The National Academies of Sciences, Engineering, and Medicine
Keck Center, Room 105
500 Fifth Street, NW, Washington DC 20001
June 5-6, 2017

WORKSHOP ON DEVELOPING A METHODOLOGICAL RESEARCH PROGRAM FOR LONGITUDINAL STUDIES

Remote Sensing Opportunities for Unobtrusive Data Collection

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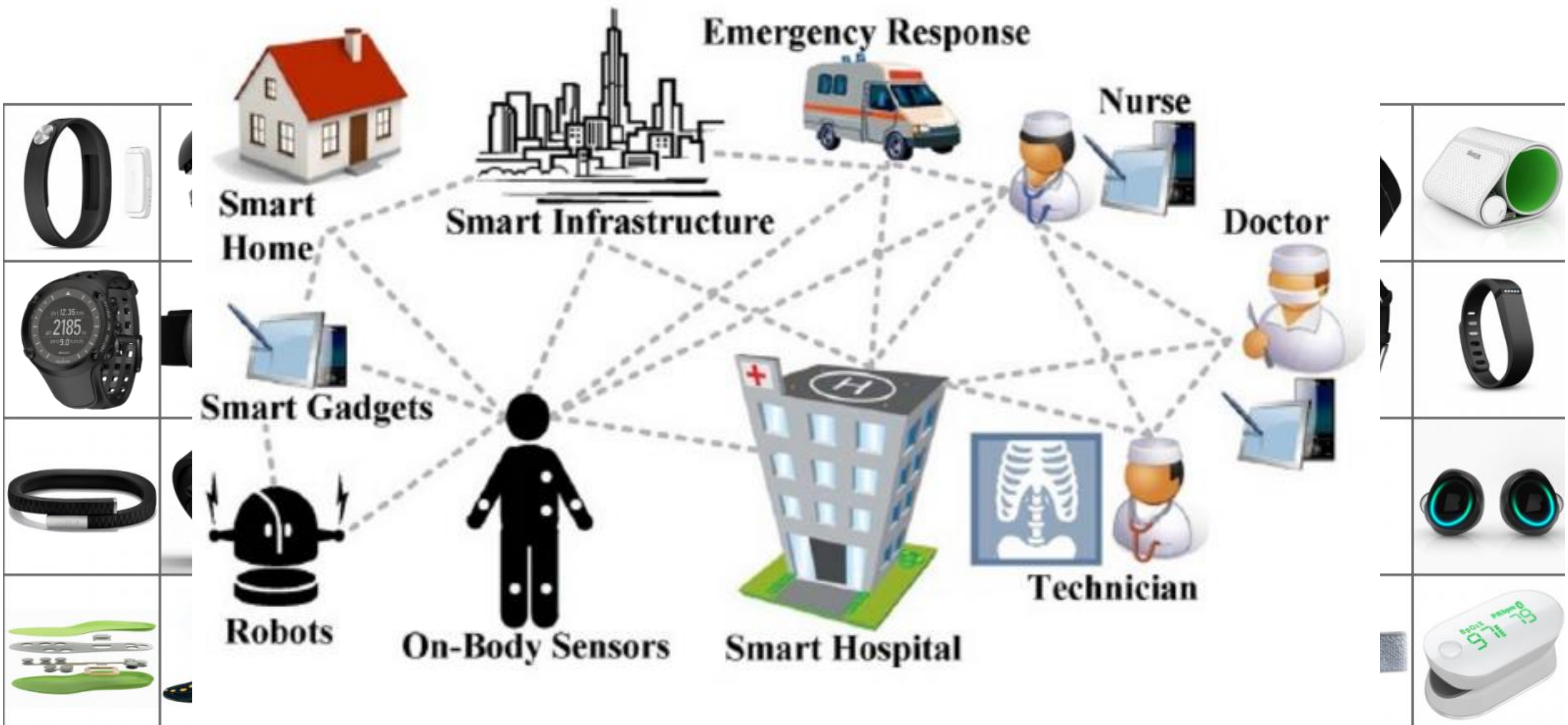
High Interest in Digital Technologies

The “Internet of Things”



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A fundamental challenge of longitudinal 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.

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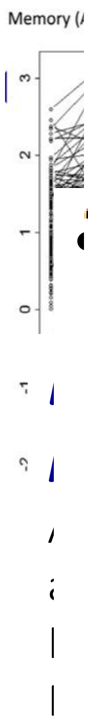
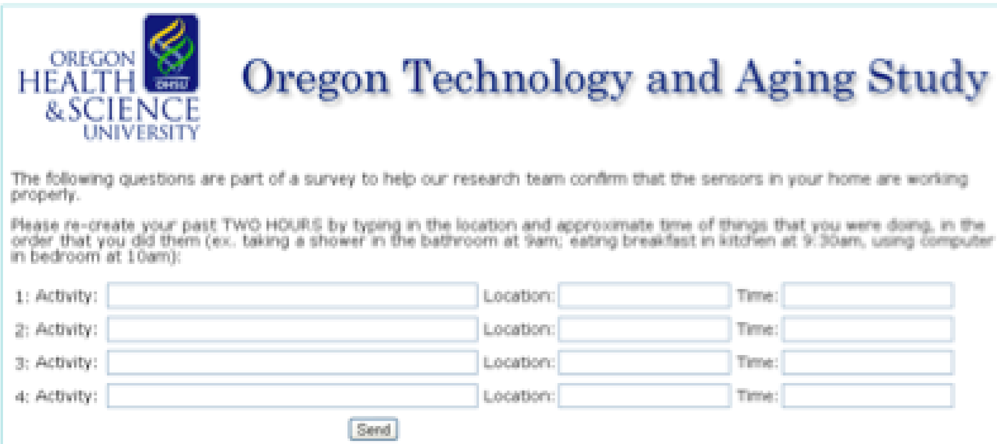
Assessment Challenges

High Self-Report Inaccuracy

Wild et al., Are you sure?: Lapses in Self-Reported Activities Among Healthy Older Adults Reporting Online, J. Appl. Gerontol. 2016



"What were you doing during the past 2 hours?"



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Oregon Technology and Aging Study

The following questions are part of a survey to help our research team confirm that the sensors in your home are working properly.

Please re-create your past TWO HOURS by typing in the location and approximate time of things that you were doing, in the order that you did them (ex. taking a shower in the bathroom at 9am; eating breakfast in kitchen at 9:30am, using computer in bedroom at 10am):

1: Activity: ______ Location: ______ Time: ______

2: Activity: ______ Location: ______ Time: ______

3: Activity: ______ Location: ______ Time: ______

4: Activity: ______ Location: ______ Time: ______

Send

- 26% No Match Between Sensors & Report
- 49% Partial Agreement
- 25% Full Match

n=95; Mean age 84 yrs

Area	Firings	Time
Kitchen 1	1	0:00:00
Bedroom 1	14	0:01:52
Kitchen 1	1	0:00:00
Living Room 1	3	0:00:22
Living Room 1	1	0:00:00
Bathroom 2	1	0:00:00
Living Room 1	1	0:00:00
Kitchen 1	1	0:00:00
Bedroom 1	4	0:01:12
Kitchen 1	5	0:00:33
Living Room 1	1	0:00:00
Kitchen 1	1	0:00:00
Living Room 1	1	0:00:00
Kitchen 1	1	0:00:00
Bedroom 1	1	0:00:00
Kitchen 1	1	0:00:00
Bedroom 1	1	0:00:00
Kitchen 1	10	0:01:03
Living Room 1	1	0:00:00
Kitchen 1	1	0:00:00
Living Room 1	1	0:00:00
Computer Room	3	0:00:14

