Life Kinetics as Outcomes in Clinical Trials

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WHY DIGITAL BIOMARKERS?

Trial Challenges / Trial Solutions

• Inability to detect objective, ecologically valid, meaningful functional change
  ➤ Digital biomarkers capture real-time, real-world activity and behavior

• Inability to identify early phase I-II efficacy
  ➤ Digital biomarkers enable identification of early efficacy signals facilitated by high frequency data capture in individuals (e.g., “n-of-one” capability)

• Current late-phase trials are long, large, ‘noisy’ and expensive.
  ➤ Digital biomarkers enable reduced sample size and/or shorter trial duration with intra-individual measurement
WHY DIGITAL BIOMARKERS?

Opportunities for new discovery & outcomes

- Enable novel observations with regard to biology and potential responses (good and bad); unique outcome measures (e.g., objective caregiver burden/interaction quantification)

The fundamental limitation of current research... The ability to detect meaningful change.

Cardinal features of change - *slow decline punctuated with acute, unpredictable events* - are challenging to assess with legacy tools and methods.
Prodromal Biomarker Trajectories are Not Linear

**Change point: 10.6 years** (95% CI 5.16, unknown) prior to conversion; WMH trajectory accelerates 6.5% of the previous value annually, $p < 0.0001$

After change point, WMH increased by an additional 3.3% of the previous value annually, $p = 0.04$

Data from Dodge et al., 2014

Self Report Inaccuracy


“What were you doing during the past 2 hours?”

<table>
<thead>
<tr>
<th>Area</th>
<th>Firings</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kitchen 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Bedroom 1</td>
<td>14</td>
<td>0:01:52</td>
</tr>
<tr>
<td>Kitchen 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Living Room 1</td>
<td>3</td>
<td>0:00:22</td>
</tr>
<tr>
<td>Living Room 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Bedroom 2</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Living Room 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Kitchen 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Bedroom 1</td>
<td>4</td>
<td>0:01:12</td>
</tr>
<tr>
<td>Kitchen 1</td>
<td>5</td>
<td>0:00:33</td>
</tr>
<tr>
<td>Living Room 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Kitchen 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Living Room 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Kitchen 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Bedroom 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Kitchen 1</td>
<td>10</td>
<td>0:01:03</td>
</tr>
<tr>
<td>Living Room 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Kitchen 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Living Room 1</td>
<td>1</td>
<td>0:00:00</td>
</tr>
<tr>
<td>Computer Room</td>
<td>3</td>
<td>0:00:14</td>
</tr>
</tbody>
</table>

- 26% No Match Between Sensors & Report
- 49% Partial Agreement
- 25% Full Match
Improving detection of change: The case for continuous, objective, multi-domain measures

Early detection

Baseline 3 years 6 years

Symptoms Reported

Is this the disease onset?

Functional range
Change the clinical research paradigm

- Brief
- Episodic
- Clinic-based
- Subjective
- Obtrusive
- Inconvenient

- Pervasive Computing
- Wireless Technologies
- "Big Data Analytics"

- Real-time
- Continuous
- Home-based
- Objective
- Unobtrusive
- Ambient

- New Observations & Discovery
- Maximally Effective Clinical Research
- Useful & Trusted Products & Services
- Better Outcomes for Patients & Families
Many ways to approach/collect data using digital biomarkers and pervasive computing

- **Class of data** (genetic, environmental, clinical); **frequency** (episodic, continuous); **certainty** (supervised, unsupervised); **method of capture** (device, procedure); **locus of capture** (home, work, hospital)

- In a growing diverse IoT, connected world, less focus on devices to be used; more on optimizing when, where, and how to *practically* and *reliably* capture longitudinal data.

“Resist the law of the hammer”
Demographics are important: The right tools for the job...

