Advances in Alzheimer’s Disease

James E. Galvin, MD, MPH
Professor and Associate Dean for Clinical Research
Director, Comprehensive Center for Brain Health
Director, Institute for Healthy Aging and Lifespan Studies
Disclosures

• Research Support
  • National Institutes of Health
  • Florida Department of Health
  • Association for Frontotemporal Degeneration
  • Alzheimer Drug Discovery Fund
  • Mangurian Foundation
  • Langbert Foundation

• Clinical Trials
  • Biogen
  • Axovant

• Consultant
  • Biogen, Axovant, Roche, Eisai, Lilly

• Royalties and License Agreements
  • Eisai, Pfizer, Roche, Lilly, Biogen, Quintiles

I own no stocks or equities in any Pharmaceutical or Biotechnology Companies
Acknowledgements

• Galvin Lab
  • Magdalena Tolea, PhD
  • Stephanie Chrisphonte, MD
  • Keri Greenfield, MSN, ANP, GNP
  • Catherine Robson, MSN, FNP
  • Niurka Shkolnick, LCSW
  • Amie Rosenfeld, DPT
  • Katty Saravia
  • Kadesha Stewart
  • Angelina Kelly

• New York University
  • Stella Karantzoulis, PhD
  • Victoria Raveis, PhD
  • Ab Brody, PhD
  • Licet Valois, MSW
  • Yael Zweig, MSN, ANP, GNP

• Washington University
  • John Morris, MD

• University of Kansas
  • David Johnson, PhD

• Penn State University
  • Marie Boltz, PhD

• Pace University
  • Jean Bear-Lehman, PhD
What is healthy brain aging?

• The absence of cognitive decline
  • Occurs into the 10\textsuperscript{th} decade of life
  • Still carry out their activities of daily living
  • Lead a productive and happy life

• With age, it may take longer to do things or recall information, but it usually comes back

• Memory loss is \textbf{not} a normal part of the aging process
What is Dementia?

• A general word to describe:
  • Change in memory and thinking abilities
  • Interferes with everyday function
  • Not caused by another disease

• Not really a diagnosis

• There are over 100 different causes of dementia
What is Alzheimer’s Disease (AD)?

- Most common cause of dementia
- 5.4 million Americans have AD
  - 250,000 age <65 years (early-onset)

<table>
<thead>
<tr>
<th>AD Prevalence by Age in Adults ≥65 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>65-74</td>
</tr>
<tr>
<td>75-84</td>
</tr>
<tr>
<td>≥85</td>
</tr>
</tbody>
</table>

- Annual treatment costs > $200 billion
  - Costs increase as disease progresses
  - 3rd most expensive disease after cardiovascular and cancer
- Sixth leading cause of death in the US (over age 70)
- Makes up 50% of all nursing home beds
  - Median cost (2013) = $84,000
Forecast of Alzheimer’s Disease Prevalence

- 2009: 5.2 Million (est)
- 2030: 7.7 Million (est)
- 2050: 16.0 Million (est)

The Neuropathology of AD

Mixed pathology is most common cause of the clinical picture of AD.

AD: Alzheimer disease
I: Vascular disease
LB: Lewy body disease
Comprehensive Center for Brain Health

• Center of Excellence devoted to world-class comprehensive clinical care and cutting-edge research advances

• Prevention, treatment and cure of neurodegenerative diseases

• Expertise in:
  • Healthy brain aging and Prevention Services
  • Alzheimer’s Disease and cognitive disorders
  • Parkinson’s Disease and movement disorders
  • Therapy, counseling, and rehabilitative services
  • State of the art brain imaging and mapping
  • Basic and Translational Science Laboratories

• Translate basic, clinical, behavioral and social research into innovative programs and practices that improve health outcomes and reduce health disparities
# Chronic Diseases in South Florida

## Prevalence of Chronic Disease in Medicare Beneficiaries (2013 Data)

<table>
<thead>
<tr>
<th></th>
<th>National</th>
<th>Florida</th>
<th>Palm Beach County</th>
<th>Broward County</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beneficiaries</td>
<td>34,126,305</td>
<td>2,243,566</td>
<td>174,150</td>
<td>119,379</td>
</tr>
<tr>
<td>Mean Age, y</td>
<td>71</td>
<td>73</td>
<td>75</td>
<td>73</td>
</tr>
<tr>
<td>Gender, % Female</td>
<td>55.1</td>
<td>54.7</td>
<td>56.2</td>
<td>55.8</td>
</tr>
<tr>
<td>Dual-eligible, %</td>
<td>21.7</td>
<td>19.3</td>
<td>11.2</td>
<td>23.9</td>
</tr>
<tr>
<td><strong>Alzheimer’s Disease¹ (%)</strong></td>
<td><strong>9.8</strong></td>
<td><strong>11.3</strong></td>
<td><strong>11.5</strong></td>
<td><strong>12.7</strong></td>
</tr>
<tr>
<td>Depression (%)</td>
<td>15.4</td>
<td>16.4</td>
<td>15.2</td>
<td>17.9</td>
</tr>
<tr>
<td>Coronary Heart Disease (%)</td>
<td>28.5</td>
<td>37.1</td>
<td>42.7</td>
<td>37.8</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>27.0</td>
<td>28.5</td>
<td>28.9</td>
<td>29.1</td>
</tr>
<tr>
<td>COPD (%)</td>
<td>11.9</td>
<td>13.6</td>
<td>9.7</td>
<td>12.4</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>55.5</td>
<td>60.8</td>
<td>60.3</td>
<td>58.8</td>
</tr>
<tr>
<td>Hypercholesterolemia (%)</td>
<td>44.7</td>
<td>55.5</td>
<td>60.2</td>
<td>52.9</td>
</tr>
<tr>
<td>Strokes (%)</td>
<td>3.8</td>
<td>4.5</td>
<td>4.6</td>
<td>4.8</td>
</tr>
</tbody>
</table>

¹Includes related dementias
Aging and Dementia Research Program

Diagnose

Treat

Cure

Prevent

Outpatient (Pre-Diagnosis)
Provider           Patient

Inpatient (Pre/Post Diagnosis)
Provider           Patient

Outpatient (Post-Diagnosis)