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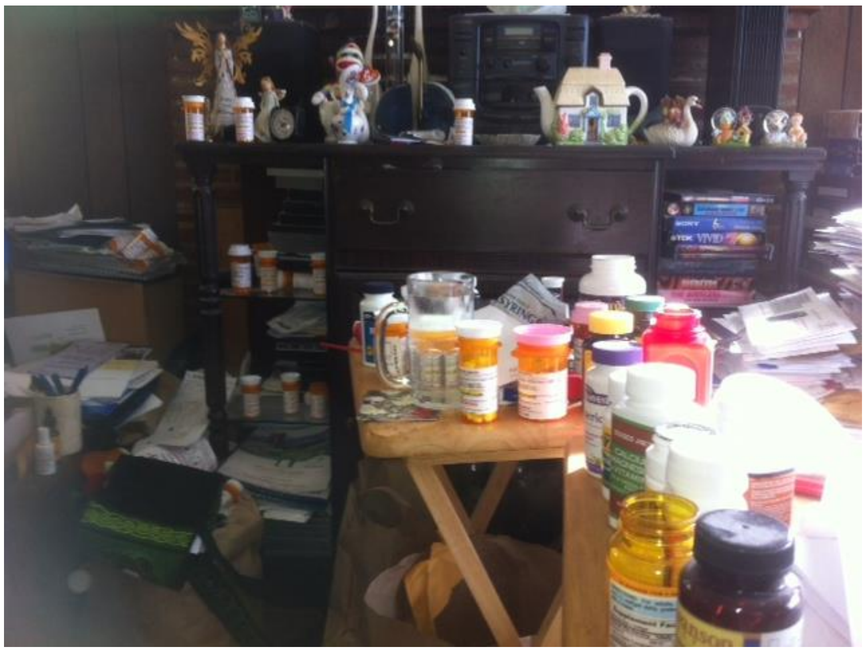
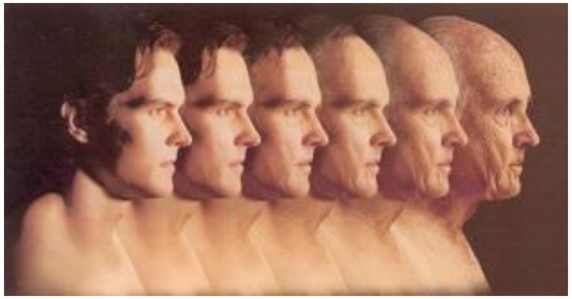
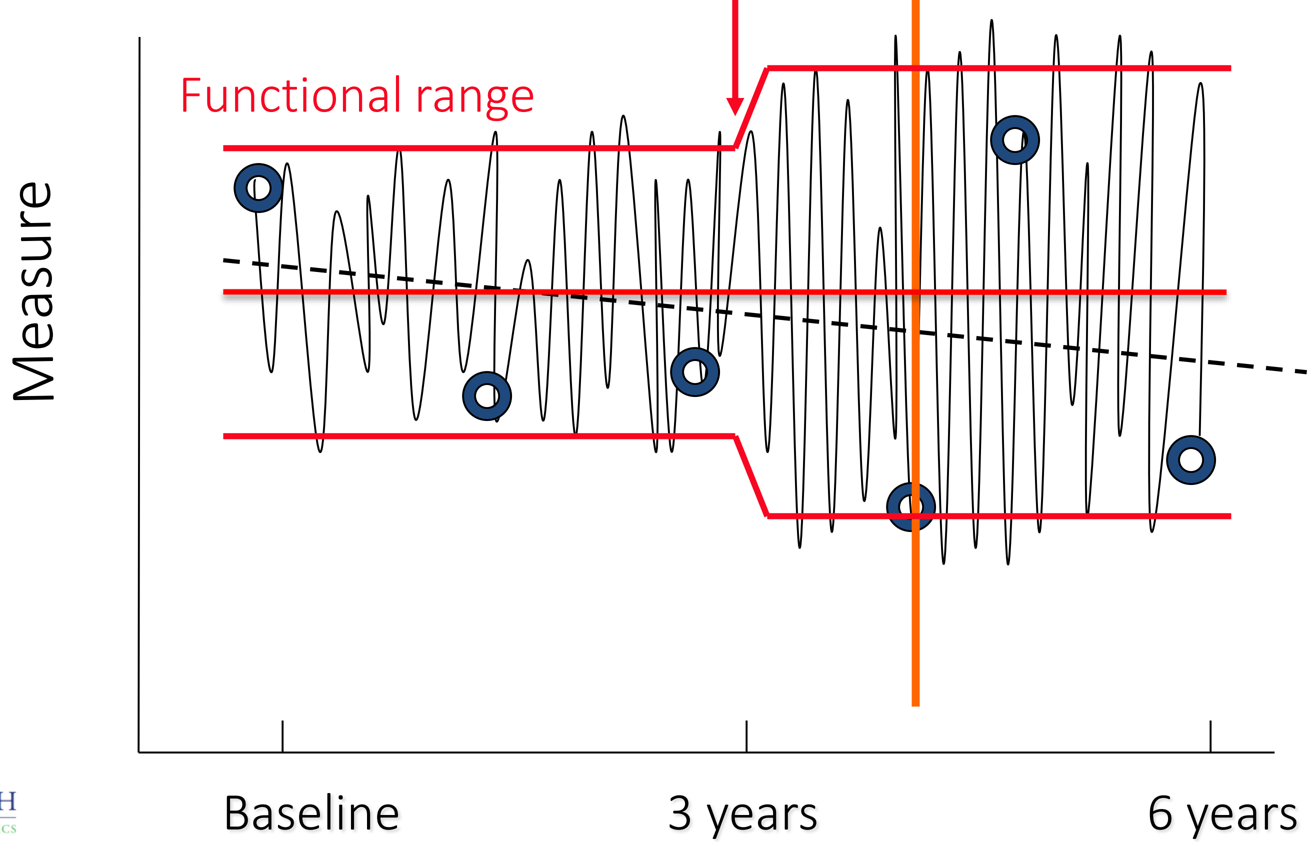
How may new technologies advance longitudinal research?



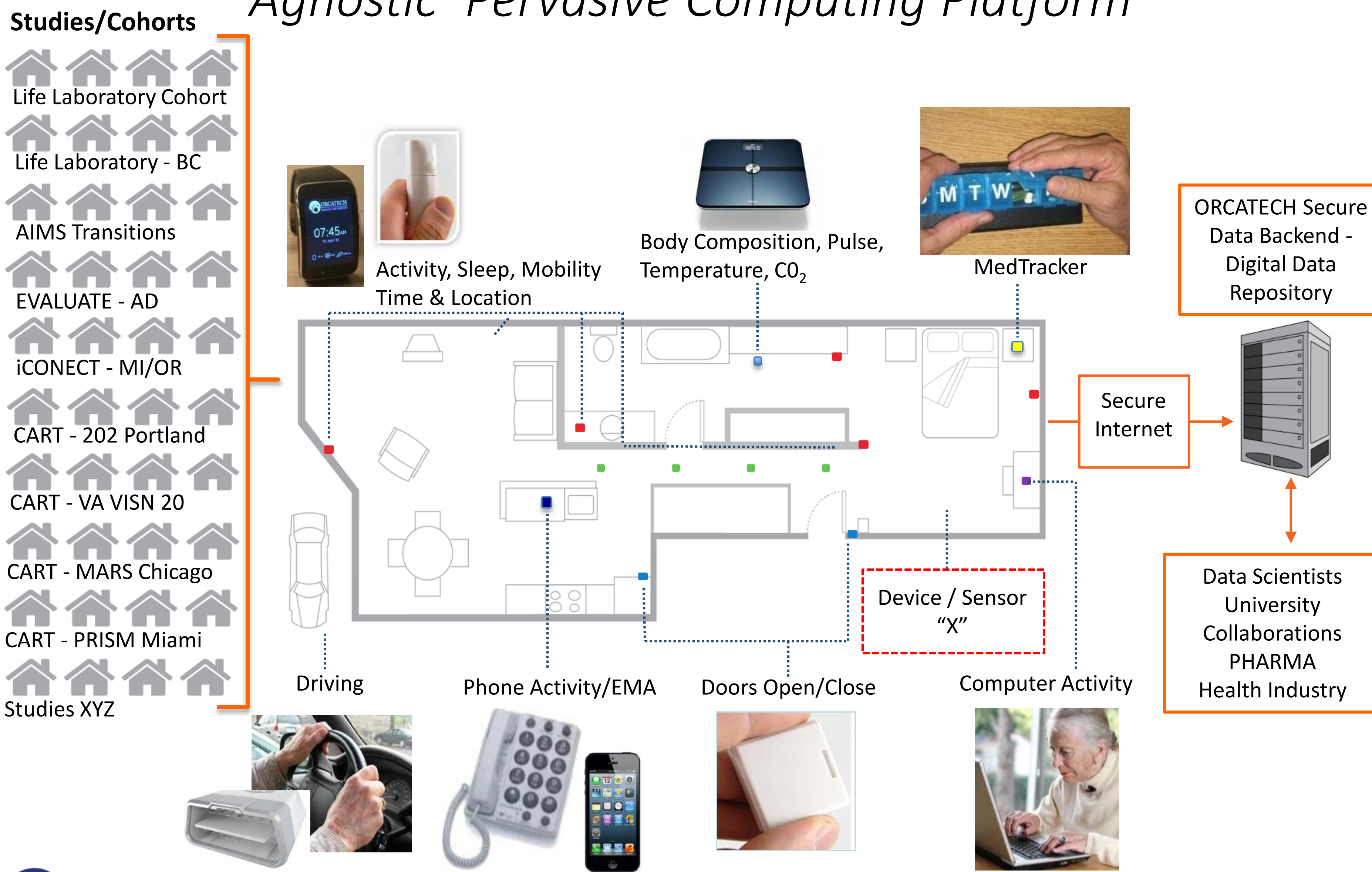
Improving detection of change: The case for more continuous, objective, multi-domain measures





