Alzheimer’s disease: balancing cure with care

Lessons from Johns Hopkins

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Dementia has higher societal and economic impact than other important chronic diseases. NIH research funding lags far behind.

<table>
<thead>
<tr>
<th></th>
<th>Annual ($bn)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Care</td>
</tr>
<tr>
<td>Heart disease</td>
<td>$102</td>
</tr>
<tr>
<td>Cancer</td>
<td>$77</td>
</tr>
<tr>
<td>Dementia</td>
<td>$109</td>
</tr>
</tbody>
</table>


Objectives

• Overview of challenges in developing a cure

• Where did Dementia Care come from?

• Practically illustrate ‘Dementia Care’
35.5 million people have dementia today
The number of living cases doubles every 20 years
115.3 million people with dementia by 2050—NEW CASES
Major causes of dementia

- Alzheimer disease
- Lewy body diseases (Parkinson ++)
- Frontotemporal degeneration
- Brain vascular disease
  - Large infarcts, “microbleeds,” insufficiency
- OVER 80 other proposed causes
- MOST CASES MIXED, esp “OLD-OLD”
Alzheimer’s disease: the current “amyloid hypothesis”

Amyloid protein builds up in brain

Many processes triggered

Tau altered in nerve cells

Nerve cells die

Symptoms
Treatment under “amyloid hypothesis”

- Amyloid protein builds up in brain
- Stop/reduce amyloid production
- Many processes triggered
- Tau altered in nerve cells
- Nerve cells die
- Symptoms

Prevent build up or remove amyloid
Failures of “anti-amyloid” therapies

NULL—comparable to placebo
• Alzhemed: anti-plaque formation (Neurochem)
• Flurizan: anti-plaque formation (Myriad)
• Bapineuzamab: removal (J+J/Pfizer/Elan)
• Solaneuzumab: removal (Lilly)
• BMS708163: removal (Bristol Meyers Squibb)

NEGATIVE—worse than placebo
• LY450139: GSI anti-amyloid production (Lilly)
• RAGE Inhibitor: removal (Pfizer)
Future tests of the amyloid hypothesis

- Different drugs

- Earlier stages, especially asymptomatic will require biomarkers to target & assess
Facing reality: balancing “cure” with “care”

- Rational treatment development ongoing in AD
- Use of biomarkers is critical and evolving
- A long, hard slog: decades?

- **Near and medium term outcome**: extend the time course of MCI and dementia

- We must take proper care of 100+ million patients & caregivers worldwide
“There exists currently an effective, systematic care & treatment model for patients with dementia…”

Position Statement of the American Association for Geriatric Psychiatry Regarding Principles of Care for Patients With Dementia Resulting From Alzheimer Disease

Constantine G. Lyketsos, M.D., M.H.S.,
Christopher C. Colenda, M.D., M.P.H.,
Cornella Beck, Ph.D., R.N., F.A.A.N., Karen Blank, M.D.,
Murali P. Doraiswamy, M.D., Douglas A. Kalman, M.D.,
Kristine Yaffe, M.D.
Dementia Care started in Memory Clinics

Johns Hopkins Memory and Alzheimer’s Treatment Center

STATE OF THE ART “DEMENTIA CARE” DEVELOPED AT HOPKINS

- Comprehensive, accurate diagnosis and medical management
- Comprehensive caregiver & family support & education guided by Johns Hopkins Dementia Care Needs Assessment
- Psychosocial interventions provided by dementia-care specialist psychologist, nurses, occupational therapists
- Access to clinical trials protocols for novel research therapies targeting Alzheimer’s & related conditions
Epidemiology of dementia progression informs dementia care

Cache County Dementia Progression Study (DPS)

R01AG21136, R01AG11380, R01AG18712, R01HG02213
Potentially modifiable factors

- Medical co-morbidity
- FDA approved meds
- Neuropsychiatric symptoms
- Psychotropic medications
- Early activities, especially mental
- Setting: caregiver closeness, coping style
Latent classes of trajectories in AD

335 probable AD cases
Growth mixture models
MMSE over time
Over time, low GMHR ratings, but not comorbidities or medications, were associated with poorer outcomes (MMSE: $\beta = -1.07 \ p = 0.01$; CDR-sb: $\beta = 1.79 \ p < 0.001$; NPI: $\beta = 4.57 \ p = 0.01$).
High blood pressure and AD progression