Collaboration with I-SENSE to build external sensor devices

Graph showing percentage of single impairment, dual impairment, and no impairment over time (0, 15, 30, 45, 60, 75, 90)
The AD8 Interview (either informant or patient)
- 2-3 minutes to complete
- In-person, phone, or web

<table>
<thead>
<tr>
<th>Question</th>
<th>YES, A change</th>
<th>NO, No change</th>
<th>N/A, Don’t know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Problems with judgment (e.g. falls for scams, bad financial decisions,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>buys gifts inappropriate for recipients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced interest in hobbies/activities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Repeats questions, stories or statements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trouble learning how to use a tool, appliance or gadget (e.g. VCR,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>computer, microwave, remote control)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forgets correct month or year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difficulty handling complicated financial affairs (e.g. balancing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>checkbook, income taxes, paying bills)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difficulty remembering appointments</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily problems with thinking and/or memory</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TOTAL AD8 SCORE

Remember, “Yes, a change” indicates that you think there has been a change in the last several years cause by cognitive (thinking and memory) problems.

- Report cognitive loss in comparison with patient’s premorbid function
- Report interference with usual daily activities
- Consistent change, even when patient’s brief test performance is “normal”, may detect earliest symptomatic stages of dementia
- Less biased by race, culture, education or SES
- Dependent on a reliable, observant informant

Galvin JE et al, Neurology, 2005
The AD8

<table>
<thead>
<tr>
<th>Variable</th>
<th>AD8 &lt; 2</th>
<th>AD8 ≥ 2</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>75.3 (7.2)</td>
<td>75.5 (7.5)</td>
<td>ns</td>
</tr>
<tr>
<td>ApoE, % ε4</td>
<td>30.1</td>
<td>48.7</td>
<td>.003</td>
</tr>
<tr>
<td>Dementia Ratings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDR-SB, range 0-18</td>
<td>0.06 (0.19)</td>
<td>2.8 (2.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AD8, range 0-8</td>
<td>0.3 (0.5)</td>
<td>5.0 (2.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MMSE, range 30-0</td>
<td>28.5 (1.5)</td>
<td>25.8 (4.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Biomarker Studies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PiB Amyloid, units</td>
<td>0.12 (.23)</td>
<td>0.45 (.42)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CSF Ab42, pg/ml</td>
<td>590.7 (266.2)</td>
<td>435.6 (209.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CSF tau, pg/ml</td>
<td>303.6 (171.2)</td>
<td>500.5 (261.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CSF p-tau181, pg/ml</td>
<td>52.2 (23.9)</td>
<td>76.7 (39.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- Works across cultures/languages

Galvin JE et al., *JAMA Neurol* 2007; 64:725-730; Galvin JE et al., *Brain* 2010;133:3290-300
AD8 Discriminative Properties

- AUC: 0.917 (95% CI: 0.88-0.95)
- Sensitivity: 92%
- Positive PV: 93%

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>No dementia</td>
<td>------</td>
</tr>
<tr>
<td>AD</td>
<td>0.958</td>
</tr>
<tr>
<td>VaD</td>
<td>0.984</td>
</tr>
<tr>
<td>Mixed AD/VaD</td>
<td>0.981</td>
</tr>
<tr>
<td>DLB</td>
<td>0.844</td>
</tr>
<tr>
<td>FTD</td>
<td>0.951</td>
</tr>
<tr>
<td>Aphasia + memory</td>
<td>0.910</td>
</tr>
<tr>
<td>Mood disorder</td>
<td>0.929</td>
</tr>
<tr>
<td>Other cognitive disorders</td>
<td>0.874</td>
</tr>
</tbody>
</table>

Galvin JE et al, Neurology, 2006
Combining informant interview and performance

**Dementia**

AUC=0.97
(95%CI: 0.93-0.99)

Combining a cut-off of ≥ 2 on the AD8 and ≤ 5 on 10-item word list recall:
- Sensitivity: 94.1%
- Specificity: 81.8%

**MCI**

AUC=0.91
(95%CI: 0.8-1.0)

Sensitivity: 85.0%
Specificity: 84.2%

Galvin JE et al, Archives Neurol 2007
1. **ATTENTION AND CONCENTRATION**

**0**  Normal attention, concentration and interaction with his/her environment and surroundings

**0.5**  Mild problems with attention, concentration, and interaction with environment and surroundings, may appear drowsy during day

**1**  Moderate problems with attention and concentration, may have staring spells or spend time with eyes closed, increased daytime sleepiness

**2**  Significant portion of the day is spent sleeping, not paying attention to environment, when having a conversation may say things that are illogical or not consistent with topic