Platform for Continuous Remote Assessment: *ORCATECH*

'Agnostic' Pervasive Computing Platform



Kaye et al. Journals of Gerontology, 2011; Lyons et al. Frontiers in Aging Neuroscience, 2015

Illustrative Examples & Principles:

Assessment of key functional and wellness domains - motor function, mobility, medication adherence, sleep behaviors, mood, cognition

"Don't Panic. It's only a prototype"

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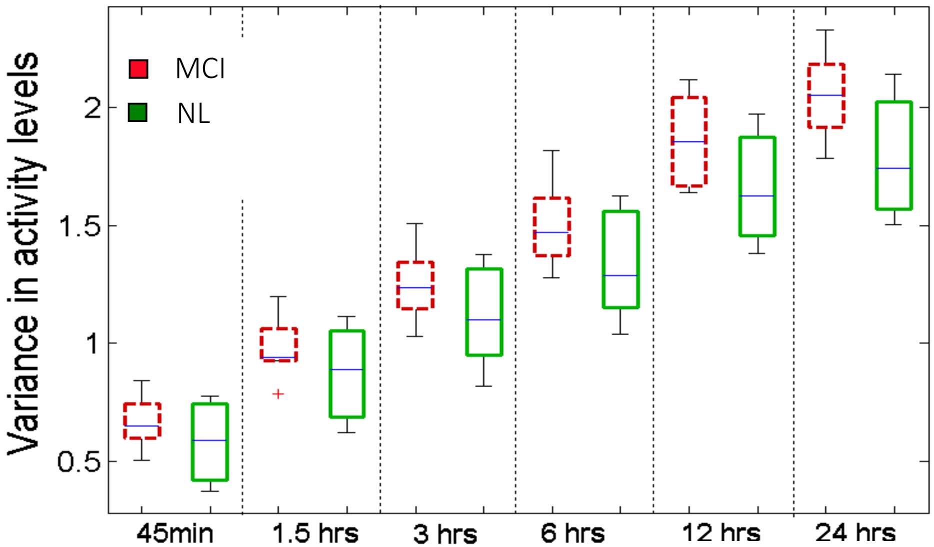
Physical Activity and Mobility Behaviors:

Differentiation of early MCI

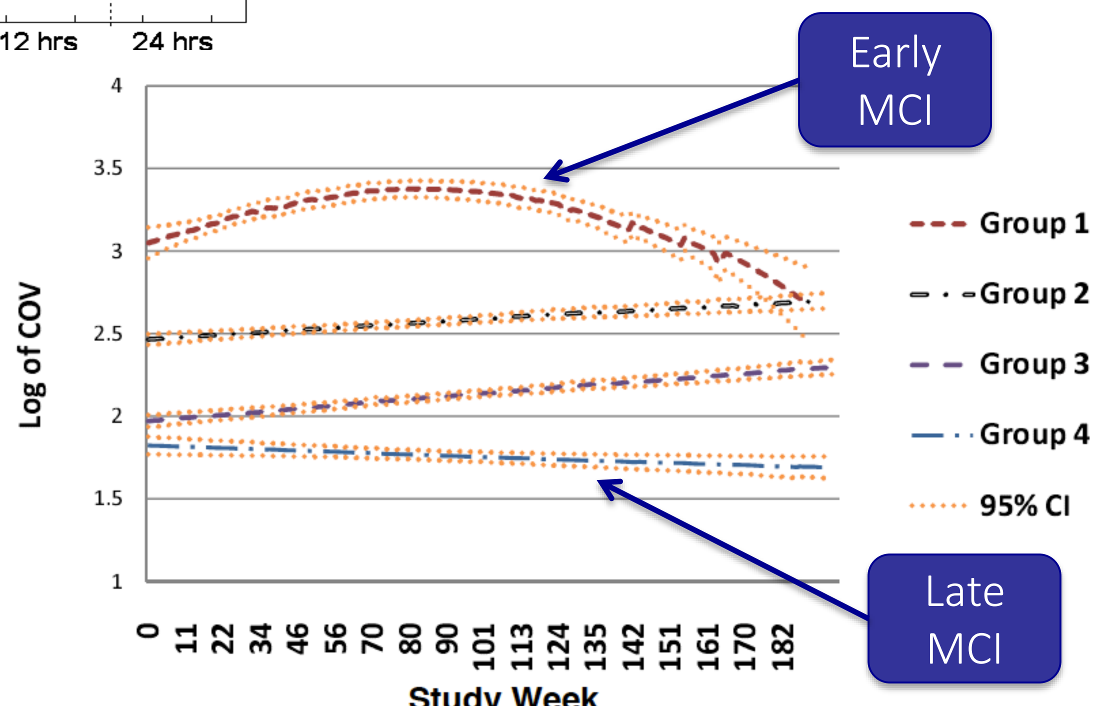


Activity patterns associated with MCI

Hayes et al. Alzheimers Dement, 2008

Trajectories of gait speed over time

Dodge, et al. Neurology, 2012



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Physical Activity and Mobility Behaviors

Room activity distributions differentiating MCI vs not MCI (n=85)

Room	Bedroom	Bathroom	Kitchen	Living Room	Combined
$F_{0.5}$ Score*	0.842	0.829	0.813	0.826	0.856

*$F_{0.5}$ Scores window size ω = 20 weeks; slide size = 4 weeks (with leave-one-subject-out cross validation)

