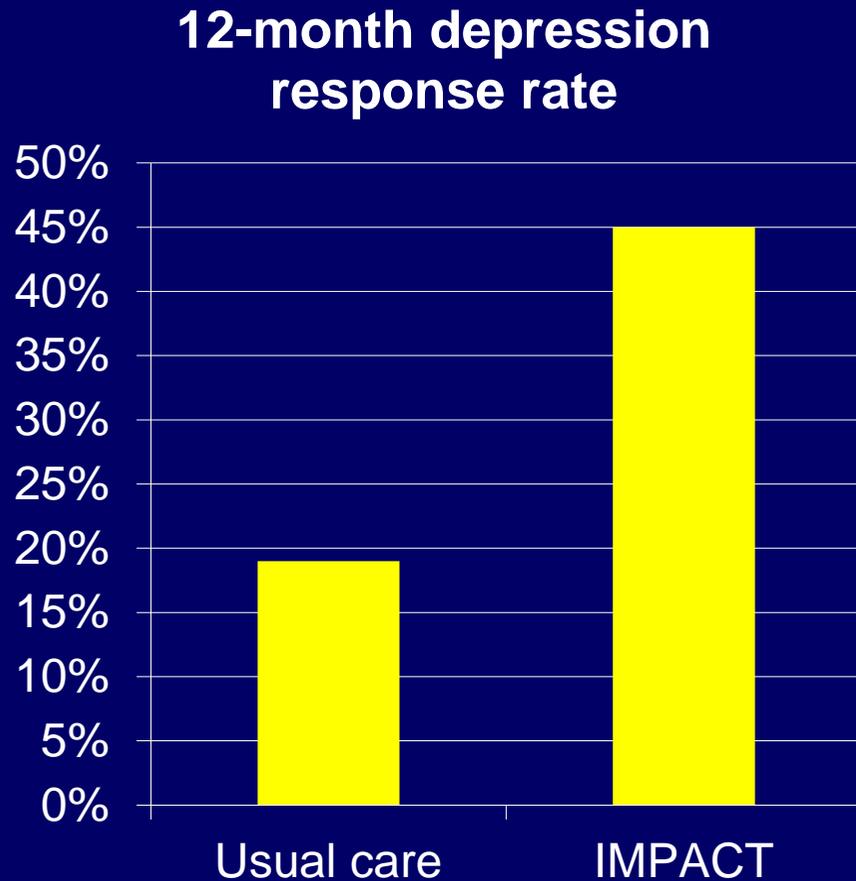
- ◆ **Executive dysfunction (as measured by impaired initiation/perseveration (IP) on DRS) but not memory impairment predicted:**
  - **Delayed antidepressant response<sup>1</sup>**
  - **Greater risk of relapse, recurrence and symptom fluctuation following response<sup>2</sup>**
- ◆ **White matter hyperintensities predicted executive dysfunction<sup>3,4</sup> and poorer treatment response<sup>4</sup> (but not in all studies<sup>5</sup>)**

# ECT

- ◆ **Geographic variation in usage.**
- ◆ **Likely underutilized in certain areas.**
- ◆ **Most effective treatment for severe depression, especially depression with psychosis.**
- ◆ **Think of ECT in patients with refractory depression plus not eating/suicidal.**