Rosenberg, et al., AJGP, 2008
Conclusion: A low percentage of individuals with AD in the community are taking cholinesterase inhibitors or memantine. This study suggests that women, particularly those with an APOE34 allele, may benefit the most from these medications.
NPS are UNIVERSAL

Steinberg et al, Int J Ger Psychiatry, 2008
Depression, agitation, apathy, psychosis accelerate severe dementia and death

Rabins et al, Alzheimer’s and Dementia, 2012
Conclusions: Psychotropic medication use was associated with more rapid cognitive and functional decline in AD, and not with improved NPS. Clinicians may tend to prescribe psychotropic medications to AD patients at risk of poorer outcomes, but one cannot rule out the possibility of poorer outcomes being caused by psychotropic medications.
Cognitive Stimulation and Cognitive and Functional Decline in Alzheimer’s Disease: The Cache County Dementia Progression Study

Katherine A. Treiber,1 Michelle C. Carlson,2 Chris Corcoran,3,4 Maria C. Norton,1,4,5 John C. S. Breitner,6,7 Kathleen W. Piercy,4,5 Michael Scott DeBerard,1 David Stein,1 Beth Foley,8 Kathleen A. Welsh-Bohmer,9 Amber Frye,1 Constantine G. Lyketsos,10,* and JoAnn T. Tschang1,4,*

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2Bloomberg School of Public Health, The Johns Hopkins University, Baltimore, Maryland.  
3Department of Mathematics and Statistics, 4Center for Epidemiologic Studies, and 5Department of Family, Consumer and Human Development, Utah State University, Logan.  
6Douglas Mental Health Research Centre and 7Department of Psychiatry, McGill University, Montreal, Québec, Canada.  
8Department of Communicative Disorders and Deaf Education, Utah State University, Logan.  
9Department of Psychiatry and Behavioral Sciences and Bryan Alzheimer’s Disease Research Center, Duke University Medical Center, Durham, North Carolina.  
10Department of Psychiatry, Bayview Medical Center, The Johns Hopkins University, Baltimore, Maryland.
Early mental activities = slower progression
Caregiver–Recipient Closeness and Symptom Progression in Alzheimer Disease. The Cache County Dementia Progression Study

Maria C. Norton,1,2,3 Kathleen W. Piercy,1,3 Peter V. Rabins,4 Robert C. Green,5,6,7 John C. S. Breitner,8,9 Truls Østbye,10 Christopher Corcoran,3,11 Kathleen A. Welsh-Bohmer,12,13 Constantine G. Lyketsos,4,* and JoAnn T. Tschanz2,3,*

1Department of Family, Consumer and Human Development, 2Department of Psychology, and 3Center for Epidemiologic Studies, Utah State University, Logan.
4Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland.
5Department of Neurology, and 6Department of Medicine (Genetics), Boston University School of Medicine, Massachusetts.
7Department of Epidemiology, Boston University School of Public Health, Massachusetts.
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10Department of Community and Family Medicine, Duke University Medical Center, Durham, North Carolina.
11Department of Mathematics and Statistics, Utah State University, Logan.
12Department of Psychiatry and Behavioral Sciences, and 13Bryan Alzheimer’s Disease Research Center, Duke University Medical Center, Durham, North Carolina.
Dementia Care common activities

- Treat neuropsychiatric symptoms (NPS)
- Reduce medication load
- Manage co-morbidities
- Prevent delirium
- Treat cognitive symptoms
- Support patients: activities, safety
- Caregivers: communication, skills, respite
Alzheimer’s & Dementia 9 (2013) 602–608

Neuropsychiatric symptoms in Alzheimer’s disease: Past progress and anticipation of the future

Targets for treatment

Accepted by FDA
• Agitation: Cache + CitAD + IPA (2001; 2011; 2014)
• Psychosis: Jeste Criteria (2000)

Proposed to regulators
• Affective disorder: Olin criteria (2002)
• Apathy: Robert criteria (2010)
Use The DICE Approach

Describe
- Caregiver describes problematic behavior
  - Context (who, what, when and where)
  - Social and physical environment
  - Patient perspective
  - Degree of distress to patient and caregiver

Investigate
- 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

Create
- 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

Evaluate
- Provider evaluates whether “CREATE” interventions have been implemented by caregiver and are safe and effective

Kales, Gitlin, Lyketsos, JAGS, 2014
Antipsychotics for agitation
(findings similar for psychosis)

