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Preventing Cognitive Decline and Dementia

Demetrius M. Maraganore, MD, FAAN  
B.J. and Eve Wilder Professor  
Department of Neurology  
University of Florida  
Gainesville, FL
Disclosures

I came to Florida to find the Fountain of Youth

- To preserve and improve brain health
- by preventing cognitive decline and dementia

MCI AD VaD LBD FTD PPA All*

ICD-10 codes
G31.84 F03.50 G31.83 G31.09 G31.01
G30.0 G30.8 G30.9
FO1.51
290.41
331.19
331.11

ICD-9 codes
331.83 G31.84 G31.09 G31.01
249.9
331.0
290.40

N 44,068 99,555 31,332 8,968 2,138 512 161,852
Sex
Male 19,160 (43.5%) 31,227 (31.4%) 12,314 (39.3%) 4,485 (50.0%) 990 (46.3%) 223 (43.6%) 59,096
Female 6,366 (14.4%) 12,367 (12.4%) 6,561 (20.9%) 973 (10.1%) 217 (9.2%) 47 (9.4%) 22,845
Unknown 13 (0.3%) 19 (0.3%) 16 (0.2%) 1 (0.0%) 1 (0.2%) 315 (0.2%)
Race
White 23,735 (53.9%) 56,458 (37.4%) 16,874 (53.9%) 5704 (63.6%) 1,392 (65.1%) 347 (67.8%) 89,855
Black 6,366 (14.4%) 12,367 (29.9%) 6,561 (19.3%) 973 (10.1%) 217 (9.2%) 47 (9.4%) 22,845
Asian 372 (0.9%) 787 (2.0%) 297 (1.0%) 90 (1.0%) 23 (1.3%) 6 (1.3%) 1,464
Unknown 6,822 (15.5%) 7,096 (6.4%) 2,007 (6.4%) 439 (4.9%) 183 (8.6%) 41 (8.0%) 14,624
Ethnicity
Hispanic 9,492 (26.0%) 25,540 (18.2%) 5,711 (17.4%) 1,974 (22.0%) 371 (17.4%) 77 (15.0%) 36,956
Unknown 2,138 (2.0%) 5,056 (1.1%) 1,158 (1.0%) 297 (3.1%) 53 (0.5%) 25 (0.5%) 3,668

Why Florida?

ADRD diagnoses registered in the OneFlorida Data Trust

<table>
<thead>
<tr>
<th>ICD-10 codes</th>
<th>MCI</th>
<th>AD</th>
<th>GBD</th>
<th>LBD</th>
<th>FTD</th>
<th>PPA</th>
<th>All*</th>
</tr>
</thead>
<tbody>
<tr>
<td>G31.84 F09</td>
<td>331.84 F03.50</td>
<td>G31.83</td>
<td>G31.09</td>
<td>G31.01</td>
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<tr>
<td>G30.0 G30.8 G30.9</td>
<td>290.40 290.41</td>
<td>331.19</td>
<td>331.11</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

OneFlorida Data Trust
- 15 million patients
- 4,100 providers
- 1,240 practices
- 22 hospitals
- 75% of Floridians

https://onefloridaconsortium.org
### The Ponce de Leon State!

<table>
<thead>
<tr>
<th></th>
<th>Over 90 in Florida</th>
<th>Over 90 Non-Demented</th>
<th>Over 90 Demented*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>187,092</td>
<td>116,458</td>
<td>70,634</td>
</tr>
<tr>
<td></td>
<td>66.36%</td>
<td>62.08%</td>
<td>74.87%</td>
</tr>
<tr>
<td>Male</td>
<td>91,511</td>
<td>67,852</td>
<td>23,659</td>
</tr>
<tr>
<td></td>
<td>32.46%</td>
<td>36.17%</td>
<td>25.08%</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>155,689</td>
<td>97,590</td>
<td>58,099</td>
</tr>
<tr>
<td></td>
<td>55.22%</td>
<td>52.02%</td>
<td>61.59%</td>
</tr>
<tr>
<td>African American</td>
<td>26,356</td>
<td>15,736</td>
<td>10,620</td>
</tr>
<tr>
<td></td>
<td>9.35%</td>
<td>8.39%</td>
<td>11.26%</td>
</tr>
<tr>
<td>American Indian</td>
<td>311</td>
<td>206</td>
<td>105</td>
</tr>
<tr>
<td></td>
<td>0.11%</td>
<td>0.11%</td>
<td>0.11%</td>
</tr>
<tr>
<td>Asian</td>
<td>2,847</td>
<td>1,937</td>
<td>910</td>
</tr>
<tr>
<td></td>
<td>1.01%</td>
<td>1.03%</td>
<td>0.96%</td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>112</td>
<td>89</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>0.04%</td>
<td>0.05%</td>
<td>0.02%</td>
</tr>
<tr>
<td>Multirace</td>
<td>2,330</td>
<td>1,788</td>
<td>542</td>
</tr>
<tr>
<td></td>
<td>0.83%</td>
<td>0.95%</td>
<td>0.57%</td>
</tr>
<tr>
<td>Unknown</td>
<td>40,862</td>
<td>36,563</td>
<td>4,299</td>
</tr>
<tr>
<td></td>
<td>14.49%</td>
<td>19.49%</td>
<td>4.56%</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>51,115</td>
<td>32,404</td>
<td>18,711</td>
</tr>
<tr>
<td></td>
<td>18.13%</td>
<td>17.27%</td>
<td>19.83%</td>
</tr>
<tr>
<td>Total</td>
<td>281,927</td>
<td>187,588</td>
<td>94,339</td>
</tr>
<tr>
<td></td>
<td>66.54%</td>
<td>68.54%</td>
<td>33.46%</td>
</tr>
</tbody>
</table>