### Computer Ownership Varies Greatly by Race and Ethnicity, Household Income and Educational Attainment

<table>
<thead>
<tr>
<th>% of U.S. adults who own a desktop or laptop computer</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. adults</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Race/ethnicity</td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Black</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Age group</td>
</tr>
<tr>
<td>18-29</td>
</tr>
<tr>
<td>30-49</td>
</tr>
<tr>
<td>50-64</td>
</tr>
<tr>
<td>65+</td>
</tr>
<tr>
<td>Household income</td>
</tr>
<tr>
<td>&lt;$30K</td>
</tr>
<tr>
<td>$30K-$49,999</td>
</tr>
<tr>
<td>$50K-$74,999</td>
</tr>
<tr>
<td>$75K+</td>
</tr>
<tr>
<td>Educational attainment</td>
</tr>
<tr>
<td>Less than high school</td>
</tr>
<tr>
<td>High school</td>
</tr>
<tr>
<td>Some college</td>
</tr>
<tr>
<td>College+</td>
</tr>
<tr>
<td>Community type</td>
</tr>
<tr>
<td>Urban</td>
</tr>
<tr>
<td>Suburban</td>
</tr>
<tr>
<td>Rural</td>
</tr>
</tbody>
</table>

Source: Pew Research Center survey conducted March 17 - April 12, 2015. Whites and blacks include only non-Hispanics. N=950

### Smartphone Owners More Likely to be Younger, More Affluent and Highly Educated

<table>
<thead>
<tr>
<th>% of U.S. adults who own a smartphone, e.g. iPhone, Android, Blackberry or Windows phone</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. adults</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Race/ethnicity</td>
</tr>
<tr>
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<tr>
<td>Urban</td>
</tr>
<tr>
<td>Suburban</td>
</tr>
<tr>
<td>Rural</td>
</tr>
</tbody>
</table>

Source: Pew Research Center survey conducted June 10 - July 12, 2015. Whites and blacks include only non-Hispanics. N=2,001

### A majority of older internet users go online on a daily basis

<table>
<thead>
<tr>
<th>% of internet users in each age group who go online ...</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-29</td>
</tr>
<tr>
<td>30-49</td>
</tr>
<tr>
<td>50-64</td>
</tr>
<tr>
<td>65+</td>
</tr>
</tbody>
</table>

Source: Pew Research Center’s Internet Project July 18 - September 30, 2013 tracking survey.
Home as a Hub

• “1/3 of your life is spent sleeping” (plus bathroom, meals, social engagement...)
• Where you are when you’re sick (or about to be).
• Home-based health care ("Medical Homes", HCBS) is an embodied principle in the ACA and current health care organizations.
• Populations driving the majority of health care expenditures are home-anchored (older adults, chronic pain, Alzheimer’s families)
• Direct-to-home telemedicine.
Technology ‘Agnostic’ Pervasive Computing Platform: The Life Laboratory

Life Laboratory
Aims Study
Life Lab BC
Study/Site X

Activity, Sleep, Mobility
Time & Location

Body Composition, Pulse,
Temperature, CO₂

MedTracker

Central Secure
Data Backend

Secure Internet

Device / Sensor
“X”

Driving
Phone Activity
Doors Open / Close
Computer Activity


MedTracker

Computer Activity
To effectively use pervasive computing technologies & *established* devices →

**Four key processes**

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**UNDERSTAND THE STAKEHOLDERS/KEY QUESTIONS**
ROI (Response Over Internet) surveys, Focus Groups, Participant/End-User Assessment

<table>
<thead>
<tr>
<th>Situation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
<td>I only use a landline phone. I do not use a cell phone.</td>
</tr>
<tr>
<td>☐</td>
<td>I use my landline often, but have a cell phone for emergencies.</td>
</tr>
<tr>
<td>☐</td>
<td>I use both a landline phone and a cell phone, depending on which one is more convenient.</td>
</tr>
<tr>
<td>☐</td>
<td>I use my cell phone most of the time, even at home, but I still have a landline that I use occasionally.</td>
</tr>
<tr>
<td>☐</td>
<td>I don't have a landline phone, I just use a cell phone.</td>
</tr>
</tbody>
</table>

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**UNDERSTAND REAL WORLD USE**
Life Lab: Large Scale Deployments Relevant Health & Wellness Measures & Interventions in Everyday Environments

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**UNDERSTAND THE DATA**
ORCATECH Data Repository, Data Aggregation, Measurement Analytics & Outcomes

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**UNDERSTAND THE TECHNOLOGIES**
Point of Care ‘Smart Apartment’ Lab: Focused Sensor/Measurement Technology Development & Assessment
What can you see?

