



### Language Biomarkers of Brain Health

#### Rhoda Au, Ph.D. 2<sup>nd</sup> International Symposium on Language Resources and Intelligence 12-17-18

# **Global Burden of Dementia**



# Can We Prevent the Tsunami Wave of Dementia?



# So Far the Answer is No



# Alzheimer's Disease: What Stands Between Us and a Cure?

#### Eli Lilly's Experimental Alzheimer's Drug Fails in Large Trial

#### **INVESTOR'S BUSINESS DAILY**

Merck's Alzheimer's Drug Fails; Are Biogen, Roche, AstraZeneca Next? ALLISON GATLIN | 2/15/2017

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Adapted by Drs. Dana Penney and Randall Davis from Fig 3 of *Criteria For Preclinical Alzheimer's Disease*, Alzheimer's Association report (2010), which in turn cites Jack C R, et al., Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade, *The Lancet*, **9**:1, Jan 2010, pp 119-128.

# The Impact



Alzheimer's Association. "Changing the Trajectory of Alzheimer's Disease." *Washington DC* (2010).





# Leveraging Framingham



## Framingham Cognitive Aging Preclinical-Incident Dementia



Cognitive Impairment Detection Challenge FHS Two-Method Approach

The Traditional Approach

Boston Process Approach

- Preserve traditional measures
- Expand test beyond single score
- Focus on path to final response
  - Value of incorrect responses

# Logical Memory Error Measures

#### **Traditional scores**

None

**Qualitative Scores** 

Confabulations – related Intrusions – related Confabulations – unrelated Intrusions – unrelated

## Framingham Cognitive Aging Today Preclinical-Incident Disease



## Framingham Cognitive Aging Today Asymptomatic-Preclinical-Incident Disease



# What is Preclinical?

- •65+ years old
  - •Measures differentiate cognitively intact vs. clinically demented
- •45-65 years old
  - •Measures differentiate cognitively intact vs. preclinical
- <45 years old
  - Measures differentiate cognitively intact vs.
     cognitively intact



## BPA on Steroids Digital Voice

#### Not Demented: 2009





#### Mild Cognitive Impairment:2015



## **Digital Voice Markers** evidation Cognitive Impairment



Sample Demographics	N	% Men	Ave. Age (s.d.)	Education <sup>^</sup>
No Dementia (ND)	35	60.0	83 <u>+</u> 8	2.0
Cognitively Impaired-ND (CIND)	58	40.4	83 <u>+</u> 8	1.5
Dementia*	107	37.5	83 <u>+</u> 6	1.7

#### **Audio Features**

A. Acoustic Features

e.g., pitch, Harmonic-to-Noise ratio, jitter

- B. Quantitative Audio Features e.g., #fillers, speed, pauses length, answer delay
- C. Linguistic Features e.g., part of speech tags, tree depth, frequency

#### Analysis

We used audio analysis, speech transcription, and language processing to automatically reduce voice segments from participants into a set of digital biomarkers for the early detection and diagnosis of dementia:

- Input: Acoustic, quantitative and linguistic features
- Target: Participant's cognitive status
- Machine Learning: Random Forest classifier
- Performance Metric: Area Under the Curve (AUC)
- Validation Strategy: 10-fold cross validation



#### MANUALLY TRANSCRIBED DATASET

Limited to 127 participants: Dementia (n=45, mean age=83<u>+</u>7) ND (n=82; mean age=65<u>+</u>17)

# All 0.91 [0.85, 0.97] Linguistic Features 0.9 [0.82, 0.98] Audio + Linguistic 0.89 [0.82, 0.97] Audio Features Only 0.76 [0.66, 0.86] Health & Demographic 0.82 [0.71, 0.93]

Mean AUC Scores and 95th CI

## **FDA Digital Health Initiative**



The FDA has implemented the *Digital Health Innovation Action Plan* 

Promote the development and use of digital health technologies



## **Digital Health Initiative**



#### Digital health technologies may act as susceptibility/risk biomarkers

Sources: https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM524904.pdf https://www.ncbi.nlm.nih.gov/books/NBK326791/pdf/Bookshelf\_NBK326791.pdf

## **Digital Biomarkers**



Source: Kaye, J., Gregor, M., Matteck, N., Asgari, M., Bowman, M., Ybarra, O., & Dodge, H. (2014). SOCIAL BIOMARKERS FOR EARLY SIGNS OF DEMENTIA: INCREASED SPOKEN WORD COUNTS AMONG OLDER ADULTS WITH MILD COGNITIVE IMPAIRMENT (MCI). Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 10(4), P915-P916.

# **Digital Voice Biomarkers**









## What Else?

# **Cognitive Impairment**

# **Cognitive Health**

## Sustaining brain health across life span













#### What We Need to Do Precision Brain Health



#### What It Will Take Paradigmatic Shift

Dimension	Current Mindset From	🔶 70 New Mindset	
Investment Focus	Finding the cure for Alzheimer's disease and related disorders	Finding how to prevent brain related disorders	
Research Focus	Siloed, a-priori hypothesis-driven research to find treatments for Alzheimer's diseases	Understanding lifelong health and experiences of sub-populations to optimize their brain health	
Research Scope	Isolating single or small set of factors associated with disease	Deploying scalable, multi-factorial solutions to diverse populations with and without disease risk	
Care Focus	Diagnosing and treating dementia	Monitoring and sustaining brain health	
Healthcare Delivery	Stove-piped 烟道式 Healthcare Institutions	Healthcare Ecosystem	
Data Capture	In clinic, sporadic time point, highly invasive, often self reported data collection	Continuous, passive capture of brain related data with rich demographic metadata	
Health Information Management	Raw, unusable cognitive and related data stored in disparate sources.	Networked, secure, seamless, integrated, sharable, cloud based platform made widely available	

#### What We Want to Do Next Build Plug and Play System



#### Where We Want to Do It Test Platform Robustness Across Diverse Study Sites



#### What We Have Learned



Easy data use/sharing



#### Ambient Technology Sustainable Remote Monitoring







## Where Next?















#### What Ultimate Success Will Look Like Open Science, Scalable, Integrated Research & Care Platform



### **Impact of Success**



#### Think Different, Be Different



# When a fast shot forces 15-year-old Chris Chen to the floor, it seems like the point is over

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RONDHEIM TABLE TENNIS CLUB

# Thanks.