# What about Treatment of Geriatric Depression in Primary Care?

## IMPACT improves outcomes, saves money\*



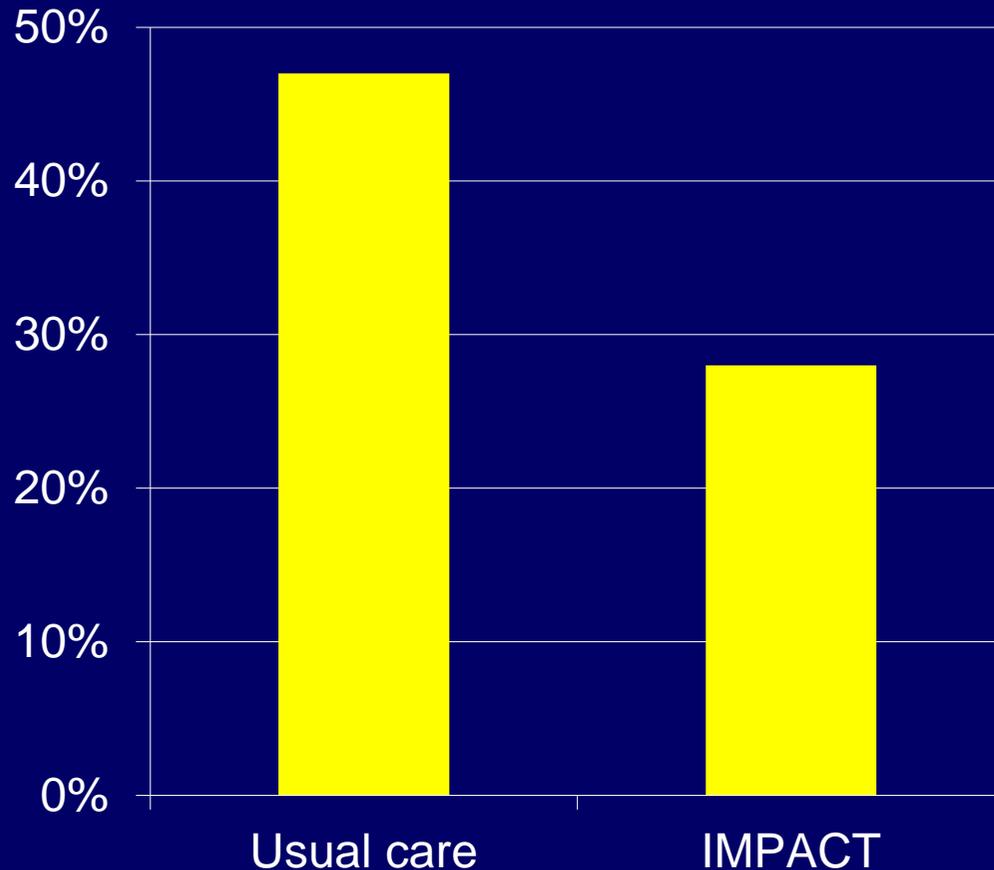
\* In a geriatric population

\*\* Includes intervention costs

Unutzer et al., 2002; Unutzer et al., 2008.

# IMPACT improves other health measures

Pts with hard cardiac events over 8 years (pts w/o baseline CVD)



- Improved physical functioning
- Decreased pain
- Reduced suicidal ideation (even long after intervention)
- Improved access to preferred treatment

# Conclusions Regarding Management of Geriatric Depression

- ◆ Treat to remission, not response
- ◆ If patients are partial responders at 6 weeks, they have a good chance to be full responders by 12 weeks: stay the course
- ◆ If patients are partial responders at 12 weeks, despite adequate dose: change medications
- ◆ Switching antidepressants is as effective as augmentation (about 50% will respond) but is associated with fewer side effects and lower costs.
- ◆ All patients, even those with first episodes, are candidates for at least one year, preferably two years of maintenance pharmacotherapy.<sup>1</sup>
- ◆ The dose that gets you well, keeps you well.

# Conclusions, Continued

- ◆ **Co-existing symptoms of anxiety pose risks for slow and incomplete response during acute treatment and for early recurrence during maintenance treatment. No evidence base for treating co-existing anxiety optimally in geriatric depression. Pay attention to residual symptoms of anxiety and poor sleep.**
- ◆ **Co-existing medical illness moderates response to long term treatment: patients with greater medical burden show more brittle recovery.**
- ◆ **Watch for caregiver depression: this also means burn-out in long term care clinicians**

# Major and Mild Neurocognitive Disorders

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- ◆ Redefining the Diagnostic Criteria
- ◆ Biomarkers
- ◆ Treatment strategies
- ◆ Prevention
- ◆ Pharmacotherapy of Behavioral Disorders in Dementia

# **Alzheimer's Disease: Redefining the Criteria**

**Pre-Clinical Alzheimer's Disease**

**MCI of Alzheimer's Disease**

**Dementia due to Alzheimer's  
Disease**

# **Mild Neurocognitive Disorder: DSM 5**

- ◆ Change in cognition
- ◆ Impairment in at least one cognitive domain
- ◆ Independence in functional abilities remain
- ◆ Cognitive assessment:
  - episodic memory impairment most frequent
- ◆ Etiology of MCI is consistent with AD pathology (rule out vascular, medical traumatic causes)
- ◆ Provide evidence of longitudinal decline
- ◆ Genetics consistent with AD (APOE4, PS1, PS2, APP)