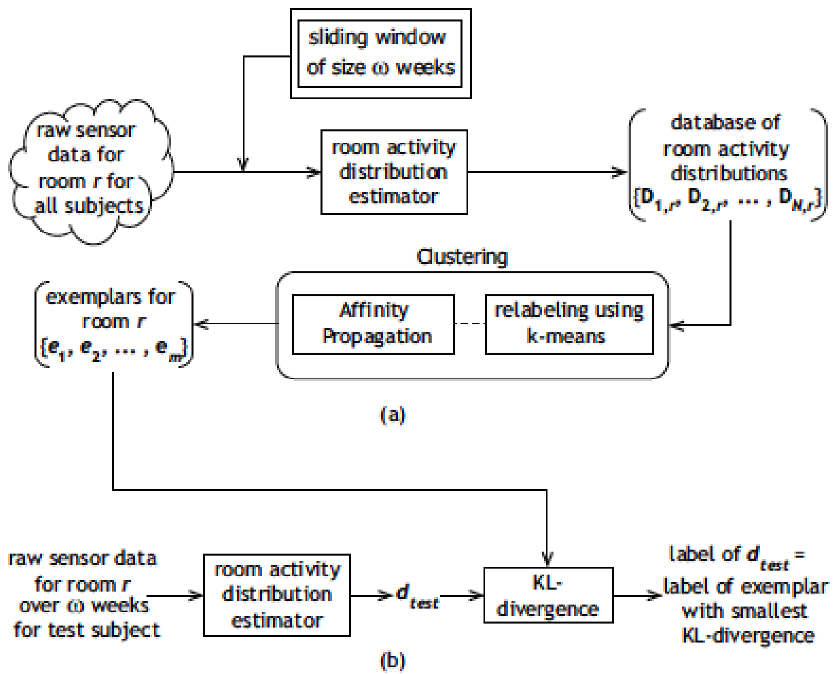
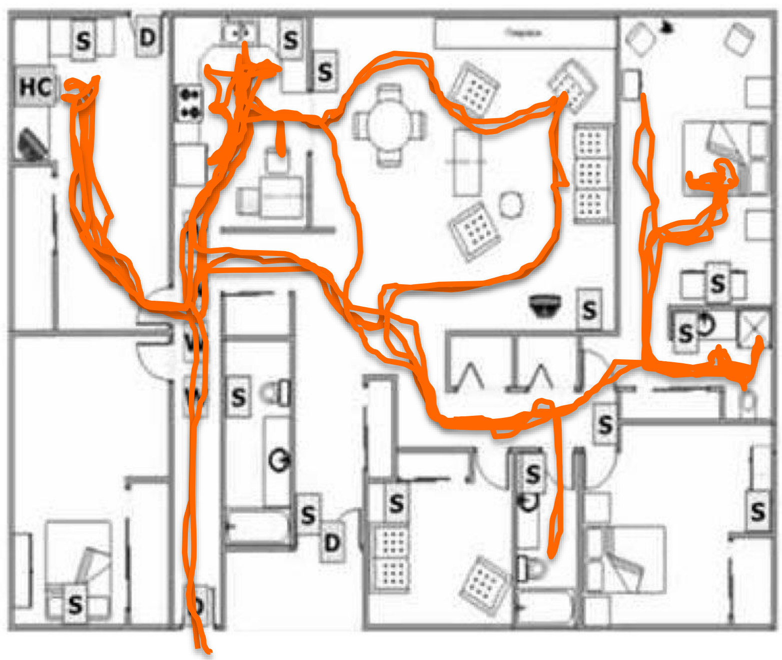


Fig. 2. General overview of the cognitive status recognition process using distributions corresponding to room r. (a) Training Stage. (b) Test Stage.



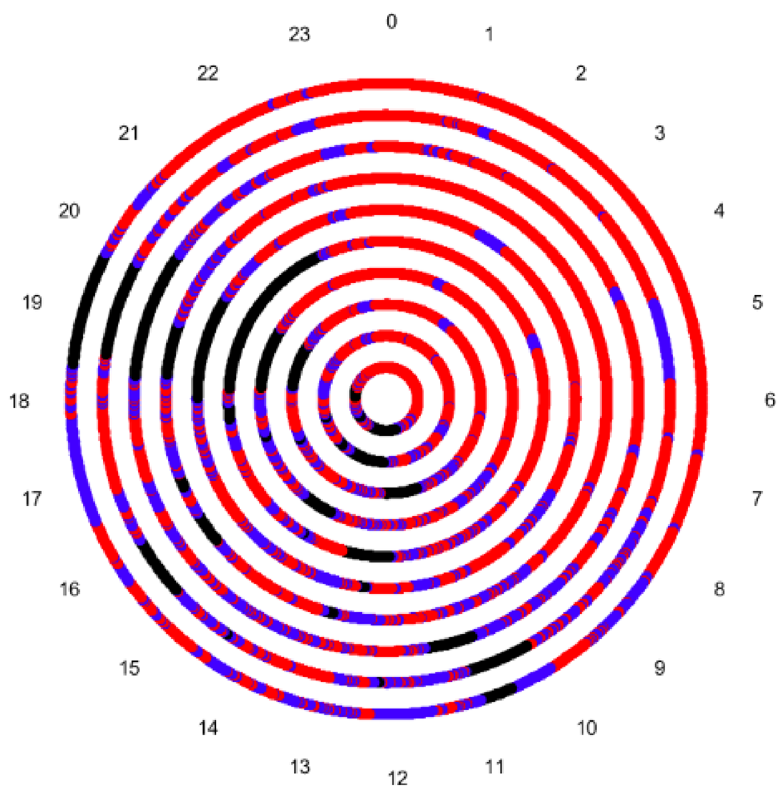
Akl et al. Journal of Ambient Intelligence and Smart Environments, 2015

Dyad Analysis

Together

Separate

Out of Home



Together: 1285 minutes (21.4 hrs/day)
Apart: 155 minutes (2.6 hrs/day)

Christy Reynolds, 2017, unpublished

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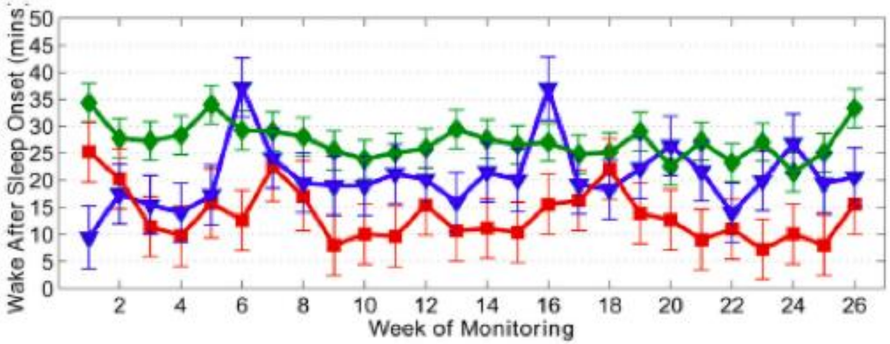
Night-time Behavior & Sleep

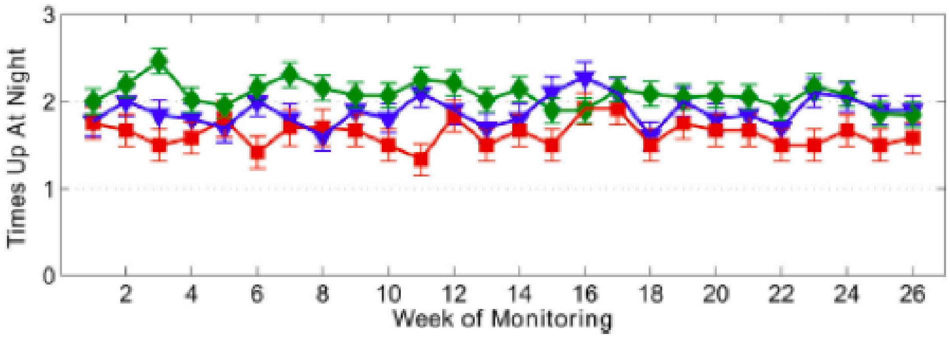
Differentiation of MCI

Normal -

NA-MCI -

A-MCI -





Objective Measure	Intact	aMCI	naMCI	P value
Movement in Bed (sensor firings)	9.4 ± 0.4	7.8 ± 0.9	10.9 ± 0.7	p < 0.05 (aMCI < naMCI)
Wake After Sleep Onset (mins)	27.2 ± 1.2	13.5 ± 2.6	20.6 ± 2.0	p < 0.001 (aMCI < intact, naMCI)
Settling Time (mins)	2.5 ± 0.07	2.3 ± 0.15	3.1 ± 0.11	p < 0.001 (naMCI > intact, aMCI)
Times up at night (# times)	2.1 ± 0.04	1.6 ± 0.10	1.9 ± 0.08	p < 0.001 (aMCI < intact, naMCI)
Total Sleep Time (hrs)	8.3 ± 0.04	8.5 ± 0.09	8.5 ± 0.07	NS

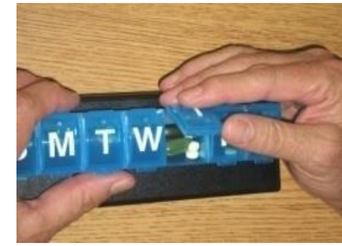
No Differences Between Groups in Self-Report Measures