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Study ID</th>
<th>SMD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>Breder, 2004</td>
<td>0.27 (0.05, 0.48)</td>
</tr>
<tr>
<td></td>
<td>Mintzer, 2007</td>
<td>0.31 (0.10, 0.52)</td>
</tr>
<tr>
<td></td>
<td>Streim, 2004/Streim, 2008</td>
<td>0.30 (0.05, 0.55)</td>
</tr>
<tr>
<td></td>
<td>Subtotal (I-squared = 0.0%, p = 0.954)</td>
<td>0.29 (0.16, 0.42)</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>DeDeyn, 2004</td>
<td>0.28 (0.02, 0.53)</td>
</tr>
<tr>
<td></td>
<td>Deberdt, 2004</td>
<td>0.39 (0.55, 0.62)</td>
</tr>
<tr>
<td></td>
<td>Schneider, 2006/Sultur, 2008</td>
<td>0.29 (0.05, 0.52)</td>
</tr>
<tr>
<td></td>
<td>Street, 2000</td>
<td>0.19 (0.07, 0.31)</td>
</tr>
<tr>
<td></td>
<td>Subtotal (I-squared = 0.0%, p = 0.454)</td>
<td>0.19 (0.07, 0.31)</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Ballard, 2005</td>
<td>0.14 (0.05, 0.33)</td>
</tr>
<tr>
<td></td>
<td>Palacau, 2008</td>
<td>-0.13 (-0.66, 0.39)</td>
</tr>
<tr>
<td></td>
<td>Schneider, 2006/Sultur, 2008</td>
<td>-0.03 (-0.27, 0.21)</td>
</tr>
<tr>
<td></td>
<td>Tarot, 2006</td>
<td>0.19 (0.05, 0.46)</td>
</tr>
<tr>
<td></td>
<td>Zhong, 2004/Zhong, 2007</td>
<td>0.24 (0.05, 0.54)</td>
</tr>
<tr>
<td></td>
<td>Subtotal (I-squared = 36.4%, p = 0.165)</td>
<td>0.05 (-0.45, 0.55)</td>
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<tr>
<td>Risperidone</td>
<td>Brodaty, 2003/Brodaty, 2005</td>
<td>0.37 (0.14, 0.39)</td>
</tr>
<tr>
<td></td>
<td>Deberdt, 2004</td>
<td>0.14 (-0.11, 0.39)</td>
</tr>
<tr>
<td></td>
<td>DeDeyn, 1999</td>
<td>0.31 (0.05, 0.57)</td>
</tr>
<tr>
<td></td>
<td>Katz, 1999</td>
<td>0.38 (0.17, 0.50)</td>
</tr>
<tr>
<td></td>
<td>Mintzer, 2006</td>
<td>0.04 (-0.16, 0.23)</td>
</tr>
<tr>
<td></td>
<td>Schneider, 2006/Sultur, 2008</td>
<td>0.10 (-0.17, 0.37)</td>
</tr>
<tr>
<td></td>
<td>Subtotal (I-squared = 43.7%, p = 0.114)</td>
<td>0.22 (0.09, 0.35)</td>
</tr>
<tr>
<td></td>
<td>Overall (I-squared = 27.1%, p = 0.139)</td>
<td>0.20 (0.13, 0.27)</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis

Favors Placebo * Favors Treatment

AHRQ Comparative Effectiveness Review 2011
Effectiveness of Atypical Antipsychotic Drugs in Patients with Alzheimer’s Disease

Lon S. Schneider, M.D., Pierre N. Tariot, M.D., Karen S. Dagerman, M.S., Sonia M. Davis, Dr.P.H., John K. Hsiao, M.D., M. Saleem Ismail, M.D., Barry D. Lebowitz, Ph.D., Constantine G. Lyketsos, M.D., M.H.S., J. Michael Ryan, M.D., T. Scott Stroup, M.D., David L. Sultzer, M.D., Daniel Weintraub, M.D., and Jeffrey A. Lieberman, M.D., for CATIE-AD Study Group

BACKGROUND
Second-generation (atypical) antipsychotic drugs are widely used to treat psychosis, aggression, and agitation in patients with Alzheimer’s disease, but their benefits are uncertain and concerns about safety have emerged. We assessed the effectiveness of atypical antipsychotic drugs in outpatients with Alzheimer’s disease.