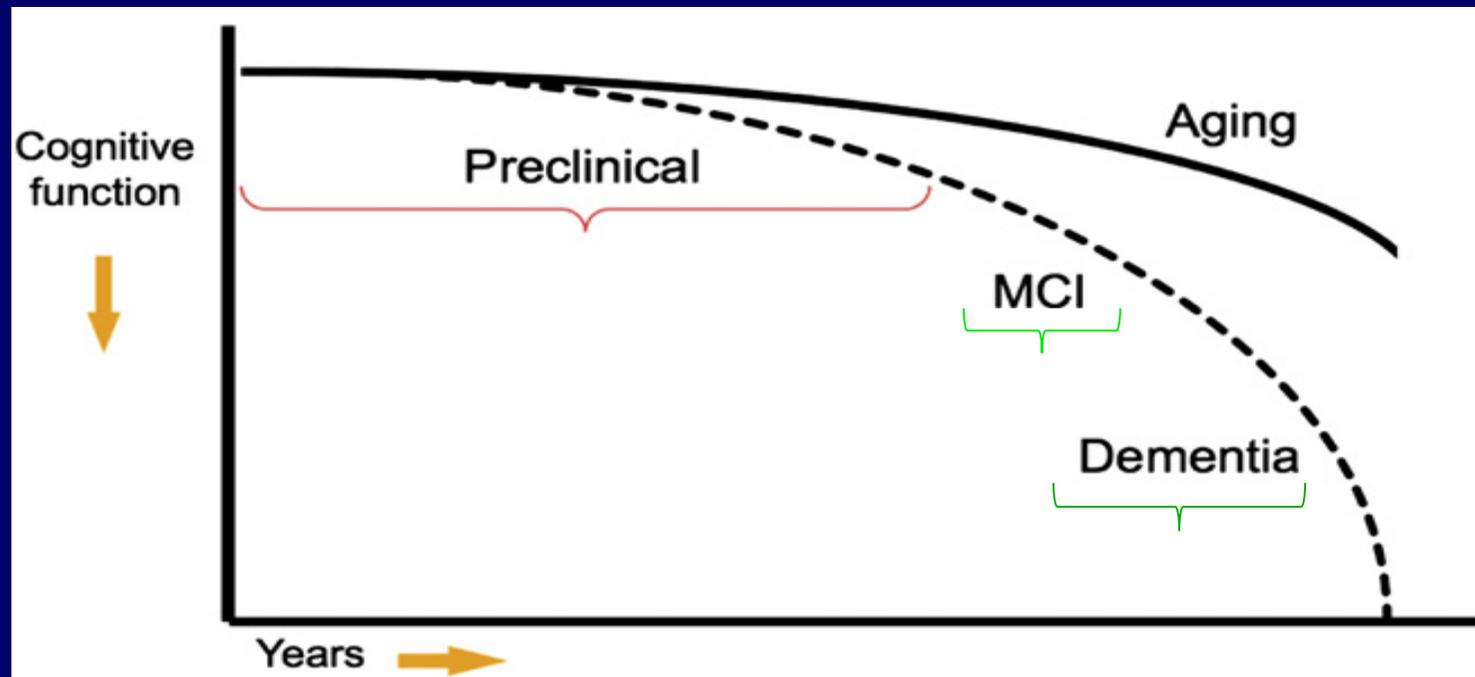
# Major Neurocognitive Disorder: DSM 5

- ◆ A. Evidence of significant cognitive decline from a previous level of performance in one or more areas of cognitive domains (complex attention, executive function, learning and memory, language, perceptual-motor or social cognition) based on:
  - ◆ 1. Concern of the individual, a knowledgeable informant or the clinician that there has been a significant decline in cognitive function; and
  - ◆ 2. substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.
- ◆ B. The cognitive deficits interfere with independence in everyday activities.
- ◆ C. The cognitive deficits do not occur exclusively in the context of a delirium.
- ◆ D. The cognitive deficits are not better explained by another mental disorder (e.g., major depressive disorder, schizophrenia).

# Continuum of Alzheimer's Disease

Normal

Alzheimer's disease



# PET Imaging

## Positron Emission Tomography (PET)

- Fluorodeoxy-glucose (sugar) measures brain activity; decreased with dementia
- Amyloid tracers detect amyloid without autopsy; increased in Alzheimer's