**3**  Limited to no ability to pay attention to external environment or surroundings
## Properties of QDRS

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>MCI</th>
<th>AD</th>
<th>LBD</th>
<th>VaD</th>
<th>FTD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>70.1 (7.6)</td>
<td>76.2 (8.0)</td>
<td>79.8 (7.5)</td>
<td>78.4 (7.7)</td>
<td>77.2 (6.2)</td>
<td>72.7 (8.2)</td>
<td>.001</td>
</tr>
<tr>
<td>Education, y</td>
<td>16.7 (2.4)</td>
<td>15.9 (3.0)</td>
<td>15.2 (2.9)</td>
<td>14.5 (3.6)</td>
<td>14.8 (3.4)</td>
<td>16.8 (3.3)</td>
<td>.28</td>
</tr>
<tr>
<td>CDR</td>
<td>0.2 (0.3)</td>
<td>1.9 (1.6)</td>
<td>1.0 (0.6)</td>
<td>1.5 (0.9)</td>
<td>1.7 (0.9)</td>
<td>0.8 (0.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CDR-SB</td>
<td>0.03 (0.1)</td>
<td>0.4 (0.3)</td>
<td>5.7 (3.3)</td>
<td>8.8 (5.2)</td>
<td>9.3 (6.3)</td>
<td>5.2 (4.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MMSE</td>
<td>28.7 (1.6)</td>
<td>26.1 (3.3)</td>
<td>19.6 (5.5)</td>
<td>18.2 (7.7)</td>
<td>19.7 (6.0)</td>
<td>23.6 (1.4)</td>
<td>.005</td>
</tr>
<tr>
<td>Functional Activities Questionnaire</td>
<td>0.0 (0.0)</td>
<td>3.6 (4.2)</td>
<td>10.5 (8.5)</td>
<td>17.1 (10.1)</td>
<td>16.6 (13.9)</td>
<td>8.1 (9.9)</td>
<td>.001</td>
</tr>
<tr>
<td>Neuropsychiatric Inventory</td>
<td>0.9 (1.6)</td>
<td>5.6 (4.7)</td>
<td>7.7 (5.7)</td>
<td>11.6 (5.7)</td>
<td>11.4 (5.6)</td>
<td>10.5 (9.1)</td>
<td>.002</td>
</tr>
<tr>
<td>QDRS Total</td>
<td>0.3 (0.5)</td>
<td>3.5 (2.7)</td>
<td>7.2 (5.1)</td>
<td>11.7 (6.9)</td>
<td>11.6 (7.8)</td>
<td>7.4 (6.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>QDRS Cognitive Subscale</td>
<td>0.2 (0.3)</td>
<td>1.5 (0.9)</td>
<td>3.1 (1.9)</td>
<td>4.5 (2.6)</td>
<td>2.8 (2.3)</td>
<td>2.7 (2.4)</td>
<td>.005</td>
</tr>
<tr>
<td>QDRS Behavioral Subscale</td>
<td>0.2 (0.3)</td>
<td>2.0 (2.0)</td>
<td>4.2 (3.5)</td>
<td>7.5 (4.9)</td>
<td>8.8 (5.9)</td>
<td>5.4 (4.8)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Key: AD=Alzheimer’s Disease; LBD=Lewy Body Dementia; VaD=Vascular Dementia; FTD=Frontotemporal Degeneration; CDR=Clinical Dementia Rating; CDR-SB=CDR Sum of Boxes; MMSE=Mini Mental State Exam;
# Lewy Body Composite Risk Score

Please rate the following symptoms as being present or absent for at least 3 times over the past 6 months. Does the patient...

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have slowness in initiating and maintaining movement or have frequent hesitations or pauses during movement?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have rigidity (with or without cogwheeling) on passive range of motion in any of the 4 extremities?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have a loss of postural stability (balance) with or without frequent falls?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have a tremor at rest in any of the 4 extremities or head?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have excessive daytime sleepiness and/or seem drowsy and lethargic when awake?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have episodes of illogical thinking or incoherent, random thoughts?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have frequent staring spells or periods of blank looks?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have visual hallucinations (see things not really there)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appear to act out his/her dreams (kick, punch, thrash, shout or scream)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have orthostatic hypotension or other signs of autonomic insufficiency?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TOTAL SCORE**

---

Copyright 2015 *The Lewy Body Composite Risk Score* James E. Galvin
## Number-Symbol Coding Test

### KEY

<table>
<thead>
<tr>
<th>Number</th>
<th>Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>△</td>
</tr>
<tr>
<td>2</td>
<td>✕</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>⊥</td>
</tr>
<tr>
<td>5</td>
<td>[</td>
</tr>
<tr>
<td>6</td>
<td>&lt;</td>
</tr>
<tr>
<td>7</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>⊙</td>
</tr>
<tr>
<td>9</td>
<td>∧</td>
</tr>
<tr>
<td>0</td>
<td>=</td>
</tr>
</tbody>
</table>

### Practice #1

<table>
<thead>
<tr>
<th>Practice #2</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 1 0 9 4</td>
</tr>
<tr>
<td>&lt;   &lt;   ∧   ✕</td>
</tr>
<tr>
<td>8 6 5 2 7 0 1 5 6 8 9 0 4</td>
</tr>
<tr>
<td>∧   ⊥   –   +   ✕   ＜   ∧</td>
</tr>
<tr>
<td>+ =   □   ＜   ⊙   –   △   +   –   ⊙   ⊥</td>
</tr>
<tr>
<td>1 0 3</td>
</tr>
<tr>
<td>–   □   ＜   –   ⊙   ✕   +</td>
</tr>
</tbody>
</table>

### Practice #2

<table>
<thead>
<tr>
<th>Practice #2</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 1 9 8 4 2 9 3 5 4</td>
</tr>
</tbody>
</table>

Copyright 2016 Number Symbol Coding Test James E. Galvin and Florida Atlantic University
Relationship Between Imaging Biomarkers

Figure 4: Correlations between Cortical Volume and Diffusion Metrics

A. Cortical volume / WM DKI

B. Cortical volume / WM TII

C. Cortical SUVR / WM DKI

D. Cortical SUVR / WM TII
Structure-Function Connectome

- Sensory motor network
- Cingulo-opercular network
- Auditory network
- Default mode network
- Visual network
- Fronto-parietal network
- Salience network
- Subcortical network
- Attention network
High Density EEG

Normalized power (μV²)

Channel Number (from 250)
Modeling Neurodegenerative Diseases

A: AD vs. Controls

Control, N=310
AD-clinical, N=134
AD-autopsied, N=44
Preclinical

B: PD vs. PDD vs. Controls

Control (N=192); PD (N=48); PDD (N=76)

C: AD vs. DLB

Control (N=192); AD (N=130); Mixed DLB (N=84); Pure DLB (N=15)

D: Evolution of PD-MCI

Abnormal
Threshold
WM
Crystalized
Memory
Episodic
memory
Language

Preclinical
Project LEARN MORE

- Collaborative effort
  - Missouri Department of Health
  - 10 Area Agencies on Aging (AAA)
  - 4 Alzheimer Association chapters
  - Academic researchers
- 2 day training for AAA field workers
- Screened ~4000 older adults for dementia
- Incidence: 28.5%
- 244 referred for intervention
- Compared with 96 usual care controls
- Improved knowledge, mood, social support