*ICD-10 codes: F01.50, F01.51, F01.80, F01.81, F01.90, F01.91, F04, F06.0, F06.8, G30.0, G30.1, G30.2, G30.3, G31.0, G31.1, G31.2, G31.8, G31.9, G33.0, G33.1, G33.8, G33.9, G34.1, G34.2, G34.3, G34.4, G34.5, G34.6, G34.7, G34.8, G34.9, G35.0, G35.1, G35.2, G35.3, G35.4, G35.5, G35.6, G35.7, G35.8, G35.9, G36.0, G36.1, G36.2, G36.3, G36.4, G36.5, G36.6, G36.7, G36.8, G36.9, G37.0, G37.1, G37.2, G37.3, G37.4, G37.5, G37.6, G37.7, G37.8, G37.9

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### Outline

- Definitions of cognitive decline and dementia
- Risk factors for cognitive decline and dementia
- Predicting cognitive decline and dementia
- Preventing cognitive decline and dementia
- Call to action: preserving brain health
- Questions???
Definitions of cognitive decline and dementia

Definitions

• Cognitive decline
  – age-related decrement in memory and other cognitive measures
  – scoring in the normal range
  – without significant impairment in activities of daily living

• Mild cognitive impairment
  – age-related decrement in memory and other cognitive measures
  – scoring below the normal range
  – without significant impairment in activities of daily living

• Dementia
  – age-related decrement in memory and other cognitive measures
  – scoring below the normal range
  – with significant impairment in activities of daily living
  – The most common cause is Alzheimer’s disease
An age-related clinical continuum…

Risk factors for cognitive decline and dementia
**Lifetime risks**

1 in 5 women and 1 in 10 men will develop Alzheimer’s in their lifetime.

**APOE genotypes made simple**

Odds are your Alzheimer’s disease risk will be lowered by the test.

*Genotype frequencies from 23andMe; risk estimate from Olmsted Co, MN*
Amyloid positivity (PET or CSF)
Timing of amyloid deposition and disease onset is genotype dependent

Race differences in dementia risk not due to genetic factors
Modifiable lifestyle and health factors are likely responsible
Income disparities in dementia risk also not due to genetics.
Brain Boosters: Fads, Facts and Fundamentals
Session One: Preventing Cognitive Decline and Dementia
September 17, 2019

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**Early Unopposed Menopause:**
*Natural or Surgical*

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Table 1. Survey of the literature reveals at least 20 modifiable risk factors for Alzheimer’s disease and related disorders

<table>
<thead>
<tr>
<th>Factors that Increase Risk</th>
<th>Factors that Decrease Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic (APOE ε4, other susceptibility genes)</td>
<td>Genetic (APOE ε2)</td>
</tr>
<tr>
<td>Metabolic (cholesterol, diabetes, obesity)</td>
<td>Social (education, income, engagement)</td>
</tr>
<tr>
<td>Vascular (cardiovascular disease, hypertension, stroke)</td>
<td>Lifestyle (physical &amp; mental exercise, high work complexity)</td>
</tr>
<tr>
<td>Infectious/Inflammatory (chronic periodontitis, others)</td>
<td>Diet (Mediterranean, polyunsaturated and fats from fish)</td>
</tr>
<tr>
<td>Head trauma (multiple concussions)</td>
<td>Vitamins (B6/ B12/ Folate, A, C, D, E)</td>
</tr>
<tr>
<td>Diet (homocysteine, Standard American Diet, deficiencies)</td>
<td>Medications (NSAIDs, statins, early HRT, antihypertensives)</td>
</tr>
<tr>
<td>Lifestyle (smoking, alcohol abuse)</td>
<td></td>
</tr>
<tr>
<td>Sleep (poor quality, disorders)</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>Early menopause (natural or surgical)</td>
<td></td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
<td></td>
</tr>
<tr>
<td>Certain medications</td>
<td></td>
</tr>
</tbody>
</table>