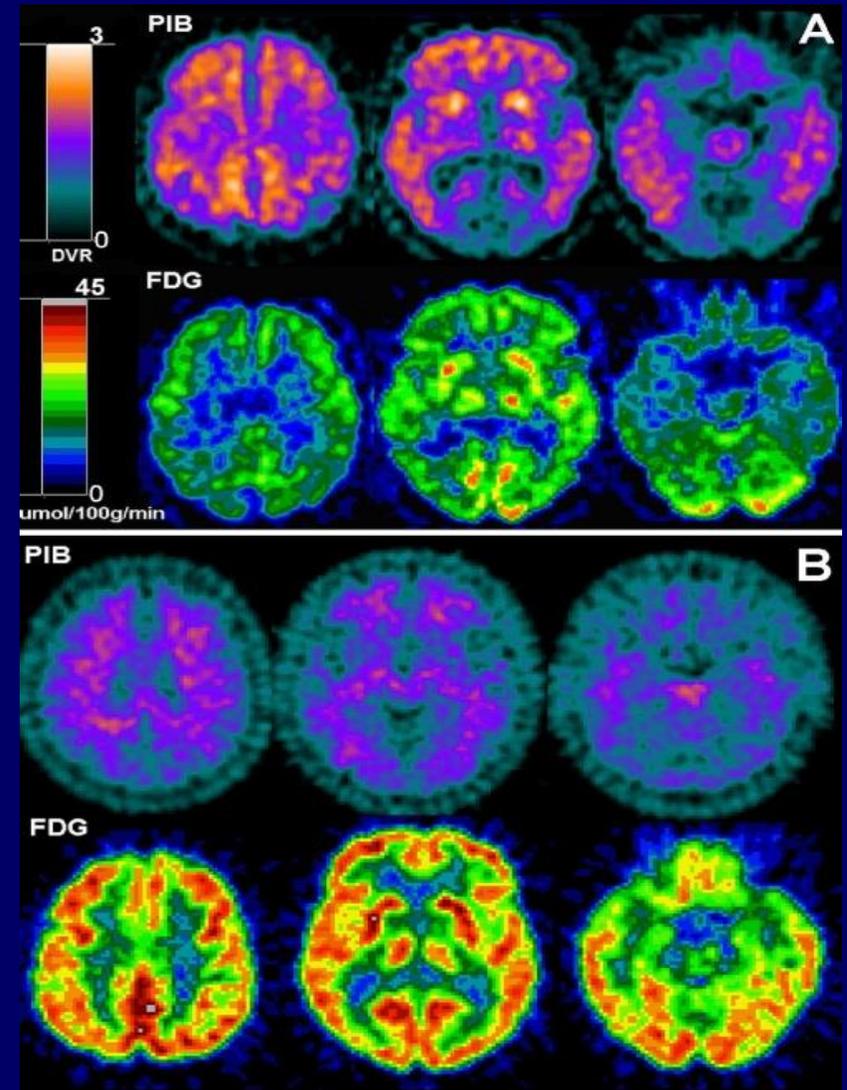
**AD**  
Amyloid

Sugar

**Normal**

Amyloid

Sugar

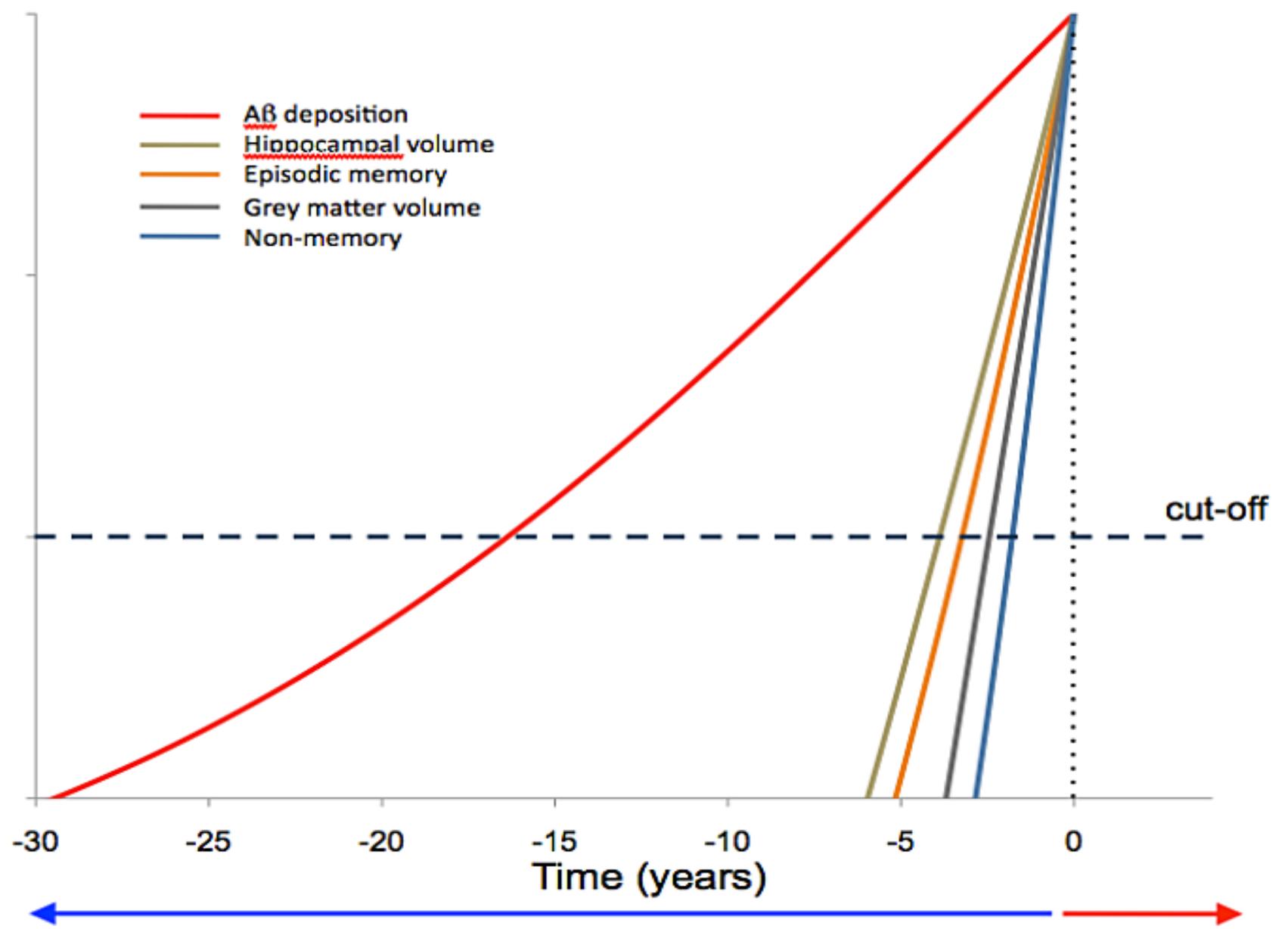


abnormal

CDR 1.0

- A $\beta$  deposition
- Hippocampal volume
- Episodic memory
- Grey matter volume
- Non-memory

normal



cut-off

-30      -25      -20      -15      -10      -5      0

Time (years)

non-demented

demented

# Irreversible Dementias

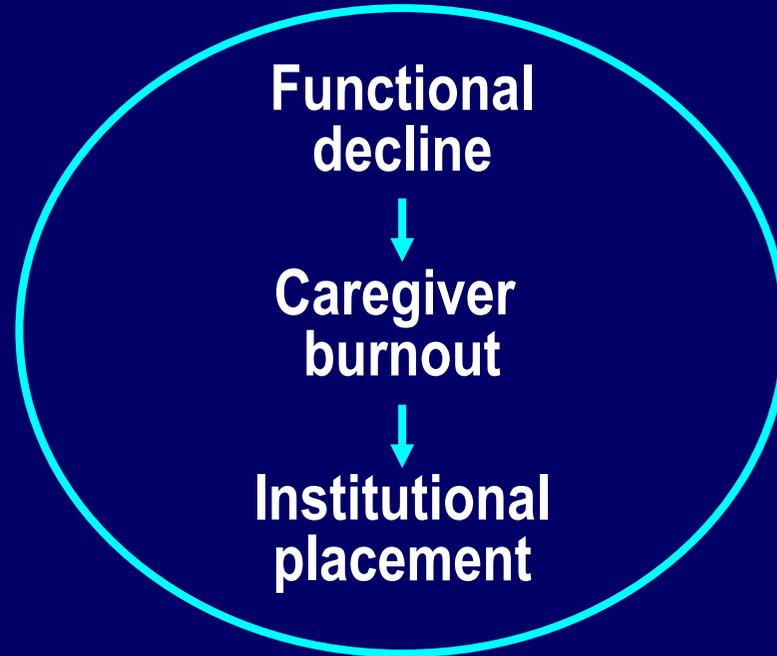
- ◆ Alzheimer's disease
- ◆ Vascular Dementia
- ◆ Lewy Body Dementia
- ◆ Frontotemporal Dementias (Pick's disease)
- ◆ Creutzfeldt-Jakob disease
- ◆ Parkinson's disease
- ◆ Huntington's disease
- ◆ AIDS dementia complex
- ◆ Progressive aphasia