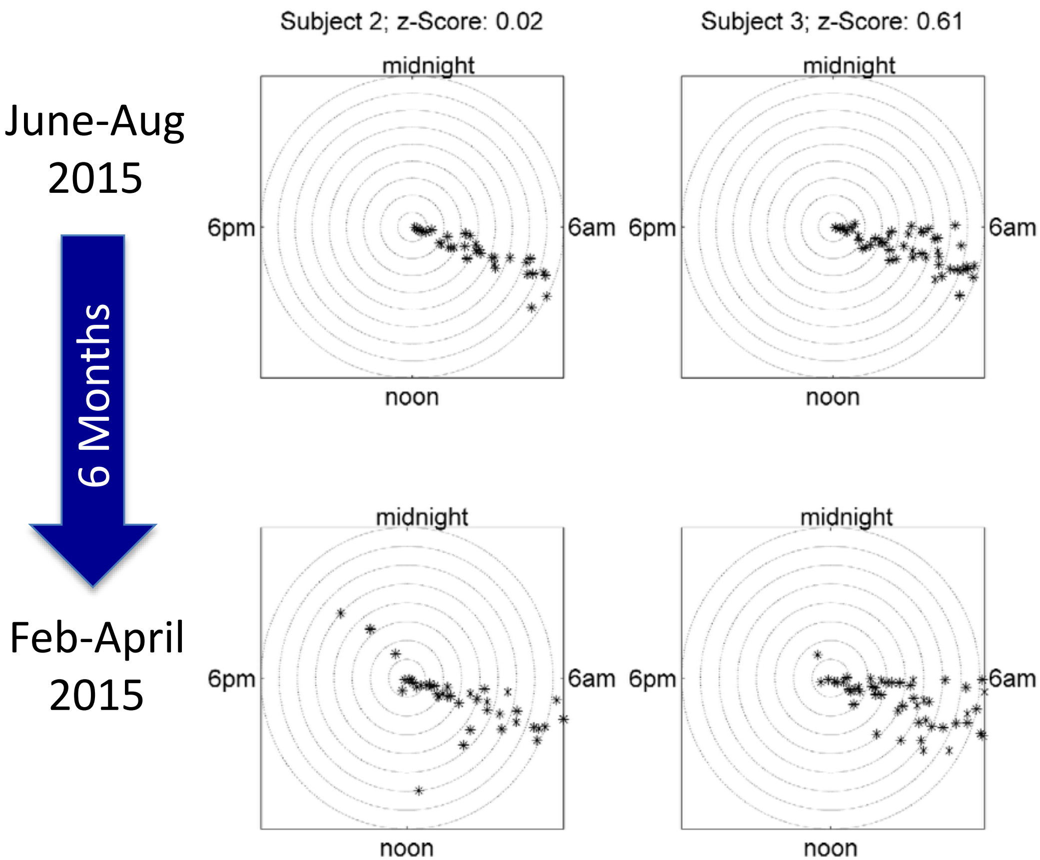
Self-Report Measure	Intact	aMCI	naMCI	P value
Subjective Daytime Sleepiness	1.8 ± 0.2	1.5 ± 0.3	2.0 ± 0.3	0.69
Subjective Insomnia	1.3 ± 0.2	0.8 ± 0.3	1.6 ± 0.3	0.21
Subjective Restlessness	1.0 ± 0.1	0.4 ± 0.3	0.7 ± 0.2	0.34
Times up at night	1.1 ± 0.1	1.0 ± 0.3	1.0 ± 0.2	0.77

Hayes, et al. Alzheimer Dis Assoc Disord. 2014
Hayes, et al. IEEE Eng Med Biol Soc, 2010

Cognition: Prospective Memory (Medication Adherence)

Continuous monitoring of medication adherence may identify patients experiencing cognitive decline





- Individuals with lower cognitive function have more 'spread' in the timing of taking their medications ($p < .014$)
- Increase over time in the spread of timing of taking their medications ($P < .012$)

Austin, et al. Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring, 2017

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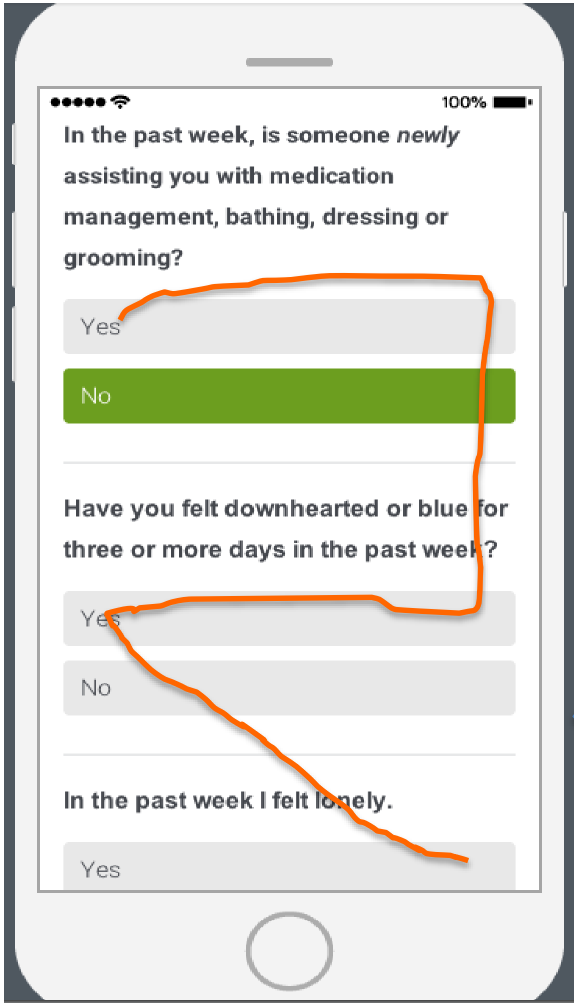
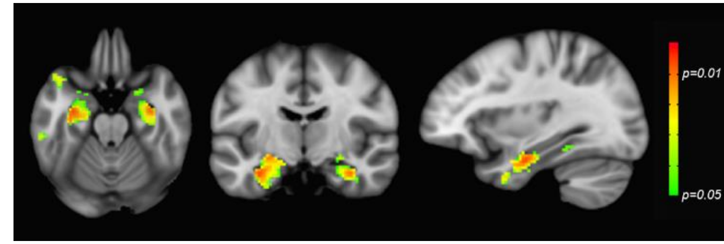
Cognition, Behavior, Motor Function: Computer Use