Effect of Project Learn MORE on delay in transitions of care

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds Ratio£</td>
<td>3.32</td>
</tr>
<tr>
<td>(1.25, 8.83£)</td>
<td></td>
</tr>
<tr>
<td>Relative Risk Reduction (%)</td>
<td>64.10</td>
</tr>
<tr>
<td>(14.96, 84.84)</td>
<td></td>
</tr>
<tr>
<td>Absolute Risk Reduction (%)</td>
<td>14.67</td>
</tr>
<tr>
<td>(3.70, 25.64)</td>
<td></td>
</tr>
<tr>
<td>Number Needed to Treat</td>
<td>6.82</td>
</tr>
<tr>
<td>(3.90, 27.03)</td>
<td></td>
</tr>
</tbody>
</table>

Galvin et al, Clinical Interventions Aging 2014
FAU Center for Advanced Redesign of Eldercare Services (FAU CARES)

Mobile Personalizes Geriatric Care to Improve Health Outcomes and Reduce Healthcare Costs
Aging and Dementia Research Program

Diagnose

Cure

Treat

Prevent

Outpatient (Pre-Diagnosis)
- Provider
- Patient

Inpatient (Pre/Post Diagnosis)
- Provider
- Patient

Outpatient (Post-Diagnosis)
- Provider
- Patient

Collaboration with I-SENSE to build external sensor devices

Brain imaging data from different modalities and positions

Graph showing percentage of single and dual impairment across different age groups
Combination Therapy: Long Term Effects

**Predicted Mean Cognition Score**

- **No treatment**
- **ChEI alone**
- **COMBO**

<table>
<thead>
<tr>
<th>Years</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment</td>
<td>10.0</td>
<td>20.0</td>
<td>30.0</td>
<td>40.0</td>
</tr>
<tr>
<td>ChEI alone</td>
<td>9.5</td>
<td>19.0</td>
<td>29.0</td>
<td>39.0</td>
</tr>
<tr>
<td>COMBO</td>
<td>9.0</td>
<td>18.5</td>
<td>28.0</td>
<td>37.5</td>
</tr>
</tbody>
</table>

**Cohen's d**

- **ChEI alone vs no treatment**
  - Year 1: 0.47***
  - Year 2: 0.39**
  - Year 3: 0.32**
  - Year 4: 0.23*

- **COMBO vs no treatment**
  - Year 1: 0.56***
  - Year 2: 0.73***
  - Year 3: 0.76***
  - Year 4: 0.77***

- **COMBO vs ChEI alone**
  - Year 1: 0.10
  - Year 2: 0.34**
  - Year 3: 0.44***
  - Year 4: 0.49***

---

**Predicted Mean Level of Dependence**

- **No treatment**
- **ChEI alone**
- **COMBO**

<table>
<thead>
<tr>
<th>Years</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment</td>
<td>80.0</td>
<td>70.0</td>
<td>60.0</td>
<td>50.0</td>
</tr>
<tr>
<td>ChEI alone</td>
<td>79.5</td>
<td>69.0</td>
<td>59.0</td>
<td>49.0</td>
</tr>
<tr>
<td>COMBO</td>
<td>79.0</td>
<td>68.5</td>
<td>58.0</td>
<td>48.0</td>
</tr>
</tbody>
</table>

**Cohen's d**

- **ChEI alone vs no treatment**
  - Year 1: 0.47***
  - Year 2: 0.39**
  - Year 3: 0.32**
  - Year 4: 0.23*

- **COMBO vs no treatment**
  - Year 1: 0.56***
  - Year 2: 0.73***
  - Year 3: 0.76***
  - Year 4: 0.77***

- **COMBO vs ChEI alone**
  - Year 1: 0.23
  - Year 2: 0.46***
  - Year 3: 0.62***
  - Year 4: 0.73***
Aducanumab Therapy for Alzheimer’s Disease

Change in measurements of Amyloid B-protein over 54 weeks of trial demonstrating significant dose-response effect

Change in measurements of cognitive function (CDR-SB and MMSE) over 54 weeks of trial demonstrating significant treatment response

RVT-101 in Dementia with Lewy Bodies (DLB)

- **Significant unmet need:** no drugs approved in the U.S. or EU

- **Cholinergic deficits are a prominent feature of DLB:** Cholinergic neurotransmission is more dysfunctional in DLB than Alzheimer’s disease

- **Increasing acetylcholine improves cognition and function in DLB:** RVT-101 promotes the release of acetylcholine

- **5HT_{2A} activity is a driver of visual hallucinations:** RVT-101 inhibits the activity of the 5HT_{2A} receptor

- **24-week Phase 2b study**

---

Single successful study could serve as basis for approval of RVT-101 in DLB when combined with Alzheimer’s filing
Interprofessional Education Initiatives

**Clinicain Partners Program:** 3-day internship for rural clinicians. Increased care and diagnostic confidence and to significant practice change.

**Dementia Friendly Hospital Program:** Training program for hospital staff. Increased knowledge and care confidence, increased dementia recognition of dementia, and creation of new programs to improve hospital discharge outcomes.

**Project Learn MORE:** State-wide intervention to increase dementia detection. Significant increases in dementia detection with appropriate referrals for resources, delays in nursing home placement and reduced mortality.

**Family-centered, Function Focused Care:** Program to incorporate family caregivers into hospital discharge planning teams. Increased caregiver preparedness, reduced caregiver anxiety, increased patient mobility, reduced post-discharge delirium, and reduced 30-day readmission rates.

**WeCare:** Demonstration of a transdisciplinary collaborative care model. Increased caregiver and patient confidence, reduced caregiver burden, and increased patient satisfaction with care.