# Diagnostic Evaluation of Dementia

- ◆ History from patient *and* relative or friend
- ◆ Clinical exam
- ◆ Blood work: CBC, Chem profile, Thyroid function tests, Syphilis serology, Vit B12, Folate
- ◆ Structural Brain Imaging: CT or MRI
- ◆ Neuropsychological testing
- ◆ Functional Imaging (SPECT or PET scan)
- ◆ EEG
- ◆ HIV Testing
- ◆ Genetics: APOE4
- ◆ CSF: tau, Amyloid beta 1-42

# Psychiatric Factors that Impact on the Trajectory of DAT

**Psychosis**  
Delusions  
Hallucinations  
Social withdrawal



**Cognitive deficits**  
Attention  
Memory  
Executive function

**Mood disorder**  
Depression  
Mania  
Bipolar illness

**Co-morbidity**  
Medical illness  
Movement disorders  
Substance abuse

**Non-cognitive deficits**  
Aggressiveness  
Agitation  
Behavioral disturbance

# The Cholinesterase Inhibitors: Indications and Uses

Medication	FDA Indication	Off-Label Uses
Aricept (donepezil)	Mild, moderate, and severe AD	<ul style="list-style-type: none"> <li>*MCI</li> <li>*Non-AD dementias               <ul style="list-style-type: none"> <li>-DLB</li> <li>-Vascular</li> <li>-PD</li> <li>-Huntington's</li> <li>-FTD</li> </ul> </li> <li>-Psychotropic-induced memory disturbance</li> <li>-ADHD</li> <li>-Attentional sx in PDD</li> <li>-Mania</li> <li>-Augmentation in negative symptom schizophrenia</li> <li>-TBI</li> <li>-ECT recovery</li> </ul>
Exelon (rivastigmine)  Also patch	Mild to moderate AD	
Razadyne (galantamine)	Mild to moderate AD	

# The Cholinesterase Inhibitors: Differentiating Characteristics

	Donepezil	Rivastigmine*	Galantamine and “ER”
<b>Dosage Strengths (mg)</b>	5,10,23 mg	1.5,3,6	4,8,12 ER: 8,16,24
<b>Oral Solution</b>	1 mg/ml	2 mg/ml	4 mg/ml
<b>Starting Dose</b>	5 mg q d	1.5 mg bid	4 mg bid
<b>Maximum Recommended Dose</b>	10 mg q d	6 mg bid	8 or 12 mg bid ER: 16 or 24 mg q d
<b>T<sub>1/2</sub> (hours)</b>	73	5	6 to 8
<b>Plasma protein binding</b>	96%	40%	18%
<b>CYP450 substrate of</b>	2D6/3A4	NA	2D6/3A4
<b>CYP450 inhibitor of</b>	NA	NA	NA

**Exelon Patch:** 4.6 mg/24 hours for 4 weeks, then 9.5 mg/24 hours, up to 13.3 mg/24 hours.

# Clinical/Safety Issues

- ◆ **Before use, assess medical and psychosocial factors**
- ◆ **Side effects lower with slower titration**
  - **Common: nausea, vomiting, dyspepsia, anorexia, diarrhea, insomnia, fatigue, increased urination, cramps**
  - **Uncommon: syncope, bradycardia, confusion, depression, agitation**
- ◆ **Caution with liver/ gastric disease, COPD, bradycardia, inadequate supervision of adherence**
- ◆ **Dropout due to adverse event in 7-32% of patients in clinical trials (vs. placebo 1-8%)**

# Goals of Therapy with Cholinesterase Inhibitors

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- ◆ Delay cognitive decline
- ◆ Delay functional decline
- ◆ Treat and/or prevent development of behavioral symptoms
- ◆ Don't expect a cure
- ◆ Downhill slope of illness will continue, yet quality of life may likely improve

# Memantine - NMDA antagonist

- ◆ Approved in Europe 2002, U.S. October 2003
- ◆ Moderate affinity NMDA antagonist
- ◆ Half Life: 60-80 hours
- ◆ Renally excreted (serum level may rise with renal insufficiency and alkalinization of urine)
- ◆ Minimal Hepatic P450 metabolism and interactions
- ◆ Dosing: 5 mg/day up to 10 mg twice daily over 4 weeks
- ◆ Namenda XR 28 mg once daily dosage formulation:
  - 7 mg/day up to 28 mg/day over 4 weeks

# Update on AD Research

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# Aducanumab

- ◆ Biogen Phase Ib Trial reported March 20, 2015
- ◆ 166 subjects with mild AD
- ◆ Significant cognitive advantages on CDR-SB and MMSE after 54 weeks
- ◆ Highest dose produced greatest clinical benefit and highest percentage of ARIA-E (amyloid related imaging abnormalities-sulcal effusion)
- ◆ Phase III Trials began Fall, 2015
- ◆ Clinical Trials Information:
  - <http://www.alzforum.org/therapeutics>