Some Self-Report Data is Necessary



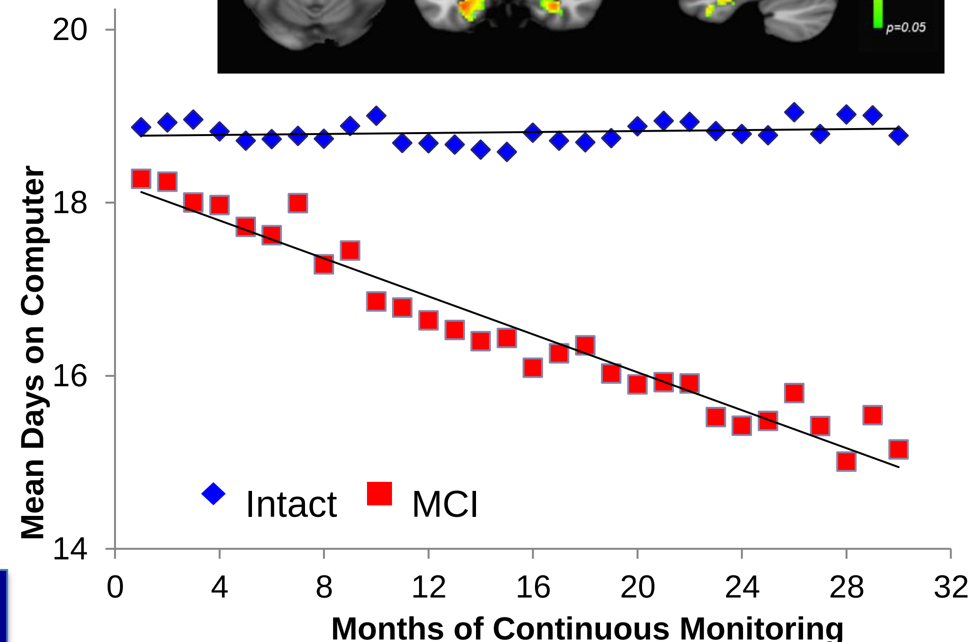


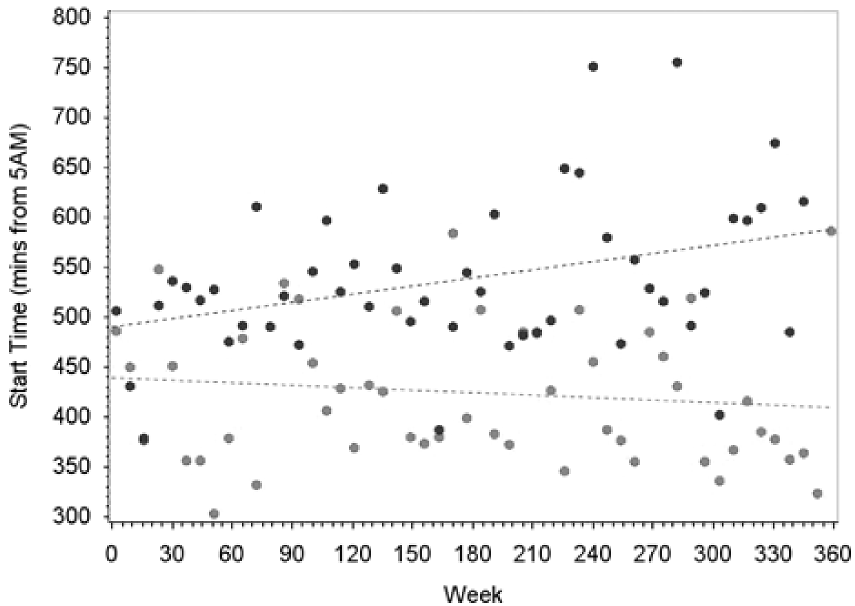
Table 4
Associations between cognitive status and mouse movement variability derived from one week of data

	Outcome, movement curvature (IQR_K)		Outcome, time spent idling (IQR_Idle)	
Covariate	Coefficient	*P* value	Coefficient	*P* value
MCI (reference: cognitively intact group)	0.013	.008**	386.8	.04*
Age (y)	−0.001	.03*	−15.0	.31
Education (y)	0.002	.05	−12.4	.70

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

Kaye, et al. Alzheimers Dement. 2014; Silbert et al., Alzheimers Dement, 2015; Seelye et al. Alzheimers Dement.: Diagnosis, Assessment & Disease Monitoring, 2015; Seelye et al. Alzheimer's Disease & Assoc. Disorders, 2015

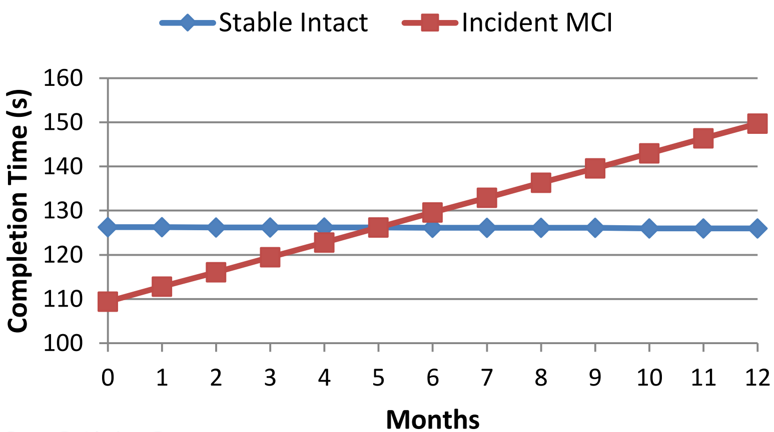
Cognition: Computer Use



Time of Day Completed: Longitudinal scatter plot of differences in median questionnaire start time of day (minutes from 5 AM) by week for MCI (Black) and cognitively intact (gray) participants. Points are the median start time of day for the group during each week.

Seelye et al. Alzheimer's Disease & Assoc. Disorders, 2015

Longitudinal change in survey completion time by group



Time to Complete: Longitudinal Change in Survey Completion Time (in seconds) by Group in the 12 month period *before* MCI diagnosis (calculated regression lines from the mixed effect model)

Seelye et al. under review, 2017

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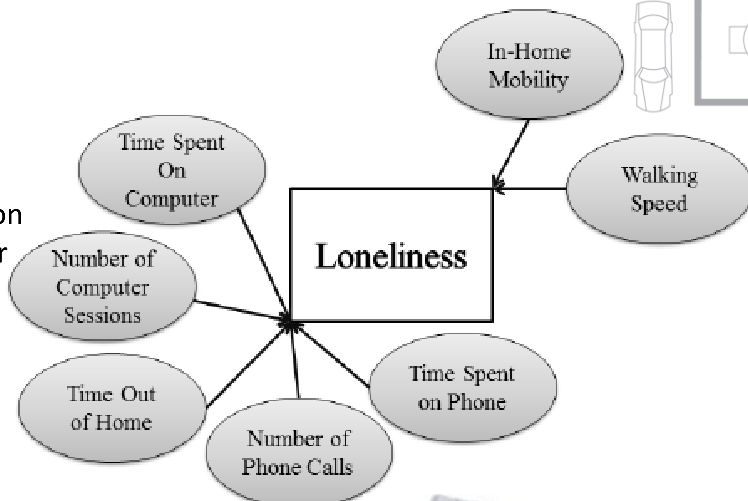
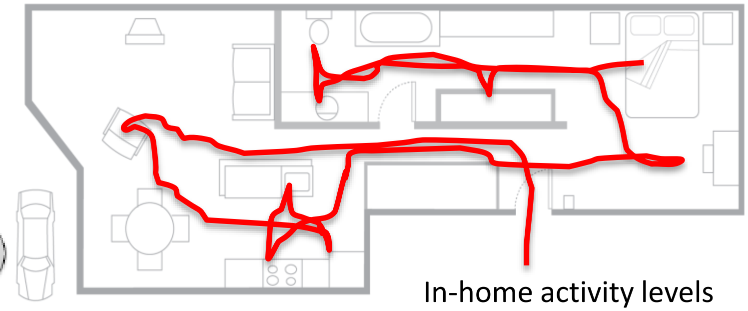
Objective in-home monitoring to identify meaningful behaviours changing during a loneliness intervention

Intervention: "Capturing Time: Journaling Your Journey" -- designed to improve negative emotions such as loneliness, depression, anxiety, and low self-esteem.

Computer use (time on computer; computer sessions)

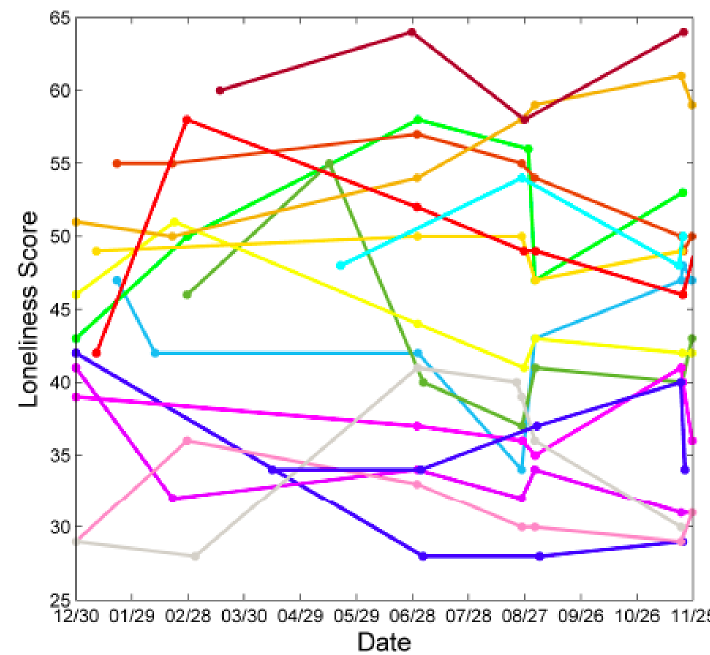




In-home activity levels (mobility, walking speed)