FEB-MAR
Healthy

Week 8
Week 7
Week 6
Week 5
Week 4
Week 3
Week 2
Week 1

12 AM
10 PM
9 PM
8 PM
7 PM
6 PM
5 PM
4 PM
3 PM
2 PM
1 PM
12 PM

Room 1
Room 2
Room 1
Room 2
Room 1
Room 1

Bedroom 1
Bedroom 2
Bedroom 1
Bedroom 2
Bedroom 1

Kitchen 1
Living Room 1

PT-OCT 2013

Treatment with Sinemet

SEPT-OCT 2012

Healthy Diagnosed with Parkinson’s Disease
Parkinson’s disease: Mobility changes prior to PD diagnosis; remotely identified response to therapy
Extended Period of Monitoring with Therapy – Stable Walking Speed (at slow speed)

PD Diagnosis

Treatment

Sinemet 25/100 BID
Sinemet 25/100 TID
Sinemet: 25/100 qAM
25/100 q PM
25/100 q Evening
Parkinson’s disease: Times up (out of bed) at night over time

- PD Diagnosed
- Sinemet Begun
- Sinemet Increased
- Patient Asking to Increase Dosage

Relative Frequency %


0 or 1 | 2 | >=3

Orcatech
Sensing Life Kinetics
What can you see?
Differentiation of early MCI: Total Activity & Walking


Activity patterns associated with mild cognitive impairment


Trajectories of walking speed over time


MCI cases 9X more likely in Slow Group
Early MCI - “high variability at baseline, then decreasing over time”

Late MCI - “low variability and declining”

Trajectories of COV of Weekly Walking Speeds
Differentiation of MCI: Night-time Behavior & Sleep

### Differentiation of early MCI: Night-time Behavior & Sleep

<table>
<thead>
<tr>
<th>Objective Measure</th>
<th>Intact</th>
<th>aMCI</th>
<th>naMCI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Movement in Bed (sensor firings)</td>
<td>9.4 ± 0.4</td>
<td>7.8 ± 0.9</td>
<td>10.9 ± 0.7</td>
<td>p &lt; 0.05 (aMCI &lt; naMCI)</td>
</tr>
<tr>
<td>Wake After Sleep Onset (mins)</td>
<td>27.2 ± 1.2</td>
<td>13.5 ± 2.6</td>
<td>20.6 ± 2.0</td>
<td>p &lt; 0.001 (aMCI &lt; intact, naMCI)</td>
</tr>
<tr>
<td>Settling Time (mins)</td>
<td>2.5 ± 0.07</td>
<td>2.3 ± 0.15</td>
<td>3.1 ± 0.11</td>
<td>p &lt; 0.001 (naMCI &gt; intact, aMCI)</td>
</tr>
<tr>
<td>Times up at night (# times)</td>
<td>2.1 ± 0.04</td>
<td>1.6 ± 0.10</td>
<td>1.9 ± 0.08</td>
<td>p &lt; 0.001 (aMCI &lt; intact, naMCI)</td>
</tr>
<tr>
<td>Total Sleep Time (hrs)</td>
<td>8.3 ± 0.04</td>
<td>8.5 ± 0.09</td>
<td>8.5 ± 0.07</td>
<td>NS</td>
</tr>
</tbody>
</table>
Every Day Cognition: Medication adherence as a measure of cognitive function

- Adherence assessed continuously x 5 wks with MedTracker taking a
- Mean Age - 83 yrs
- Based on ADAScog: Lower Cognition Group vs Higher Cognition Group

Significantly Worse Adherence in Lower Cognition Group

Individual patterns of medication adherence over time

Hayes, 2009
Every Day Cognition: Computer use changes over time in MCI (without formal cognitive tests)

- At Baseline: Mean 1.5 hours on computer/per day
- Over time:
  - Less use days per month
  - Less use time when in session
  - More variable in use pattern over time

Cognition and Computer Use

Table 4
Associations between cognitive status and mouse movement variability derived from one week of data

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Outcome, movement curvature (IQR_K)</th>
<th>Outcome, time spent idling (IQR_Idle)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coefficient</td>
<td>P value</td>
</tr>
<tr>
<td>MCI (reference: cognitively intact group)</td>
<td>0.013</td>
<td>.008**</td>
</tr>
<tr>
<td>Age (y)</td>
<td>-0.001</td>
<td>.03*</td>
</tr>
<tr>
<td>Education (y)</td>
<td>0.002</td>
<td>.05</td>
</tr>
</tbody>
</table>

Abbreviations: IQR, interquartile range; MCI, mild cognitive impairment.
NOTE. *P < .05, **P < .01.