# Amyloid Prevention Trials

- ◆ **Anti-Amyloid Treatment in Asymptomatic AD (A4) (ADCS)**
  - asymptomatic cognitively normal older adults. Biomarker evidence of disease used to enroll high risk individuals and follow treatment effects
  - Solanezumab

# IDEAS Study

## Imaging Dementia-Evidence for Amyloid Scanning

- ◆ The IDEAS Study was developed in response to the 2013 CMS Decision on amyloid PET imaging in dementia:
  - “the evidence is insufficient to conclude that the use of positron emission tomography (PET) amyloid-beta (A $\beta$ ) imaging is reasonable and necessary for the diagnosis or treatment of illness or to improve the functioning of ... Medicare beneficiaries with dementia or neurodegenerative disease.”
- ◆ 18,488 Medicare beneficiaries age 65 and older, referred by dementia specialist. Must meet approved use criteria (AUC).
- ◆ Enrollment began February, 2016 and will continue over 24 months at roughly 200 U.S. sites.
- ◆ Study participants will be recruited into one of two sub-groups: (1) progressive, unexplained MCI, and (2) dementia of uncertain cause.
- ◆ Aims: To determine if Amyloid PET improves diagnostic assessment, impacts treatment decisions and improves health outcomes

# Behavioral Symptoms of Dementia Definitions

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- ◆ **The Psychosis of AD (Jeste and Finkel)**
- ◆ **Neuropsychiatric Symptoms of AD**
- ◆ **BPSD (Behavioral and Psychological Symptoms of Dementia)**
- ◆ **Includes:**
  - **agitation, aggression, wandering, delusions, hallucinations, repetitive vocalizations, mood disturbances.**

# The DICE Approach



Describe

Investigate

Create

Evaluate

- Caregiver describes problematic behavior
  - Context (who, what, when and where)
  - Social and physical environment
  - Patient perspective
  - Degree of distress to patient and caregiver
- Provider investigates possible causes of problem behavior
  - Patient
    - Medication side effects
    - Pain
    - Functional limitations
    - Medical conditions
    - Psychiatric comorbidity
    - Severity of cognitive impairment, executive dysfunction
    - Poor sleep hygiene
    - Sensory changes
    - Fear, sense of loss of control, boredom
  - Caregiver effects/expectations
  - Social and physical environment
  - Cultural factors
- Provider, caregiver and team collaborate to create and implement treatment plan
  - Respond to physical problems
  - Strategize behavioral interventions
    - Providing caregiver education and support
    - Enhancing communication with the patient
    - Creating meaningful activities for the patient
    - Simplifying tasks
    - Ensuring the environment is safe
    - Increasing or decreasing stimulation in the environment
- Provider evaluates whether “CREATE” interventions have been implemented by caregiver and are safe and effective

Consideration of Psychotropic Use (Acuity/Safety)

# Conventional Antipsychotics in Dementia

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- ◆ Limited efficacy, substantial toxicity
- ◆ Associated with a risk of falls
- ◆ Cardiac toxicity (i.e., thioridazine)
- ◆ Associated with EPS
  - Parkinsonism (bradykinesia, rigidity, tremor)
  - Akathisia
  - Tardive dyskinesia: 28% after 1 year, 50% after 2 years, 63% after 3 years

# Atypical Antipsychotic Dosing in Dementia

- ◆ Risperidone: 0.5-2.0 mg/day
- ◆ Olanzapine : 2.5 mg-10 mg/day
- ◆ Quetiapine: 25 mg-200 mg plus per day
- ◆ Aripiprazole: 5-10 mg/day
- ◆ Clozapine, Ziprasidone, Paliperidone, Asenapine, Iloperidone, Lurasidone: Insufficient Data.
- ◆ TD incidence<sup>1</sup>:
  - Risperidone (1 mg/day): 1 year: 5.3%; 2 year: 7.2%
  - Olanzapine (4.3 mg/day): 1 year: 6.7%; 2 year: 11%

# Atypical Antipsychotics and Cerebrovascular Adverse Events

- ◆ **Class warning for elevated risk of cerebrovascular adverse events**
  - **Risperidone (3.8%) vs. Placebo (1.5%); N=1230**
  - **Olanzapine (1.3%) vs. Placebo (.4%); N=1882**
  - **Aripiprazole (1.3%) vs. Placebo (.6%); N=938**
  - **Quetiapine (0.3%) vs. Placebo (1.9%); N=568**
  - **Excellent Review:**
- ◆ **Sacchetti, et al. Cerebrovascular Accidents in Elderly People Treated with Antipsychotic Drugs: A Systematic Review. Drug Saf 2010; 33 (4): 273-288.**

# FDA Warning on Mortality: Atypical Antipsychotics

- ◆ Announced April 11, 2005
- ◆ **Boxed Warning:** atypical antipsychotics used to treat dementia-related psychosis carry an “increased risk of death compared with placebo”
- ◆ 17 PCTs reviewed enrolling 5106 elderly pts with dementia related behavioral disorders
- ◆ Rate of death in drug treated patients was 4.5% vs. 2.6% in placebo group
- ◆ Risk of death 1.6 to 1.7 times that seen in placebo group
- ◆ Cause of death - heart related or infectious
- ◆ Four drugs involved in trials: aripiprazole, olanzapine, risperidone, quetiapine
- ◆ 7 medications will have warning including clozapine, ziprasidone and Symbyax (olanzapine/fluoxetine)
- ◆ 2008: Warning extended to conventional antipsychotics