**Dementia Symptom Management at Home:** Program to improve home health care. Increased provider knowledge and confidence.
Family-centered, function-focused care (Fam-FFC)

A multi-component, educational-empowerment intervention to improve functional outcomes and patient/family experience

- Draws upon function-focused care work in long-term care and the community
- Adapted to acute care with improved functional outcomes
- Jointly-developed treatment goals, care plans, discharge planning, post-acute follow-up

Patient Outcomes 2 months post-discharge:
- Reduced Delirium (p=.03)
- Improved ADL (p=.02)
- Improved Walking Performance (p=.001)

Family Caregiver Outcomes 2 months post-discharge:
- Increased Preparedness (p=.04)
- Reduced Anxiety (p=.008)

<table>
<thead>
<tr>
<th>Hospital Outcomes</th>
<th>Non-Intervention</th>
<th>Intervention</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge to nursing home</td>
<td>11 (26)</td>
<td>12 (27)</td>
<td>.56</td>
</tr>
<tr>
<td>Utilization of post-acute rehabilitation</td>
<td>27 (64)</td>
<td>29 (66)</td>
<td>.69</td>
</tr>
<tr>
<td>Readmission to hospital within 30 days</td>
<td>10 (24)</td>
<td>3 (7)</td>
<td>.02</td>
</tr>
<tr>
<td>Delirium 2 months post-discharge</td>
<td>12 (29)</td>
<td>3 (7)</td>
<td>.05</td>
</tr>
<tr>
<td>Failed to return to baseline function 2 months post-discharge</td>
<td>21 (15)</td>
<td>5 (12)</td>
<td>.003</td>
</tr>
<tr>
<td>Length of stay</td>
<td>4.4 (2.0)</td>
<td>4.0 (2.1)</td>
<td></td>
</tr>
</tbody>
</table>

Quality Improvements in Dementia Care

- Determination of presence and severity of differential diagnosis of the specific type of dementia
- Evaluation for reversible causes of dementia
  - Appropriate use of medical tests and evaluations
- Active case finding and treatment for excess disability due to comorbid medical conditions and assessment of impact of co-morbid diseases on cognitive status
- Active case finding and treatment for patient depression, psychoses, behavioral disturbances, sleep disorders, and hazardous activities (e.g., driving, alcohol and substance abuse)
- Active case finding for caregiver burden and depression and ascertainment of family dynamics
- Needs assessment of patient-caregiver dyad
- Pharmacotherapy of dementia syndrome with stage-appropriate medications
- Referral for physical, occupational, speech and language, cognitive therapies
- Non-pharmacological therapies for psychological and behavioral disturbances
- Consideration and close monitoring of pharmacotherapy for behavioral disturbances
- Referral to patient and caregiver educational programs and/or community support agencies
- Counseling and care coordination services
  - Facilitated communication between all clinicians involved in patient care
- Active surveillance and tracking of patient- and caregiver-centered outcomes
- Active monitoring and support of the caregiver's emotional and physical health
- Development of transition-in-care plans and appropriate referrals for palliative and hospice services

Clinical Translational Research Unit (CTRU) to translate clinical, health services, behavioral, and social research from:

- Basic science discoveries
- Individual and population level treatments
- Innovative programs, practices, and policies
- Incorporate and translate findings from FAU, Scripps, and Max Planck scientists into drugs, devices, and delivery systems
- Biostatistics, Bioinformatics, and Biorepository capacity
- Link translational research to clinical care at consortium hospitals
- ~8000 square feet at Office Building One on FAU Boca Campus
Aging and Dementia Research Program

Diagnose

Treat

Cure

Prevent

Outpatient (Pre-Diagnosis) Provider           Patient

Inpatient (Pre/Post Diagnosis) Provider           Patient

Outpatient (Post-Diagnosis) Provider           Patient

Collaboration with I-SENSE to build external sensor devices
Marine Biomedical & Biotechnology Research

• Oceans cover over 70% of the earth’s surface and within them there is an amazing diversity of life
• Developing therapeutic products from natural sources
• Support multi-disciplinary research projects exploring ocean-based drug discovery
• Sample library from deep fore reefs, vertical walls, and boulder zones covering Atlantic and Caribbean waters with additional samples from Galapagos, Western Pacific, Mediterranean, Indian, West African, and Bering Seas
Dementia Treatment and Cure Initiative

• Specialty unit dedicated to developing, testing, and validating new treatments to prevent, treat, or cure dementia

• Tie in with basic science and drug discovery efforts at Harbor Branch and Jupiter campuses, Scripps, and Max Planck

• Dynamic network of clinical, translational, and basic scientists working on developing novel molecules

• Move promising ideas from the lab to the patient (“bench” to “bedside”) considerably faster than a traditional research environment
Aging and Dementia Research Program

Diagnose

Cure

Prevent

Treat

- Collaborate with iSENSE to build external sensor devices
Clinical Expression of AD may evolve from different etiologies

- Can prevent or treat AD by addressing:
  - AD pathology (plaques, tangles)
  - Other pathologies and mechanisms

Multiple Chronic Conditions (MCCs) and AD

- Coronary heart disease (CHD), diabetes mellitus (DM), and Alzheimer’s disease and related dementias (AD) affect older adults of all backgrounds, but may be more prevalent in minority populations.
- MCCs often have complex, bidirectional relationships with each other.
- Poorly recognized and controlled medical conditions may increase the risk of cognitive impairment.
  - CHD and DM increase the risk of AD.
  - AD leads to poor compliance, worse health outcomes, and increased costs in CHD and DM.

### Prevalence of Chronic Disease in Medicare Beneficiaries (2013 Data)

<table>
<thead>
<tr>
<th>Condition</th>
<th>National</th>
<th>Florida</th>
<th>Palm Beach County</th>
<th>Broward County</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beneficiaries</td>
<td>34,126,305</td>
<td>2,243,566</td>
<td>174,150</td>
<td>119,379</td>
</tr>
<tr>
<td>Alzheimer’s Disease</td>
<td>9.8%</td>
<td>11.3%</td>
<td>11.5%</td>
<td>12.7%</td>
</tr>
<tr>
<td>Depression (%)</td>
<td>15.4%</td>
<td>16.4%</td>
<td>15.2%</td>
<td>17.9%</td>
</tr>
<tr>
<td>Coronary Heart Disease</td>
<td>28.5%</td>
<td>37.1%</td>
<td>42.7%</td>
<td>37.8%</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>27.0%</td>
<td>28.5%</td>
<td>28.9%</td>
<td>29.1%</td>
</tr>
<tr>
<td>COPD (%)</td>
<td>11.9%</td>
<td>13.6%</td>
<td>9.7%</td>
<td>12.4%</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>55.5%</td>
<td>60.8%</td>
<td>60.3%</td>
<td>58.8%</td>
</tr>
<tr>
<td>Hypercholesterolemia (%)</td>
<td>44.7%</td>
<td>55.5%</td>
<td>60.2%</td>
<td>52.9%</td>
</tr>
<tr>
<td>Strokes (%)</td>
<td>3.8%</td>
<td>4.5%</td>
<td>4.6%</td>
<td>4.8%</td>
</tr>
</tbody>
</table>
Multicultural Community Dementia Screening