METHODS
In this 42-site, double-blind, placebo-controlled trial, 421 outpatients with Alzheimer’s disease and psychosis, aggression, or agitation were randomly assigned to receive olanzapine (mean dose, 15.5 mg per day), quetiapine (mean dose, 66.5 mg per day), risperidone (mean dose, 1.0 mg per day), or placebo. Doses were adjusted as needed, and patients were followed for up to 36 weeks. The main outcomes were the time from initial treatment to the discontinuation of treatment for any reason and the number of patients with at least minimal improvement on the Clinical Global Impression of Change (CGIC) scale at 12 weeks.

RESULTS
There were no significant differences among treatments with regard to the time to the discontinuation of treatment for any reason: olanzapine (median, 8.1 weeks), quetiapine (median, 5.3 weeks), risperidone (median, 7.4 weeks), and placebo (median, 8.0 weeks) (P=0.52). The median time to the discontinuation of treatment due to adverse events was 22.1 weeks for olanzapine and 26.7 weeks for quetiapine (9.1 weeks) and placebo (9.0 weeks) (P=0.002). The time to the discontinuation of treatment due to adverse events was longer for quetiapine than for olanzapine (P=0.028). Overall, 28% of patients who received olanzapine, 16% of patients who received quetiapine, 15% of patients who received risperidone, and 8% of patients who received placebo discontinued their assigned treatment owing to intolerability (P=0.009). No significant differences were noted among the groups with regard to improvement on the CGIC scale. Improvement was observed in 22% of patients assigned to olanzapine, 26% of patients assigned to quetiapine, 29% of patients assigned to risperidone, and 21% of patients assigned to placebo (P=0.22).

CONCLUSIONS
Adverse effects offset advantages in the efficacy of atypical antipsychotic drugs for the treatment of psychosis, aggression, or agitation in patients with Alzheimer’s disease. (ClinicalTrials.gov number, NCT00175548.)
Both conventional and atypical antipsychotics associated with significantly higher 12-month mortality than other psychotropics. Haloperidol is one of the largest “offenders.”

Kales et al, AJP 2007

Kales et al, AJP 2013
### Divalproex for agitation

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Treatment</th>
<th>Measures</th>
<th>Duration</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tariot P 2001</td>
<td>172 dementia nursing home and secondary mania</td>
<td>Valproate 20-30mg/kg/d</td>
<td>BRMS, CMAI, CGI</td>
<td>6 weeks</td>
<td>DVS=PBO</td>
</tr>
<tr>
<td>Porsteinsson A 2001</td>
<td>56 nursing home dementia &amp; agitation</td>
<td>Valproate individualized vs. PBO</td>
<td>BPRS-agitation</td>
<td>6 weeks</td>
<td>DVS&gt;PBO ?</td>
</tr>
<tr>
<td>Sival RC 2002</td>
<td>42 dementia hospitalized</td>
<td>Valproate</td>
<td>SADS-9 target aggression</td>
<td>3 weeks</td>
<td>DVS=PBO</td>
</tr>
<tr>
<td>Tariot P 2005</td>
<td>153 nursing home pAD with agitation</td>
<td>Valproate target 750/d vs. placebo</td>
<td>BPRS, CMAI</td>
<td>6 weeks</td>
<td>DVS=PBO</td>
</tr>
<tr>
<td>Hermann N 2007</td>
<td>14 AD—MMSE below 10</td>
<td>Valproate</td>
<td>NPI agitation-aggression, CMAI</td>
<td>6 weeks</td>
<td>DVS&lt;PBO</td>
</tr>
</tbody>
</table>
# Antidepressants for agitation or NPS

(Placebo controlled)

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects/Design</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Duration</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lawlor BA 1994</td>
<td>10 AD with agitation</td>
<td>Trazodone vs. Buspirone vs. PBO</td>
<td>BPRS, DMAS</td>
<td>12 weeks</td>
<td>TRA&gt;PBO</td>
</tr>
<tr>
<td>Auchus AP 1997</td>
<td>15 AD outpatients</td>
<td>Fluoxetine vs. Haloperidol vs. PBO</td>
<td>Agitation</td>
<td>4 weeks</td>
<td>FLU=PBO</td>
</tr>
<tr>
<td>Teri L 2001</td>
<td>149 AD agitation</td>
<td>Haloperidol vs. trazodone, vs. behavior mgmt vs. PBO</td>
<td>ADCS-CGIC</td>
<td>16 weeks</td>
<td>TRA=PBO</td>
</tr>
<tr>
<td>Lanctot K 2002</td>
<td>22 non-depressed AD w/ behavioral disturbance</td>
<td>Sertraline 100mg/d vs. PBO</td>
<td>NPI</td>
<td>4 weeks</td>
<td>SER=PBO</td>
</tr>
<tr>
<td>Pollock BG 2002</td>
<td>85 hospital dementia</td>
<td>Citalopram vs. perphenezine vs. PBO</td>
<td>NBRS</td>
<td>17 days</td>
<td>CIT&gt;PBO</td>
</tr>
<tr>
<td>Finkel SI 2004</td>
<td>24 pAD outpatients</td>
<td>Sertraline (24) vs. PBO (120) after open donepezil</td>
<td>NPI, CGI-I</td>
<td>8 weeks then 12 weeks</td>
<td>SER=PBO</td>
</tr>
</tbody>
</table>
### Effect of Citalopram on Agitation in Alzheimer Disease
The CitAD Randomized Clinical Trial