Factors that Increase Risk
- Genetic (APOE ε4, other susceptibility genes)
- Metabolic (cholesterol, diabetes, obesity)
- Vascular (cardiovascular disease, hypertension, stroke)
- Infectious/Inflammatory (chronic periodontitis, others)
- Head trauma (multiple concussions)
- Diet (homocysteine, Standard American Diet, deficiencies)
- Lifestyle (smoking, alcohol abuse)
- Sleep (poor quality, disorders)
- Depression
- Early menopause (natural or surgical)
- Sedentary lifestyle
- Certain medications

Factors that Decrease Risk
- Genetic (APOE ε2)
- Social (education, income, engagement)
- Lifestyle (physical & mental exercise, high work complexity)
- Diet (Mediterranean, polyunsaturated and fats from fish)
- Vitamins (B6/ B12/ Folate, A, C, D, E)
- Medications (NSAIDs, statins, early HRT, antihypertensives)

Predicting cognitive decline and dementia
Barriers to APOE testing

- American College of Medical Genetics
- Third Party Payers
- Fear of Discrimination or Distress

But… the train has left the station!!!

23andMe, others
From Brain Disease to Brain Health: Primary Prevention of Alzheimer’s Disease and Related Disorders in a Health System Using an Electronic Medical Record-Based Approach

A.M. Fosnacht1, S. Patel1, C. Yucus1, A. Pham1, E. Rasmussen1, R. Frigerio1, S. Walters2, D. Maraganore1

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Corresponding Author: Demetrius M. Maraganore, MD, Ruth Cain Ruggles Chairman, Department of Neurology, Medical Director, NorthShore Neurological Institute, NorthShore University HealthSystem, 2630 Ridge Ave, Evanston, IL, 60201, USA, Tel: 1-847-570-4678, Fax: 1-847-725-5565, Email: dmaraganore@northshore.org

Published online January 31, 2017, http://dx.doi.org/10.14283/jpad.2017.3

Kitty Hawk Experiment

- NorthShore University HealthSystem (Evanston, IL)
- Can we use the EMR to predict cognitive impairment and dementia (including Alzheimer’s)?
Brain Boosters: Fads, Facts and Fundamentals
Session One: Preventing Cognitive Decline and Dementia
September 17, 2019

29,246 people aged 60+ with a primary visit in 2009 • 62% women • 82% Caucasian • 2,193 (7.5%) diagnosed with AD over 5 years

The AD model: under the hood

<table>
<thead>
<tr>
<th>Variables</th>
<th>Parameter Estimate</th>
<th>95% CI</th>
<th>Odds Ratio Estimate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.38</td>
<td>0.26</td>
<td>0.50</td>
<td>1.46</td>
</tr>
<tr>
<td>Male</td>
<td>0.51</td>
<td>0.12</td>
<td>0.91</td>
<td>1.67</td>
</tr>
<tr>
<td>Family History Alzheimer's</td>
<td>0.58</td>
<td>0.36</td>
<td>0.81</td>
<td>1.79</td>
</tr>
<tr>
<td>Concussion</td>
<td>0.24</td>
<td>0.09</td>
<td>0.39</td>
<td>1.27</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.20</td>
<td>0.06</td>
<td>0.34</td>
<td>1.22</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.15</td>
<td>0.03</td>
<td>0.27</td>
<td>1.16</td>
</tr>
<tr>
<td>Sleep Behavior Disorder</td>
<td>0.78</td>
<td>0.63</td>
<td>0.93</td>
<td>2.18</td>
</tr>
<tr>
<td>Not Alcohol User</td>
<td>0.43</td>
<td>0.28</td>
<td>0.58</td>
<td>1.54</td>
</tr>
<tr>
<td>Depression</td>
<td>0.86</td>
<td>0.43</td>
<td>1.29</td>
<td>2.36</td>
</tr>
<tr>
<td>Age groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age groups (59,64]</td>
<td>Ref</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Age groups (64,69]</td>
<td>0.86</td>
<td>0.49</td>
<td>1.24</td>
<td>2.37</td>
</tr>
<tr>
<td>Age groups (69,74]</td>
<td>1.84</td>
<td>1.48</td>
<td>2.20</td>
<td>6.27</td>
</tr>
<tr>
<td>Age groups (74,79]</td>
<td>2.54</td>
<td>2.19</td>
<td>2.89</td>
<td>12.67</td>
</tr>
<tr>
<td>Age groups (79,84]</td>
<td>3.21</td>
<td>2.87</td>
<td>3.56</td>
<td>24.87</td>
</tr>
<tr>
<td>Age groups (84,89]</td>
<td>3.60</td>
<td>3.24</td>
<td>3.96</td>
<td>36.64</td>
</tr>
<tr>
<td>Age groups (89,109]</td>
<td>4.07</td>
<td>3.68</td>
<td>4.47</td>
<td>58.79</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (30,200)</td>
<td>Ref</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>BMI (25,30)</td>
<td>0.13</td>
<td>-0.02</td>
<td>0.28</td>
<td>1.14</td>
</tr>
<tr>
<td>BMI (18.5,25)</td>
<td>0.43</td>
<td>0.28</td>
<td>0.58</td>
<td>1.54</td>
</tr>
<tr>
<td>BMI (18.5,25)</td>
<td>0.86</td>
<td>0.43</td>
<td>1.29</td>
<td>2.36</td>
</tr>
</tbody>
</table>
Utilizing Data from the EMR to Predict Alzheimer’s and Dementia Risk