• Supported by 2 grants from the National Institute on Aging
• Community-based assessment of older adults (target goal 500)
  • Demographics, financial resources, preferences
  • Cognitive-Behavioral Screening (memory, mood)
  • Medical Screening (blood pressure, diabetes, lung disease, obesity)
  • Physical assessment (balance, frailty, strength)
  • Anthropometric measurements
  • Social work follow-up
• Subset have Gold Standard testing and biomarkers collected
  • MRI scans
  • PET scans
  • EEG
  • Blood and Spinal fluid
• Repository of multicultural medical, cognitive, and imaging biomarker data: 500 individuals with grant protocol (187,500 data points); a subset of 150 individuals with a Gold Standard evaluation (202,500 data points), structural and functional MRI, FDG-PET (SUVR), and high density EEG (125,000 data points) + raw and processed images.
Measurement Tools

- Body Composition Impedance
- Sphygmomanometer Blood pressure
- Dynamometer Grip Strength
- Hemoglobin A1C meter Diabetes Risk
- Stopwatch/Tape Measure
- Spirometer Forced Expiratory Volume
Body Composition

- Bone
- Water
- Lean Muscle
- Fat

Body Composition includes:
- Body
- Visceral
Diabetes and the Risk of AD

<table>
<thead>
<tr>
<th>Diabetes mellitus</th>
<th>Total population*</th>
<th>Men†</th>
<th>Women‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>1.9 (1.3 to 2.8)</td>
<td>1.8 (0.8 to 4.1)</td>
<td>1.9 (1.2 to 3.0)</td>
</tr>
<tr>
<td>No drug treatment</td>
<td>1.3 (0.7 to 2.3)</td>
<td>1.4 (0.5 to 4.0)</td>
<td>1.3 (0.7 to 2.6)</td>
</tr>
<tr>
<td>Oral medication</td>
<td>2.4 (1.4 to 4.1)</td>
<td>2.2 (0.7 to 7.4)</td>
<td>2.4 (1.3 to 4.4)</td>
</tr>
<tr>
<td>Insulin treatment</td>
<td>4.3 (1.7 to 10.5)</td>
<td>3.9 (0.5 to 29.5)</td>
<td>4.3 (1.6 to 11.8)</td>
</tr>
</tbody>
</table>

Subjects without diabetes served as reference. Values are relative risk (95% CI).

* Adjusted for age and sex.
† Adjusted for age.

<table>
<thead>
<tr>
<th>Dementia subtype</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total AD</td>
<td>1.9 (1.2 to 3.1)</td>
</tr>
<tr>
<td>Without cerebrovascular disease</td>
<td>1.8 (1.1 to 3.0)</td>
</tr>
<tr>
<td>With cerebrovascular disease</td>
<td>3.0 (1.0 to 9.3)</td>
</tr>
<tr>
<td>Vascular dementia</td>
<td>2.0 (0.7 to 5.6)</td>
</tr>
<tr>
<td>Other dementias</td>
<td>1.6 (0.5 to 5.0)</td>
</tr>
</tbody>
</table>

Subjects without diabetes served as reference.

Ott A, et al Neurology 1999
Elevated Hemoglobin A1C and Cognitive Impairment

- Hemoglobin A1C relates to average plasma glucose concentration over previous 2-3 months
- Higher amounts of A1C indicates diabetes risk, poorer control of blood glucose, and risk of heart, kidney and retinal disease
  - For diabetics, goal is below 6%
- Categories
  - Normal (reference): $\leq 5.6\%$
  - Pre-diabetes: 5.7-6.4%
  - Diabetes: $> 6.5\%$

### Adjusted Regression Model

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>Std Error</th>
<th>Sig</th>
<th>Exp(B)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>.019</td>
<td>.030</td>
<td>.519</td>
<td>1.02</td>
<td>0.96 – 1.08</td>
</tr>
<tr>
<td>Gender</td>
<td>-.421</td>
<td>.606</td>
<td>.49</td>
<td>.657</td>
<td>0.20 – 2.15</td>
</tr>
<tr>
<td>Pre-diabetes</td>
<td>.129</td>
<td>.675</td>
<td>.85</td>
<td>1.14</td>
<td>0.30 – 4.27</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.58</td>
<td>.785</td>
<td>.04</td>
<td>4.88</td>
<td>1.05 – 22.72</td>
</tr>
</tbody>
</table>

Diabetes increases risk of cognitive impairment 4.8-fold
Obesity and risk of AD

Profenno et al, Biol Psych 2010

---

Profenno et al, Biol Psych 2010
BMI Increases Risk of Cognitive Impairment

### Adjusted Regression Model for BMI

<table>
<thead>
<tr>
<th></th>
<th>Exp(B)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.04</td>
<td>1.01 – 1.07</td>
</tr>
<tr>
<td>Gender</td>
<td>.577</td>
<td>.33 – 1.01</td>
</tr>
<tr>
<td>BMI 25-29.9</td>
<td>1.51</td>
<td>0.82 – 2.76</td>
</tr>
<tr>
<td>BMI &gt; 30</td>
<td>2.20</td>
<td>1.13 – 4.32</td>
</tr>
</tbody>
</table>

Lean BMI = (1-%body fat * BMI)

### Adjusted Regression Model for Lean BMI

<table>
<thead>
<tr>
<th></th>
<th>Exp(B)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>.968</td>
<td>0.94 – 0.99</td>
</tr>
<tr>
<td>Gender</td>
<td>1.23</td>
<td>0.65 – 2.33</td>
</tr>
<tr>
<td>Lean BMI</td>
<td>1.00</td>
<td>0.89 – 1.14</td>
</tr>
</tbody>
</table>

Graph showing the relationship between BMI and FDG SUVR with regression lines and correlation coefficients R = -.415, p = .003 and R = -.436, p = .002.
Differences: Visceral and Body Fat