Fig. 1. Graphical representation of a mouse movement.
Collecting ‘non-sensible’ or difficult to capture data with frequent on-line self reports

- Weekly on-line reports provide unique insights into function: ER/clinic visits, medication changes, pain, mood, care needs...

“During the last week, have you felt downhearted or blue for more than three days?”

Table 3. Coefficients from Generalized Estimating Equation Models for Within-Subject Differences in Behavior Parameters Between Weeks with Low Mood and Weeks without Low Mood

<table>
<thead>
<tr>
<th>Behavior</th>
<th>Participants/Observations in Model</th>
<th>Difference (95% Confidence Interval) During Low Mood Week, %</th>
<th>Estimated Difference in Parameter</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking speed</td>
<td>83/8,027</td>
<td>-1% (-3 to -1%)</td>
<td>-0.6 cm/s</td>
<td>.35</td>
</tr>
<tr>
<td>Time out of residence</td>
<td>84/8,427</td>
<td>-9% (-15 to -3%)</td>
<td>-24 min/d</td>
<td>.007</td>
</tr>
<tr>
<td>Room transitions</td>
<td>54/3,977</td>
<td>-3% (-7 to -2%)</td>
<td>-0.3 per hour</td>
<td>.31</td>
</tr>
<tr>
<td>Computer use</td>
<td>67/8,640</td>
<td>-13% (-20 to -4%)</td>
<td>-10 min/d</td>
<td>.004</td>
</tr>
</tbody>
</table>

Analysis of Self-Report Data: Embedded Online Questionnaire Measures are Sensitive to Identifying Mild Cognitive Impairment

Seelye et al., ADAD, 2015

Figure 3: Screen shot showing questions presented for the weekly personal health and activity record (or PHAR) on a mobile device. “Yes” responses result in a drop-down menu that asks for further detail. The survey is tracked for timing of each item response and total time to complete the survey each week.
Internet searches to identify MCI

This dataset represents an average of 385 days of data continuous computer data from 77 participants. During this time, 54 subjects completed 8,899 searches in Bing, Google and Yahoo—the top 3 search engines. The richness of the dataset is demonstrated in Figure 1 where searches are represented in a social network graph. In this figure, each unique term a participant searched for is represented by an individual node, and nodes are joined together if they appeared in the same search (thicker edges indicate they appeared together more frequently). Larger nodes represent those terms that are searched for more frequently.

Figure 1: A social network diagram of searches in the past year. At the top, it is clear that the word “alzheimers” is searched for with words such as symptom, treatment, and brain.
Phone use: indicator of mood and cognitive function

22,595 calls; 26 people; 25 weeks

Petersen, et al. 2015
Dyad Analysis

Figure 4. Spiral plot (A) depicting the within home location of a husband and wife plotted on a 24 hour clock for 6 consecutive days using a Bluetooth beacon system (B - photo of one of the beacons deployed around the home) paired with smartwatches (C) for individual localization. Each concentric circle outward depicts one day. In A, the colors represent where the person is located (see key). The outer trace is the husband, inner trace is the wife and middle trace is the activity of PIR sensors (see inset).
Daily interaction patterns of couples

Figure 5. Movement patterns for couple living in the same home. Rooms are plotted as a function of the time the two participants spent alone in the room while the size of each room represents total hours spent in the room together. The thickness of the connecting lines represents the transition patterns of the residents: given a resident is in a particular room (e.g. the living room), the thickness of the same colored lines (gray lines) indicate the relative probability of moving from that room to each other room in the house.
Home Assessment Technologies are also Treatment Technologies: RCT to Increase Social Interaction in MCI Using Home-based Technologies