# **THE AMERICAN PSYCHIATRIC ASSOCIATION PRACTICE GUIDELINE ON THE USE OF Antipsychotics to Treat Agitation OR Psychosis IN Patients WITH Dementia**

## **Guideline Writing Group**

Victor I. Reus, M.D., *Chair* Laura J. Fochtmann, M.D., M.B.I., *Vice-Chair*

A. Evan Eyler, M.D., M.P.H. Donald M. Hilty, M.D. Marcela Horvitz-Lennon, M.D., M.P.H. Michael D. Jibson, Ph.D., M.D. Oscar L. Lopez, M.D. Jane Mahoney, Ph.D., R.N., PMHCNS-BC Jagoda Pasic, M.D., Ph.D. Zaldy S. Tan, M.D., M.P.H. Cheryl D. Wills, M.D.

## **Systematic Review Group**

Laura J. Fochtmann, M.D., M.B.I. Richard Rhoads, M.D. Joel Yager, M.D.

## **APA Steering Committee on Practice Guidelines**

Michael J. Vergare, M.D., *Chair* Daniel J. Anzia, M.D., *Vice-Chair* Thomas J. Craig, M.D. Deborah Cowley, M.D. Nassir Ghaemi, M.D., M.P.H. David A. Kahn, M.D. John M. Oldham, M.D. Carlos N. Pato, M.D., Ph.D. Mary S. Sciotto, M.D.

## **Assembly Liaisons**

John P.D. Shemo, M.D., *Chair of Area Liaisons* John M. de Figueiredo, M.D. Marvin Koss, M.D. William M. Greenberg, M.D. Bhasker Dave, M.D. Robert M. McCarron, D.O. Jason W. Hunziker, M.D.

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## APA Guidelines 2016

### **Assessment of Benefits and Risks of Antipsychotic Treatment for the Patient**

**Statement 5.** APA recommends that nonemergency antipsychotic medication should only be used for the treatment of agitation or psychosis in patients with dementia when symptoms are severe, are dangerous, and/or cause significant distress to the patient. (1B)

**Statement 6.** APA recommends reviewing the clinical response to nonpharmacological interventions prior to nonemergency use of an antipsychotic medication to treat agitation or psychosis in patients with dementia. (1C)

**Statement 7.** APA recommends that before nonemergency treatment with an antipsychotic is initiated in patients with dementia, the potential risks and benefits from antipsychotic medication be assessed by the clinician and discussed with the patient (if clinically feasible) as well as with the patient's surrogate decision maker (if relevant) with input from family or others involved with the patient. (1C)

## Dosing, Duration, and Monitoring of Antipsychotic Treatment

*Statement 8. APA recommends that if a risk/benefit assessment favors the use of an antipsychotic for behavioral/psychological symptoms in patients with dementia, treatment should be initiated at a low dose to be titrated up to the minimum effective dose as tolerated. (1B)*

*Statement 9. APA recommends that if a patient with dementia experiences a clinically significant side effect of antipsychotic treatment, the potential risks and benefits of antipsychotic medication should be reviewed by the clinician to determine if tapering and discontinuing of the medication is indicated. (1C)*

*Statement 10. APA recommends that in patients with dementia with agitation or psychosis, if there is no clinically significant response after a 4-week trial of an adequate dose of an antipsychotic drug, the medication should be tapered and withdrawn. (1B)*

## APA Guidelines 2016

*Statement 12. APA recommends that in patients with dementia who show adequate response of behavioral/psychological symptoms to treatment with an antipsychotic drug, an attempt to taper and withdraw the drug should be made within 4 months of initiation, unless the patient experienced a recurrence of symptoms with prior attempts at tapering of antipsychotic medication. (1C)*

*Statement 13. APA recommends that in patients with dementia whose antipsychotic medication is being tapered, assessment of symptoms should occur at least monthly during the taper and for at least 4 months after medication discontinuation to identify signs of recurrence and trigger a reassessment of the benefits and risks of antipsychotic treatment. (1C)*

# Antidepressants in Dementia with Agitation

- ◆ 6 RCTs with sertraline, citalopram, fluoxetine and trazadone
- ◆ Citalopram vs. Risperidone 12 week study for treatment of agitation and psychosis in hospitalized dementia patients.<sup>1</sup>
  - No efficacy differences on NBRs.
  - Equivalent EPS, more sedation with risperidone.
- ◆ CitAD Study: Citalopram more effective than placebo in treatment of agitation in dementia (NBRs). 3 weeks. Dosages greater than 20 mg/day associated with worsening cognition and QTc prolongation<sup>2</sup>
- ◆ DIADS-2 Study: sertraline not effective for depression in AD at 12 week or 24 week endpoints<sup>3</sup>

# Safety and utility of acute electroconvulsive therapy for agitation and aggression in dementia

Deepa Acharya<sup>1,2</sup>, David G. Harper<sup>1</sup>, Eric D. Achtyes<sup>3</sup>, Stephen J. Seiner<sup>4</sup>, Jack A. Mahdasian<sup>3</sup>, Louis J. Nykamp<sup>3</sup>, Lesley Adkison<sup>5</sup>, Lori Van der Schuur White<sup>3</sup>, Shawn M. McClintock<sup>6,7</sup>, Manjola Ujkaj<sup>4</sup>, Donald A. Davidoff<sup>8</sup> and Brent P. Forester<sup>1</sup>