Anton P. Porsteinsson, MD; Lea T. Drye, PhD; Braca G. Pollock, MD, PhD; D. P. Davanand, MD; Constantine Frangakis, PhD; Zahimee Ismail, MD; Christopher Marano, MD; Curtis L. Meier, PhD; Jacob F. Mirrlees, MD, MBA; Cynthia A. Munro, PhD; Gregory Pelton, MD; Peter V. Robbins, MD; Paul R. Rosenberg, MD; Lisa S. Schneider, MD; David M. Shide, JD; Daniel Weintraub, MD; Jerome Yesavage, MD; Constantine G. Lyketsos, MD, MHS; for the CitAD Research Group

**Importance** Agitation is common, persistent, and associated with adverse consequences for patients with Alzheimer disease. Pharmacological treatment options, including antipsychotics, are not satisfactory.

**Objective** The primary objective was to evaluate the efficacy of citalopram for agitation in patients with Alzheimer disease. Key secondary objectives examined effects of citalopram on function, caregiver distress, safety, cognitive safety, and tolerability.

**Design, Setting, and Participants** The Citalopram for Agitation in Alzheimer Disease Study (CitAD) was a randomized, placebo-controlled, double-blind, parallel group trial that enrolled 186 patients with probable Alzheimer disease and clinically significant agitation from 8 academic centers in the United States and Canada from August 2009 to January 2013.

**Interventions** Participants (n = 186) were randomized to receive a psychosocial intervention plus either citalopram (n = 94) or placebo (n = 92) for 9 weeks. Dosage began at 10 mg per day with planned titration to 30 mg per day over 3 weeks based on response and tolerability.

**Main Outcomes and Measures** Primary outcome measures were based on scores from the 18-point Neurobehavioral Rating Scale agitation subscale (NBRS-A) and the modified Alzheimer Disease Cooperative Study-Clinical Global Impression of Change (mADCS-CGIC). Other outcomes were based on scores from the Cohen-Mansfield Agitation Inventory (CMAI) and the Neuropsychiatric Inventory (NPI), ability to complete activities of daily living (ADLs), caregiver distress, cognitive safety (based on scores from the 30-point Mini Mental State Examination [MMSE]), and adverse events.

**Results** Participants who received citalopram showed significant improvement compared with those who received placebo on both primary outcome measures. The NBRS-A estimated treatment difference at week 9 (citalopram minus placebo) was −0.93 (95% CI, −1.80 to −0.06), P = .04. Results from the mADCS-CGIC showed 40% of citalopram participants having moderate or marked improvement from baseline compared with 26% of placebo recipients, with estimated treatment effect (odds ratio [OR]) of being at or better than a given CGIC category of 2.13 (95% CI, 1.23-3.65), P = .01. Participants who received citalopram showed significant improvement on the CMAI, total NPI, and caregiver distress scores but not on the NPI agitation subscale, ADLs, or in less use of rescue lorazepam. Worsening of cognition (−1.05 points; 95% CI, −1.97 to −0.13; P = .03) and QT interval prolongation (18.1 ms; 95% CI, 6.1-30.1; P = .01) were seen in the citalopram group.

**Conclusions and Relevance** Among patients with probable Alzheimer disease and agitation who were receiving psychosocial intervention, the addition of citalopram compared with placebo significantly reduced agitation and caregiver distress; however, cognitive and cardiac adverse effects of citalopram may limit its practical application at the dosage of 30 mg per day.