• 6 week RCT of daily 30 min video chats
• 89% of all possible sessions completed; Exceptional adherence – no drop-out
• Intervention group improved on executive/fluency measure.
• MCI participants spoke 2985 words on average while cognitively intact spoke 2423 words during sessions; better discrimination of MCI than conventional tests (animal fluency and delayed list recall)

Integrated View: Multi-Dimensional Data for Clinical Research

Variety
- Diverse
- Certain
- Uncertain

Veracity
- (Circle Size)
- Infrequent Measurement
- Frequent Measurement

Volume
- Small Data Size
- Large Data Size

B Biomarkers
C Clinical assessment
D Demographics
EB Everyday behavior monitoring
EF Environmental factors
EM Electronic medical record
G Genomic data
P Population trends
MAS Momentary Self-report

Data Fusion - Aggregation
Predictive Model
Outcome of Interest

Integrated View: Multi-Dimensional Data for Clinical Research

Biomarkers
Clinical assessment
Demographics
Everyday behavior monitoring
Environmental factors
Electronic medical record
Genomic data
Population trends
Momentary Self-report
Putting it all together: High dimensional data fusion model predicting care transitions

63,745,978 observations

**Model**

**Context:**
Weather, Consumer Confidence Index, etc.

24/7 Behavioral - Activity Data:
Computer use, time out of home, etc.

Weekly Self-Report:
Mood, Pain, Falls, ER Visits, Visitors, etc...

Research Assessments:
Cognition, Physical Function, Genetics, Biomarkers, etc.

Health Records:
EHR, Pharmacy, Home Care, etc.

Outcome

Care Transition

Intervention

Austin et al. 2014 GSA
Predicting Care Transitions: Sensitivity Analysis

- Likelihood of a person transitioning within next six months – ROC AUC under curve = 0.974

Area under ROC curve = 0.9744
Putting it all together: High dimensional data fusion model predicting MCI

Model

Context:
Weather, Consumer Confidence Index, etc.

24/7 Behavioral - Activity Data:
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Research Assessments:
Cognition, Physical Function, Genetics, Biomarkers, etc.

Health Records:
EHR, Pharmacy, Home Care, etc.

Outcome

MCI Transition

Intervention

49,992,645 observations

Austin et al. 2015
Predicting MCI Transitions: Sensitivity Analysis

• Likelihood of a MCI transition within the next 24 months – ROC AUC under curve = 0.95
Putting it all together: High dimensional data fusion model predicting analgesic class

66,172,380 observations

Context:
Weather, Consumer Confidence Index, etc.

24/7 Behavioral - Activity Data:
Computer use, time out of home, etc.

Weekly Self-Report:
Mood, Pain, Falls, ER Visits, Visitors, etc...

Research Assessments:
Cognition, Physical Function, Genetics, Biomarkers, etc.

Health Records:
EHR, Pharmacy, Home Care, etc.

Outcome

Analgesic Class

Intervention

Austin et al. 2015
Predicting Drug Class Effects: *Drug Action Behavioral Fingerprinting*

Example of analgesics

<table>
<thead>
<tr>
<th></th>
<th>NSAID</th>
<th>Opioid</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>94.9</td>
<td>65.9</td>
<td>67.4</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>99.9</td>
<td>98.6</td>
<td>99.6</td>
</tr>
<tr>
<td>Positive Predictive Value (%)</td>
<td>99.7</td>
<td>82.6</td>
<td>86.1</td>
</tr>
<tr>
<td>Negative Predictive Value (%)</td>
<td>99.7</td>
<td>96.6</td>
<td>98.9</td>
</tr>
<tr>
<td>Correctly Classified (%)</td>
<td>99.6</td>
<td>95.6</td>
<td>98.6</td>
</tr>
</tbody>
</table>

Logistic regression models treated as classifiers (and model fit statistics)

Observation period: July 2011 – March of 2014; 66,172,380 observations
Values are odds ratios. Values greater than 1 indicate that an increase in the associated value increases the odds of MCI, less than 0 indicates the opposite. 1 is the reference value, and is true for a "normal"
Why we need to harness the power of pervasive computing systems: *Transform clinical trials*

http://www.phrma.org/sites/default/files/Alzheimer%27s%202013.pdf
Improving clinical trials through continuous data collection: Smaller samples, more precise estimates, faster, and ecologically valid