**Visceral Fat**
- Worse Cognitive Performance
  - MoCA $r = 0.19$

**Body Fat**
- Worse Physical Performance
  - MoCA $r = 0.03$
  - Mini-PPT $r = 0.36$

**Cognitive**

- Mini-PPT $r = 0.13$
Differences: Visceral and Body Fat

**Body Fat**

- $R = -0.004, p = 0.98$
- $R = 0.017, p = 0.90$

**Visceral Fat**

- $R = -0.514, p < 0.001$
- $R = -0.523, p < 0.001$
Abdomen/Hip Ratio as Proxy Marker

MoCA $r = 0.23$

Mini-PPT $r = 0.07$

FDG SUVR

$R = -0.444, p = 0.001$

$R = -0.433, p = 0.002$
## Hypertension and risk of AD

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>Blood pressure classification</th>
<th>Outcome</th>
<th>Follow-up period</th>
<th>Results (odds ratio or relative risk; 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Launer et al.</td>
<td>3,703 Japanese-American men; never treated hypertensives 57%</td>
<td>DBP: severe high (≥95 mm Hg); high (90–94 mm Hg); normal (80–89 mm Hg); SBP; severe high (≥160 mm Hg); high (140–159 mm Hg); normal (110–139 mm Hg)</td>
<td>Dementia</td>
<td>27 (years)</td>
<td>Among those never treated, the risk for dementia was 3.8 (1.6–8.7) for severe high DBP, and 4.3 (1.7–10.8) for high DBP; the risk for dementia was 4.8 (2.0–11.0) in those with severe high SBP. BP was not associated with the risk for dementia in treated men</td>
</tr>
<tr>
<td>Kivipelto et al.</td>
<td>1,449 subjects; age 65–79</td>
<td>High SBP ≥ 160 mm Hg</td>
<td>Dementia</td>
<td>21 (years)</td>
<td>The risk for dementia was 2.3 (1.0–5.5) for high SBP</td>
</tr>
<tr>
<td>Kivipelto et al.</td>
<td>1,449 subjects; age 65–79</td>
<td>High SBP ≥ 160 mm Hg</td>
<td>AD</td>
<td>21 (years)</td>
<td>The risk for AD was 2.6 (1.1–6.6) for high SBP</td>
</tr>
<tr>
<td>Posner et al.</td>
<td>1,259 subjects; age ≥ 65</td>
<td>N/A</td>
<td>AD, VaD</td>
<td>7 (years)</td>
<td>A history of hypertension was not associated with an increased risk for AD (0.9, 0.7–1.3), but was with an increased risk for VaD (1.8, 1.0–3.2)</td>
</tr>
<tr>
<td>Kivipelto et al.</td>
<td>1,449 subjects; age 65–79</td>
<td>High SBP &gt; 140 mm Hg</td>
<td>Dementia, AD</td>
<td>21 (years)</td>
<td>High SBP was a significant risk for dementia (1.97, 1.03–3.77); no significant risk for AD (1.57, 0.78–3.14)</td>
</tr>
<tr>
<td>Luchsinger et al.</td>
<td>1,138 subjects; mean age 76.2</td>
<td>N/A</td>
<td>AD</td>
<td>5.5 (years)</td>
<td>Hypertension was not significantly associated with an increased risk for AD (1.4, 0.9–2.1)</td>
</tr>
<tr>
<td>Li et al.</td>
<td>2,356 subjects; age ≥ 65</td>
<td>DBP: borderline-high (80–89 mm Hg); normal (&lt;80 mm Hg), SBP; high (≥160 mm Hg); normal (&lt;140 mm Hg)</td>
<td>Dementia</td>
<td>8 (years)</td>
<td>Within the youngest age group (65–74), a greater risk for dementia was found in participants with high SBP (1.60, 1.01–2.55) or borderline-high DBP (1.59, 1.07–2.35) than for those with normal BP</td>
</tr>
</tbody>
</table>

AD, Alzheimer's disease; BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure; VaD, vascular dementia.
Risk Function of Age

![Graph showing the relationship between systolic blood pressure and risk function of age.](image)
Sarcopenia and Impairment

Tolea and Galvin, *Clin Intervent Aging*, 2014

### OR of having both cognitive impairment (MoCA) and physical impairment

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted</th>
<th>Adjusted 1</th>
<th>Adjusted 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Controls</strong></td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Pre-sarcopenia</td>
<td>0.90 (0.43-1.94)</td>
<td>1.09 (0.41-3.85)</td>
<td>1.54 (0.54-4.37)</td>
</tr>
<tr>
<td>Sarcopenia</td>
<td>6.02 (2.58-14.33)</td>
<td>4.09 (1.40-11.91)</td>
<td>3.46 (1.07-11.45)</td>
</tr>
</tbody>
</table>

### OR of having both cognitive impairment (AD8) and physical impairment

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted</th>
<th>Adjusted 1</th>
<th>Adjusted 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Controls</strong></td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Pre-sarcopenia</td>
<td>0.93 (0.43-1.99)</td>
<td>0.80 (0.30-2.14)</td>
<td>1.10 (0.37-3.21)</td>
</tr>
<tr>
<td>Sarcopenia</td>
<td>6.10 (2.73-14.07)</td>
<td>3.07 (1.09-8.61)</td>
<td>3.61 (1.11-11.72)</td>
</tr>
</tbody>
</table>
Functional decline depends on initial cognitive status and rate of progression

Slope of PPT decline according to change in cognitive status

- Remained normal
- Progressed normal-MCI
- Progressed normal-Dementia
- Remained MCI
- Remained Dementia
- Progressed MCI-Dementia

Slope $= \frac{-0.211}{0.279}$

Slope $= \frac{-2.288}{0.001}$

Slope $= \frac{-0.370}{0.240}$

Slope $= \frac{-2.020}{0.279}$

Slope $= \frac{-1.165}{0.001}$

Ref

AD vs. NL: Slope $= \frac{-0.666}{0.010}$

VaD vs. NL: Slope $= \frac{-4.825}{0.001}$

VaD vs. AD: Slope $= \frac{-4.094}{0.004}$

Tolea, Morris and Galvin, *Alz Dis Assoc Disord*, 2014
Lung Volumes

The FEV1/FVC ratio, is a calculated ratio used in the diagnosis of COPD
- Normal > 0.8
- COPD < 0.7
COPD Risk and Cognitive Performance