**Trial Registration** clinicaltrials.gov Identifier: NCT00898807

Study design

- 186 patients with AD and agitation
- Psychosocial intervention for all
- 9-week RCT: citalopram 30mg vs. pbo

Portseinsson et al. JAMA, 2014
### CitAD: main outcomes

<table>
<thead>
<tr>
<th></th>
<th>Citalopram</th>
<th>Placebo</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. randomized</td>
<td>94</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>No. with any week-9 data</td>
<td>86</td>
<td>83</td>
<td></td>
</tr>
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</table>

#### Primary Agitation Outcomes

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>NBRS-A(^{b})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. with ( \geq 1 ) follow-up measurement</td>
<td>90</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>No. with week-9 data</td>
<td>86</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>Estimated score at 9 weeks, mean (SE)</td>
<td>4.33 (0.31)</td>
<td>5.26 (0.31)</td>
<td></td>
</tr>
<tr>
<td>Estimated treatment effect, mean (95% CI)</td>
<td>(-0.93 (-1.80 to -0.06))(^{c})</td>
<td>.04</td>
<td></td>
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</table>

ADCS-CGIC, No. (%)

<table>
<thead>
<tr>
<th></th>
<th>Citalopram</th>
<th>Placebo</th>
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</tr>
</thead>
<tbody>
<tr>
<td>No. with week-9 data</td>
<td>86</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>Marked improvement</td>
<td>12 (14)</td>
<td>2 (3)</td>
<td></td>
</tr>
<tr>
<td>Moderate improvement</td>
<td>22 (26)</td>
<td>19 (23)</td>
<td></td>
</tr>
<tr>
<td>Minimal improvement</td>
<td>25 (29)</td>
<td>20 (25)</td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>17 (20)</td>
<td>23 (28)</td>
<td></td>
</tr>
<tr>
<td>Minimal worsening</td>
<td>6 (7)</td>
<td>11 (14)</td>
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</tr>
<tr>
<td>Moderate worsening</td>
<td>3 (4)</td>
<td>5 (6)</td>
<td></td>
</tr>
<tr>
<td>Marked worsening</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>Estimated treatment effect, OR (95% CI)</td>
<td>2.13 (1.23 to 3.69)(^{e})</td>
<td>.007</td>
<td></td>
</tr>
</tbody>
</table>

\(^{a}\) Based on a sample size of 94 in the Citalopram group and 92 in the Placebo group.

\(^{b}\) NBRS-A: Neuropsychiatric Inventory-Revised Agitation subscale.

\(^{c}\) Estimated treatment effect, mean (95% CI).

\(^{d}\) ADCS-CGIC: Alzheimer’s Disease Cooperative Study-Clinical Gerontological Interview.

\(^{e}\) Estimated treatment effect, OR (95% CI).

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Portseinson et al. JAMA, 2014
MAINTAINING INDEPENDENCE @ HOME

• Efficacy of care coordination on QOL & outcomes
• 18 month randomized controlled trial
• 303 volunteers and their caregivers (n=290)
  – Living at home in north/northwest Baltimore (28 zip codes)
• 193 augmented usual care, 110 care coordination
• Intervention: work with patient & family to meet needs
• Masked assessment every 4.5 months for 18 months

Samus et al, AJGP, 2014
Patient unmet needs

- Eval/Diagnosis: 35%
- Treat cognitive sx: 14%
- Treat neuropsych sx: 16%
- Behavior management: 21%
- Medication management: 19%
- Medication administration: 23%
- General Medical/Health care: 63%
- Allied Health care: 18%
- Safety: 90%
- ADL Assistance: 25%
- Meaningful Activities: 51%
- Legal Issues/ Care Planning: 47%
- Health Insurance: 9%
- Patient Education: 21%
- Caregiver Availability: 3%

Samus et al, AJGP, 2014
Caregiver unmet needs

- Caregiver education: 84%
- Resource referral: 88%
- Caregiver mental health: 45%
- Caregiver medical health: 24%
- Other: 6%

Samus et al, AJGP, 2014
MIND @ Home: time to leave the home

Control group—median days = 660
Care Coordination group—median days = 948
Difference = 288 days

Samus et al, AJGP, 2014
Improved self-rated quality of life

Samus et al, AJGP, 2014
Caregiver benefits

Samus et al, AJGP, 2014
Dementia Care common activities

- Treat neuropsychiatric symptoms (NPS)
- Reduce medication load
- Manage co-morbidities
- Prevent delirium
- Treat cognitive symptoms
- Support patients: activities, safety
- Caregivers: communication, skills, respite
Thank you!
Ευχαριστώ!