Conventional Approach:
Group Distributions

- High noise, lots of overlap
- Low noise, not much overlap

Distribution can be generated for EACH individual within short duration data accrual periods

Continuously Monitored Approach

Walking Speed Observed During the First 90 days for 2 subjects

Your walking speed ≠ my walking speed OR Your computer use ≠ my computer use

Courtesy of H. Dodge
Transforming Clinical Trials with High Frequency, Objective, Continuous Data: “Big Data” for Each Subject

MCI Prevention Trial – Sample Size Estimates

<table>
<thead>
<tr>
<th></th>
<th>Current Method</th>
<th>Continuous Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LM Delayed Recall*</td>
<td>Computer Use**</td>
</tr>
<tr>
<td>SAMPLE SIZE TO SHOW</td>
<td>688</td>
<td>10</td>
</tr>
<tr>
<td>50% EFFECT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAMPLE SIZE TO SHOW</td>
<td>1076</td>
<td>16</td>
</tr>
<tr>
<td>40% EFFECT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAMPLE SIZE TO SHOW</td>
<td>1912</td>
<td>26</td>
</tr>
<tr>
<td>30% EFFECT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAMPLE SIZE TO SHOW</td>
<td>4300</td>
<td>58</td>
</tr>
<tr>
<td>20% EFFECT</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Reduces required sample size and/or time to identify meaningful change.
- Reduces exposure to harm (fewer needed/ fewer exposed)
- More precise estimates of the trajectory of change; allows for *intra-individual* predictions.
- Provides the opportunity to substantially improve efficiency and inform go/no-go decisions of trials.
Proof of Concept Next Generation High Efficiency Clinical Trials (Focus on Phase II)

Traditional Trial Enrichment:
Stratification according to increased risk of AD.
Does not predict who progresses

Biomarker Enrichment
Imaging, CSF, Plasma, Genetics, other risk factors

Further Enrichment:
Stratification according to who will progress.
Can predict who progresses

Behavioral Phenotype Enrichment
Sleep hygiene, Time out of home, etc...

Efficient Longitudinal Assessment:
Continuously assessed objective measures.
Detects individual relevant change rapidly

Continuous Assessment:
Computer use, Walking speed, Activity, Mobility, etc...

Population AD Pathology Group

AD Pathology Group

Disease Progression Group(s)

Precision Phenotyped

Continuous Assessment: AD Progression

6 months

2-3 months

6 months
Acknowledgements

"The smallest act of kindness is worth more than the grandest intention."

- Oscar Wilde

Profound Thanks to My Amazing Colleagues and the Research Volunteers
Funders

alzheimer’s association

National Institute on Aging

NIBIB

Enterprise

NSF

vtech

National Heart Lung and Blood Institute

NIST

Intel

Office of Rural Health

Microsoft

NYCE

OrcataTech

Oregon Health Authority

Foundation for the National Institutes of Health

FNIH

VGO

OECD

Robert Wood Johnson Foundation

VA

Department of Veterans Affairs

Lilly

Pacific Retirement Services, Inc.
Thank You!