Table 1 Demographics and clinical characteristics ( $n = 23$ )

	Mean (SD)	N (%)
Age	73.8 (9.2)	
Education	13.9 (2.6)	
Gender		
Female	n/a	14 (60.1)
Race		
Caucasian	n/a	23 (100)
Diagnoses	n/a	
Alzheimer's disease		13 (56.5)
Vascular dementia		4 (17.4)
Mixed dementia		2 (8.7)
Frontotemporal dementia		1 (4.3)
Dementia NOS		3 (13.0)
No. ECT treatments	9.4 (range: 5–14)	
RUL		17 (73.9)
RUL to BL		2 (8.7)
BL		4 (17.4)
No. of days on unit pre-ECT	27.9 (20.1)	
Total no. of days on unit	57.3 (28.2)	
Continuation ECT recommended	n/a	15 (65.2)

NOS, not otherwise specified; ECT, electroconvulsive therapy; RUL, right unilateral; BL, bilateral; n/a, not applicable.

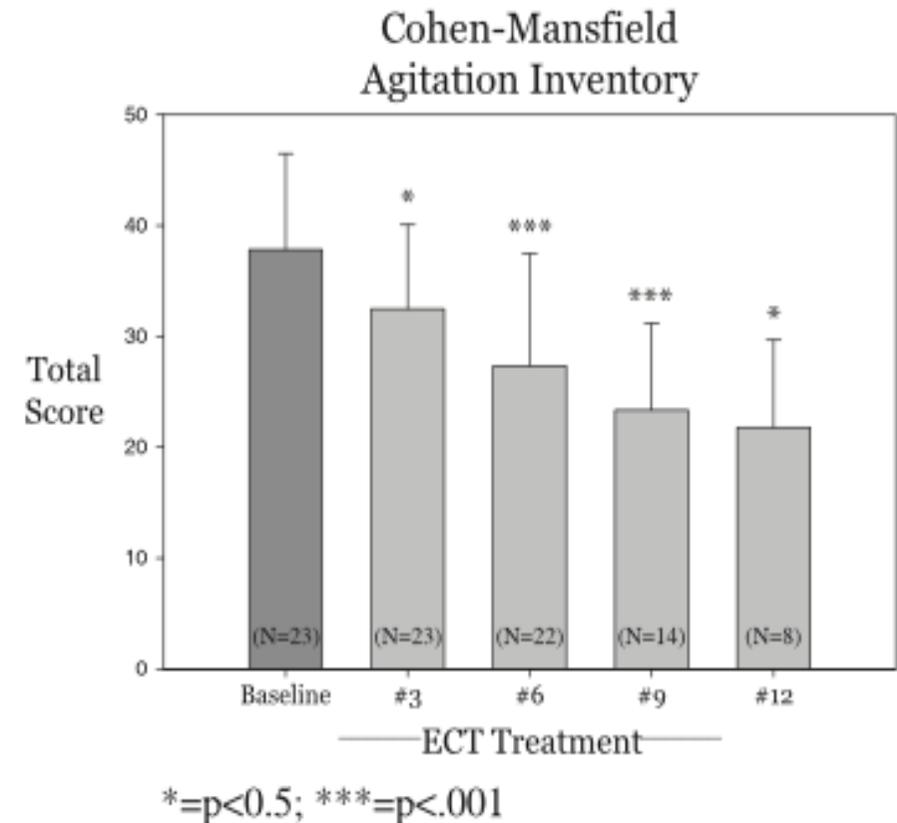


Figure 1 Cohen-Mansfield Agitation Inventory.

# **Dronabinol for the Treatment of Agitation and Aggressive Behavior in Acutely Hospitalized Severely Demented Patients with Noncognitive Behavioral Symptoms**

*Matthew R. Woodward, B.A.,  
David G. Harper, Ph.D.,  
Arkadiy Stolyar, M.D.,  
Brent P. Forester, M.D., M.Sc.,  
James M. Ellison, M.D., M.P.H.*

**40 inpatients with dementia complicated by agitation**

**Treated with dronabinol up to 10 mg/day (mean dose 7 mg/day) for 17 days**

**Significant reduction on Pittsburgh Agitation Scale (PAS) total scores and subscales of physical and verbal agitation/resisting care (p<0.0001)**

**No adverse effects led to drug discontinuation**

**Sedation (n=9), delirium (n=4), urinary tract infection (n=3), and confusion (n=2) most frequent AEs**

# Benzodiazepines

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- ◆ Minimal efficacy data
- ◆ Sedating
- ◆ Further inhibit learning and memory
- ◆ Cause falls
- ◆ Paradoxical disinhibition

# Summary

## Geriatric Depression

- Often subsyndromal with higher prevalence rates in medically compromised individuals
- Associated with high morbidity and mortality in conjunction with co-morbid medical illness
- SSRIs, SNRIs, Mirtazapine treatments of choice
- Short term psychotherapies effective (CBT, IPT, PST)

## Major and Mild Neurocognitive Disorders

- Early diagnosis is key
- Treatment to focus on cognitive, functional and behavioral symptoms
- Goal of treatment to stabilize symptoms, enhance quality of life and support caregiver all in an effort to enhance independence
- Prevention trials underway