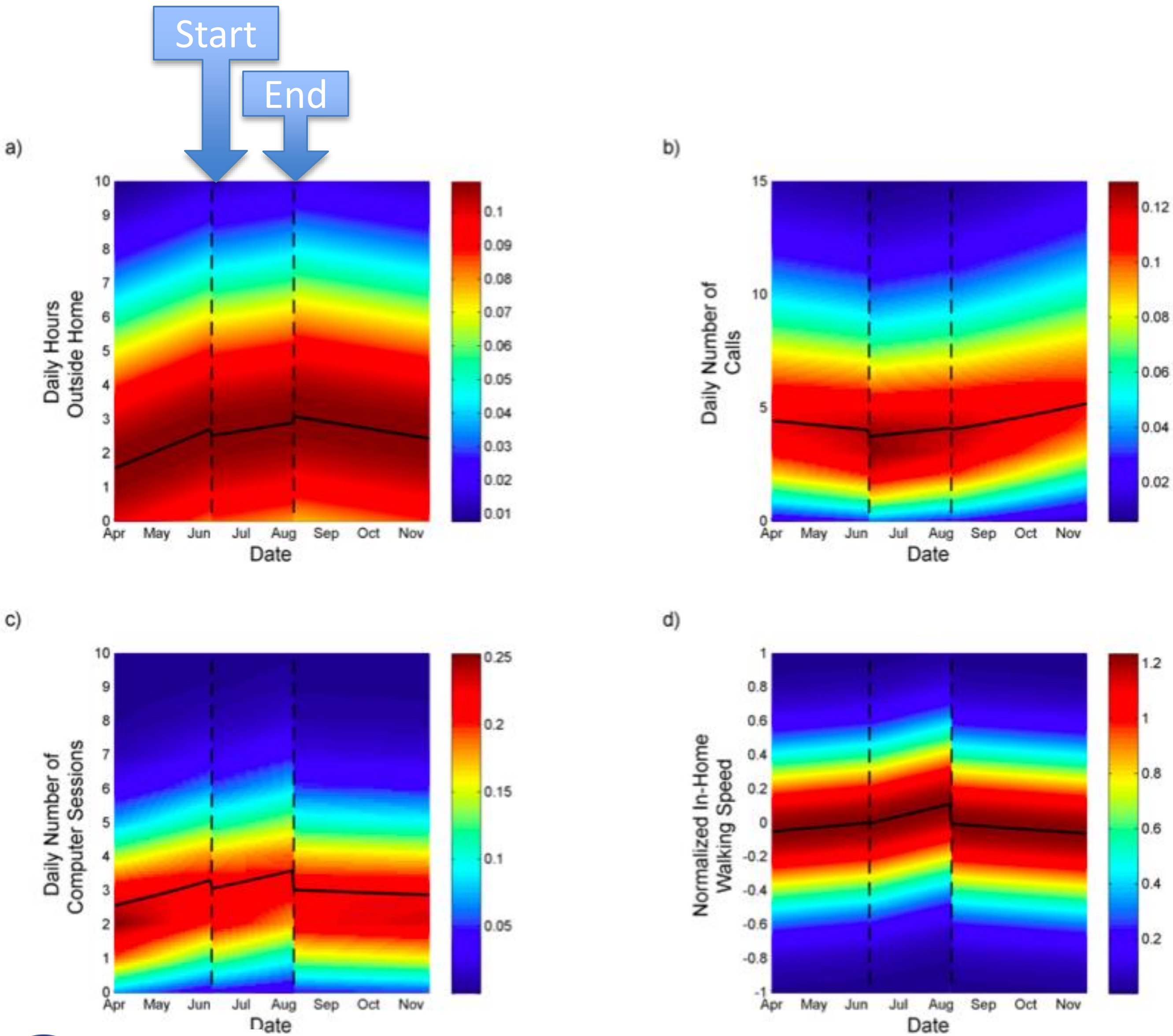
Time spent outside home

Phone use (time on phone; number of calls



Austin et al. IEEE Journal of Translational Engineering in Health Medicine 2016

Capturing Time: digital biomarker results



- ↓ Loneliness ($p<0.05$) by an average of 2.2 ± 3 points.
- ↑ Time out-of-home ($\beta=0.96$, $p<0.01$)
- ↑ Number of computer sessions (IRR=1.196, $p<0.01$)
- ↓ Daily number of calls (IRR=0.84, $p<0.05$).
- ↑ Total phone calls, after intervention (IRR=1.003, $p<0.01$)
- ↑ Walking speed over time ($\beta = 0.002$, $p<0.01$).

Austin, et al. 2017 (under review)

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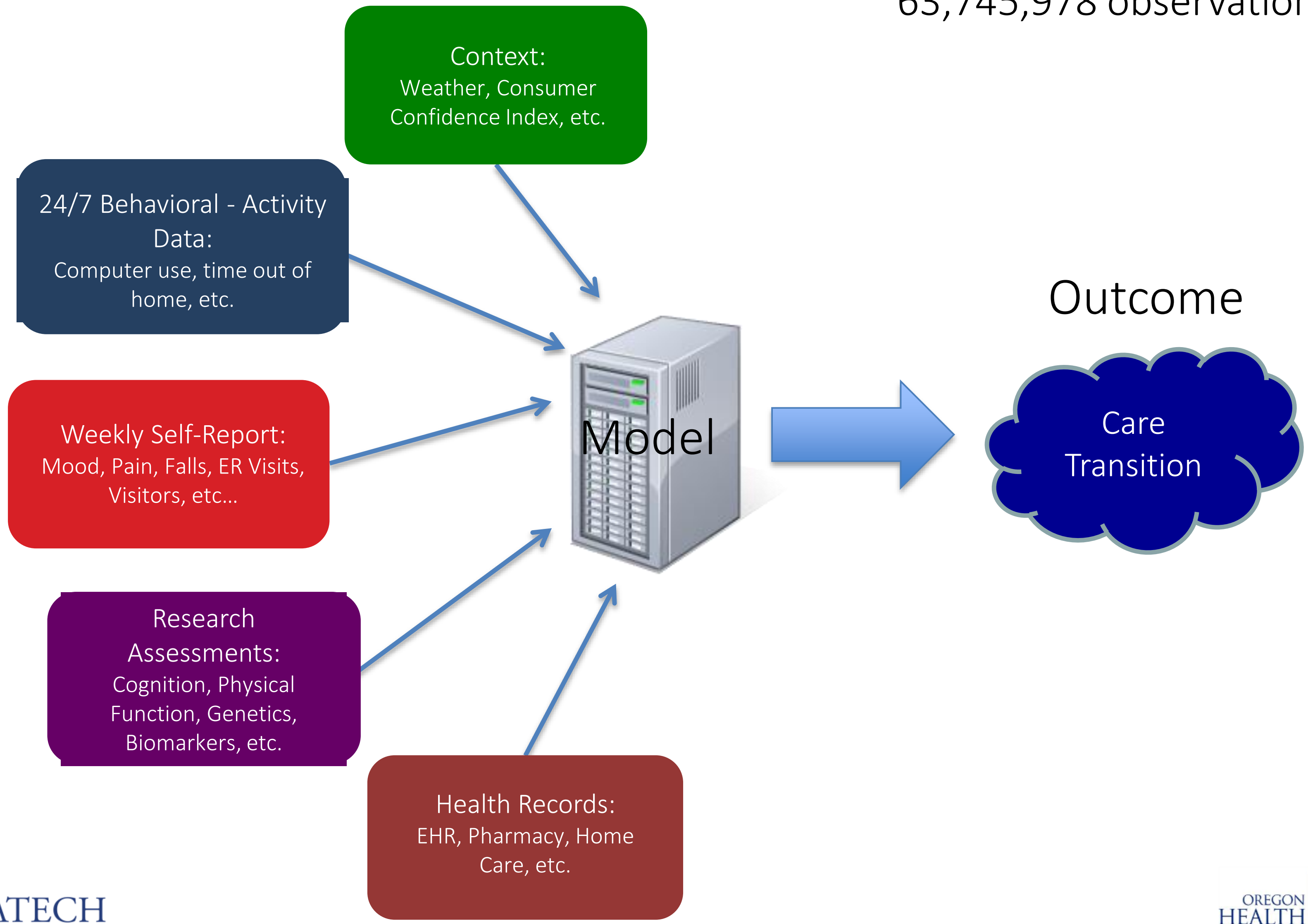
High dimensional multi-domain data fusion model predicting care transitions