1956

2006

kaye@ohsu.edu  www.orcatech.org
Study Dashboards

Your Location

View Combo Graph

May 24, 2015
May 31, 2015
Jun 7, 2015

 Resident 372

<table>
<thead>
<tr>
<th>Metric</th>
<th>Current</th>
<th>Mean</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time in Living Room</td>
<td>4.83 min</td>
<td>4.94 min</td>
<td>-01%</td>
</tr>
<tr>
<td>Time in Bedroom</td>
<td>56.00 sec</td>
<td>1.01 sec</td>
<td>-05%</td>
</tr>
<tr>
<td>Time Out of Home</td>
<td>3.75 hr</td>
<td>2.15 hr</td>
<td>+43%</td>
</tr>
<tr>
<td>Weight</td>
<td>158.16 lbs</td>
<td>156.65 lbs</td>
<td>+24%</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>Missing</td>
<td>60.00</td>
<td></td>
</tr>
<tr>
<td>Sleep Latency</td>
<td>31.00 sec</td>
<td>1.04 sec</td>
<td>-04%</td>
</tr>
<tr>
<td>Sleep Duration</td>
<td>11.97 hr</td>
<td>11.60 hr</td>
<td>+03%</td>
</tr>
<tr>
<td>Time Awake at Night</td>
<td>10.80 min</td>
<td>21.45 min</td>
<td>-16%</td>
</tr>
<tr>
<td>Motion in Bed</td>
<td>12.00 #</td>
<td>4.68 #</td>
<td>+56%</td>
</tr>
<tr>
<td>Trips out of Bed</td>
<td>4.00 #</td>
<td>4.35 #</td>
<td>-05%</td>
</tr>
<tr>
<td>Bathrooms Trips at Night</td>
<td>3.00 #</td>
<td>3.71 #</td>
<td>-12%</td>
</tr>
</tbody>
</table>

Viewable Period:
May 18, 2015 - Jun 10, 2015
Differentiation of location of two people at home

Time (sec) 0 30 60 90

Person 1

Person 2

Location
Living Room Bathroom Bedroom
Beacon

Apartment layout

Orcatech
Sensing Life Kinetics
Wavelet decomposition reveals activity periodicity
Map

Shows the user’s current location

Blue dots indicate the route

Red pin indicates the location of the next destination

Memory Marker Number. Is this significant or should this be the name or nothing at all?

Distance in feet to the next destination

Pause button to stop the walk duration timer

Current duration of the walk in HH:MM:SS

Are we giving turn by turn directions? If so they could be shown here between address and map.

Pressing back from first map page saves the state of the walk as incomplete

Going up a level from the map page saves the state of the walk as incomplete
If we are recording responses, it seems like we would start recording here since they might express a view or experience once the see the picture...

Name of marker

Main marker image. Will there ever be more than one?

This page pops up when the user arrives at the next expected marker. Can they arrive at markers out of order?

Is this duration of walk or how long they have to talk about it.

Tapping on image could toggle full screen mode

Takes user to marker prompts and starts prompt timer (I think...)
Anatomy of an office visit –
*Little time to know – Little time to help*

- **HIP**
- **DEPRESSION**
- **BACKACHE**
- **GUM**

Visit Beginning → Visit End

15.7 Minutes

Tai-Seale, 2007

n = 392 visits

The Rest of Life
Associations Between Observed In-Home Behaviors and Self-Reported Low Mood in Community-Dwelling Older Adults

• Every week participants completed an online health questionnaire that assessed nine domains of health during the last week.
• The item related to low mood asked, "During the last week, have you felt downhearted or blue for more than three days?“
• 18,960 weekly observations of mood over 3.7 yrs were analyzed; 2.6% involved low mood.

<table>
<thead>
<tr>
<th>Behavior</th>
<th>Participants/Observations in Model</th>
<th>Difference (95% Confidence Interval) During Low Mood Week, %</th>
<th>Estimated Difference in Parameter</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking speed</td>
<td>83/8,027</td>
<td>−1% (−3−1%)</td>
<td>−0.6 cm/s</td>
<td>.35</td>
</tr>
<tr>
<td>Time out of residence</td>
<td>84/8,427</td>
<td>−9% (−15 to −3%)</td>
<td>−24 min/d</td>
<td>.007</td>
</tr>
<tr>
<td>Room transitions</td>
<td>54/3,977</td>
<td>−3% (−7−2%)</td>
<td>−0.3 per hour</td>
<td>.31</td>
</tr>
<tr>
<td>Computer use</td>
<td>67/8,640</td>
<td>−13% (−20 to −4%)</td>
<td>−10 min/d</td>
<td>.004</td>
</tr>
</tbody>
</table>

Models adjusted for sex, age, chronic disease score at baseline, and individual’s mean value of the behavior parameter during the observation period. The coefficients represent the percentage difference in the parameter between weeks when low mood was reported and weeks when low mood was not reported. The estimated difference in the parameter represents the absolute numerical difference in each of the outcomes between weeks when low mood was reported and weeks when low mood was not reported.

Time for one-person trials
Precision medicine requires a different type of clinical trial that focuses on individual, not average, responses to therapy. Schork, Nature, 2015.