Aim 1: Model Building
• Use data captured by the UF EMR to develop an ADRD Prediction Model

Aim 2: Replication
• Replicate the model using the OneFlorida Data Trust registry (http://onefloridaconsortium.org)

Aim 3: Implementation
• Integrate the replicated model into the UF EMR using clinical decision support tools that identify and refer high risk patient to brain health clinic

Aim 4: Dissemination
• Share the replicated model and tools with other OneFlorida sites

Preventing cognitive decline and dementia
It's never to late!
Seniors who get aerobic exercise regularly have structurally, functionally, and biochemically stronger brains; the more intense & long, the better over time.
Mediterranean diet and age-related cognitive decline
A randomized clinical trial Valls-Pedret et al. JAMA Intern Med. 2015

Lifestyle reduces cognitive decline & dementia >60%
1000’s of Welsh men over 30 years; exercise, vegetables, smoking, drinking
A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial

Tiia Ngandu, Joen J. Laatikainen, Ali A. Scheltens, Enrico Lovati, Satu Ahvenlahti, Rikitta Antikainen, Lars Eriksson, Taitu Hjemlev, Antti J. Laive, Tiina Louniskari, Juree Lohmander, Francesca Mangiac/pgdi, Tiina Mäntylä, Sanna Sepälä, Matti Tanskanen, Petter Reiman, Anni Skogskilde Nedy, Tiina Seidenberg, Judit Toomajainen, Helsinki University Hospital, Mie Kuopio

Summary
Background: Modifiable vascular and lifestyle-related risk factors have been associated with dementia risk in observational studies. In the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER), a proof-of-concept randomised controlled trial, we aimed to assess a multidomain approach to prevent cognitive decline in at-risk elderly people from the general population.

$20 MILLION Study
but that train has left the station too…
Call to action: preserving brain health
Our greatest fear
Americans pre-retirement fear Alzheimer’s or dementia the most

Forgoing Fear:
APOE carriers benefit most from a brain health approach

- Moderate seafood intake associated with less Alzheimer’s pathology in APOE 4 carriers

- In persons with <12 years education, APOE 4 had a strong negative effect on cognition; in persons with 16+ years education, APOE 4 had less effect
  - Cook et al., (2015) Social Science and Medicine 127:159-170

- APOE 4 carriers especially benefit from physical exercise with respect to dementia or Alzheimer’s risk
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Forgoing Fear:
Little harm in brain health interventions

- Aerobic exercise
- Cognitive training
- Mediterranean diet
- Vascular risk monitoring

- Other risk monitoring
  - Head injuries
  - Sleep disorders
  - Depression
  - Social isolation
  - Alcohol excess
  - Periodontitis
  - Early menopause

The time is now!
We’re all at risk; rates and costs are soaring; we can preserve brain health!
In the cone of uncertainty

Projected Increases Between 2020 and 2025 in Alzheimer’s Dementia Prevalence by State

- 12% - 16%
- 18% - 24%
- 24% - 32%
- 30% - 38%
- 36% - 42%

Change from 2010 to 2025 for Washington, D.C. 3.1%
Created from data provided to the Alzheimer’s Association by NKC and AlzSite.