**Adjusted Regression Model**

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.03</td>
<td>1.00 – 1.06</td>
</tr>
<tr>
<td>Gender</td>
<td>0.78</td>
<td>0.43 – 1.44</td>
</tr>
<tr>
<td>FEV1/pFVC</td>
<td>8.5</td>
<td>3.1-31.2</td>
</tr>
</tbody>
</table>

**Risk of poorer cognitive performance:** OR 3.95 (95% CI: 1.73-9.09)

Every 0.5 difference in Lung Age/Chronological Age ratio effects MoCA by 1 point

![Graphs showing correlation between hippocampal volume, FDG SUVR, and FEV1/pFVC ratio](image)

**Estimate** | **Std Error** | **P-value**
---|---|---|
Lung Age/Age Ratio | -0.55 | 0.17 | .002

Clinical Expression of AD Revisited

APOE
- Amyloid plaques

Diabetes
- Infarctions

HTN
- Vascular Resistance

Obesity
- Inflammation

Physical function
- Trophic Factors

COPD
- Hypoxia

Bone Loss
- Vitamin D

Neurodegeneration
- Loss of synapses, neurons, dendrites, dendritic spines

Accumulating Pathologic Burden

Cognitive Decline

Clinical AD
Dementia Prevention Initiative

- While we cannot (yet) cure AD, there is increasing evidence AD risk is potentially modifiable (HTN, DM, cardiovascular disease, hypercholesterolemia, obesity, etc)

**Collective findings identified:**

- Specific dietary patterns and nutrient profiles associated increased AD pathology
- Changes in muscle mass, mobility and body fat associated with poorer cognitive performance
- Racial, ethnic and socioeconomic differences in health outcomes, perception, and use of medical information
- Personality profiles that increase physical and cognitive limitations
- Cognitive profiles characterizing preclinical, presymptomatic disease
- Novel cognitive tasks that portend accumulating AD brain pathology
- Brain imaging changes occurring very early in pathologic cascade

**Develop individualized risk profile:**

- Diet, physical exercise (aerobic, strength training, and flexibility), mental activities, counseling, risk reduction, and homeopathic approaches
- Comprehensive medical history and exam
- Anthropometric measurements
- Novel physical and cognitive tasks
- Dietary and physical activity profiles
- Psychological profile (personality, mood)
- Social support and network assessment
- Blood work for micro- and macro-nutrients, inflammatory/cell injury markers, lipoproteins
- MRI with novel research sequences (volume, surface area, thickness, white matter disease, vascular burden)
- CSF biomarkers of amyloid, tau, inflammation, and neuron injury

**Hypothesis:** Personalized prevention plan alters pathologic cascade in at-risk individuals

- Test tailored intervention over 3-year period to determine if personalized prevention plan can reduce dementia risk by altering biophysiological profiles and biomarkers
Falls Prevention Program

ADAC Assessment
- Family sees: 1. MD; 2. SW
- Patient sees: 1. SW; 2. NP; 3. MD

CLINIC
- Diagnostic Conference
- Dyad sees entire team

C-PROFET
- Home visit
  1. OT
  2. RA
- Eligibility
  - NP
- Informed Consent Coordinator

Questions
- Medical = NP
- Falls prevention = OT

In-Person Follow-ups
- 1. NP
- 2. Coordinator

Phone Follow-ups
- 1. Coordinator
- 2. RA

Collaboration with I-SENSE to build external sensor devices
New Initiative

Palm Beach County

The Glades

The Coast
Target Populations

Minority Status

Low SES

Rural Location

Aim 1: Epidemiologic Surveillance of ADRD, Risk Factors, and Social Determinants of Health

Root Causes
- Cultural Values
- Acculturation
- Discrimination
- Nutrition
- Physical Activity
- Smoking/Alcohol
- Injury/Exposures
- Stress
- Mental Health
- Access to Care
- Health Literacy
- Health Beliefs
- Self-Efficacy
- Transportation
- Poverty

ADRD Risk Factors
- Hypertension
- Glucose Intolerance
- Metabolic Syndrome
- Diabetes
- Vascular disease
- Hyperlipidemia
- Obesity
- Inflammation
- Frailty

Aim 2: Longitudinal Study of Transition to ADRD

Aim 3: Community Intervention
- Self Management
- Perception of Disease
- Medical Management

Aim 4: Health Provider Intervention

Outcomes

Target Populations

Minority Status

Low SES

Rural Location

Aim 1: Epidemiologic Surveillance of ADRD, Risk Factors, and Social Determinants of Health

Root Causes
- Cultural Values
- Acculturation
- Discrimination
- Nutrition
- Physical Activity
- Smoking/Alcohol
- Injury/Exposures
- Stress
- Mental Health
- Access to Care
- Health Literacy
- Health Beliefs
- Self-Efficacy
- Transportation
- Poverty

ADRD Risk Factors
- Hypertension
- Glucose Intolerance
- Metabolic Syndrome
- Diabetes
- Vascular disease
- Hyperlipidemia
- Obesity
- Inflammation
- Frailty

Aim 2: Longitudinal Study of Transition to ADRD

Aim 3: Community Intervention
- Self Management
- Perception of Disease
- Medical Management

Aim 4: Health Provider Intervention

Outcomes
Summary

• Multiple medical conditions increase the risk of neurodegeneration
  • May be multiple pathways to get Alzheimer’s, Parkinson’s, and related disorders
  • May also be multiple pathways to diagnose, treat, cure or prevent

• Efforts to prevent cognitive decline and development of dementia may be more successful when directed to at-risk individuals based on their physical functional profile

• Detection of and interventions addressing root causes may offer novel approaches to diagnosing, treating, curing, or preventing Alzheimer’s and Parkinson’s disease

• AD and PD are diseases of a lifetime; there may be many ways to build a better brain as we age

• At FAU, we are spearheading game-changing approaches to improve the lives of our patients and their families

“An Ounce of Prevention is Worth a Pound of Cure”
- Benjamin Franklin