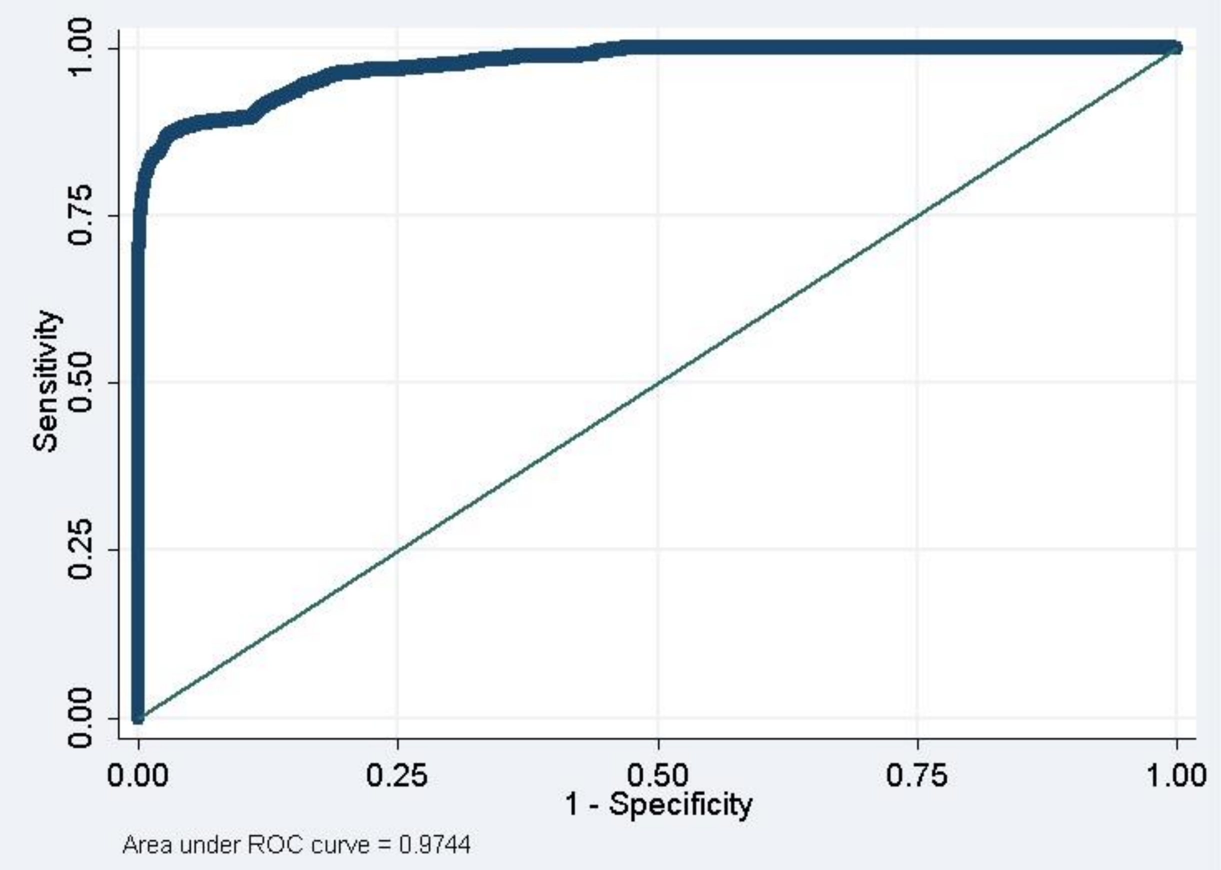
63,745,978 observations



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



Austin et al. 2014 GSA

Future Considerations

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

% of U.S. adults who own a desktop or laptop computer

U.S. adults	73
Sex	
Men	74
Women	71
Race/ethnicity	
White	79
Black	45
Hispanic	63
Age group	
18-29	78
30-49	81
50-64	70
65+	55
Household income	
<$30K	50
$30K-$49,999	80
$50K-$74,999	90
$75K+	91
Educational attainment	
Less than high school	29
High school	63
Some college	81
College+	90
Community type	
Urban	67
Suburban	78
Rural	67

Source: Pew Research Center survey conducted March 17-April 12, 2015. Whites and blacks include only non-Hispanics. N=959

PEW RESEARCH CENTER

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

% of U.S. adults who own a smartphone, e.g. iPhone, Android, Blackberry or Windows phone

U.S. adults	68
Sex	
Men	70
Women	66
Race/ethnicity	
White	66
Black	68
Hispanic	64
Age group	
18-29	86
30-49	83
50-64	58
65+	30
Household income	
<$30K	52
$30K-$49,999	69
$50K-$74,999	76
$75K+	87
Educational attainment	
Less than high school	41
High school	56
Some college	75
College+	81
Community type	
Urban	72
Suburban	70
Rural	52

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

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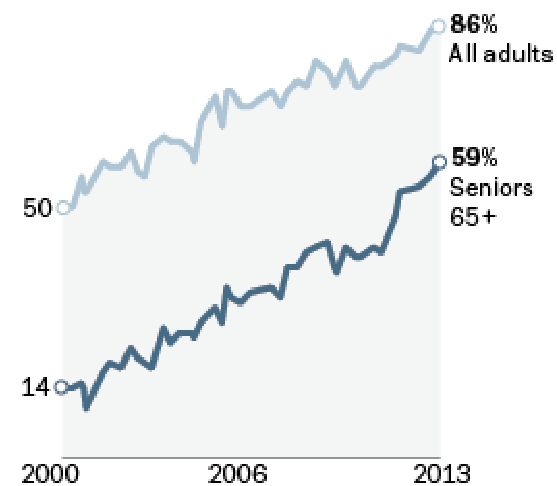
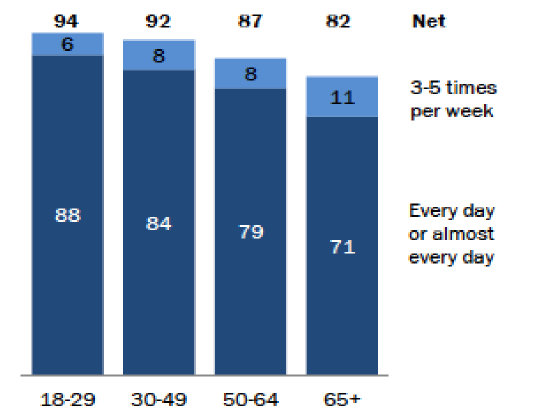
Percent of adults who go online



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

% of internet users in each age group who go online ...



Pew Research Center's Internet Project July 18-September 30, 2013 tracking survey.

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Future Directions: CART - Collaborative Aging (in Place) Research Using Technology

National Institute on Aging

Turning Discovery Into Health

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NEWSROOM

NIH initiative tests in-home technology to help older adults age in place

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January 25, 2017

Many older adults want to live at home independently as they age. Sometimes all they need is a little help from their family and friends—and the right technology. A new initiative led by the National Institutes of Health (NIH) aims to help seniors age in place by developing a research platform to study the use of health-related in-home sensors and other technologies.

CART—Collaborative Aging (in Place) Research Using Technology—unites NIH, academic, and industry experts to develop and test unobtrusive tools that record and track real-time changes in older adults' health status and activities. Launched in October 2016, the $7 million, 4-year project will take place in more than 200 homes in rural and urban communities across the United States.

"This project will provide a systematic way of investigating technology that may enable older people to remain independent and avoid hospitalizations and transitions into care facilities," said Nina Silverberg, Ph.D., of the National Institute on Aging (NIA), which leads the project.

- Interagency initiative with NIH and VA (U2C AG054397)
  - NIA, NIBIB, NCI, NINDS, NCATS, OBSSR, NINR
- To develop and validate the infrastructure for rapid and effective conduct of future research utilizing technology to facilitate aging in place, with a special emphasis on people from underrepresented groups.
- Ultimately scale to 10,000 homes
- PI: J. Kaye, ORCATECH
- Chief Science Officer: N. Silverberg, NIA
- Intel, Rush, U. Miami, U. Penn. OSU

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Thank you!

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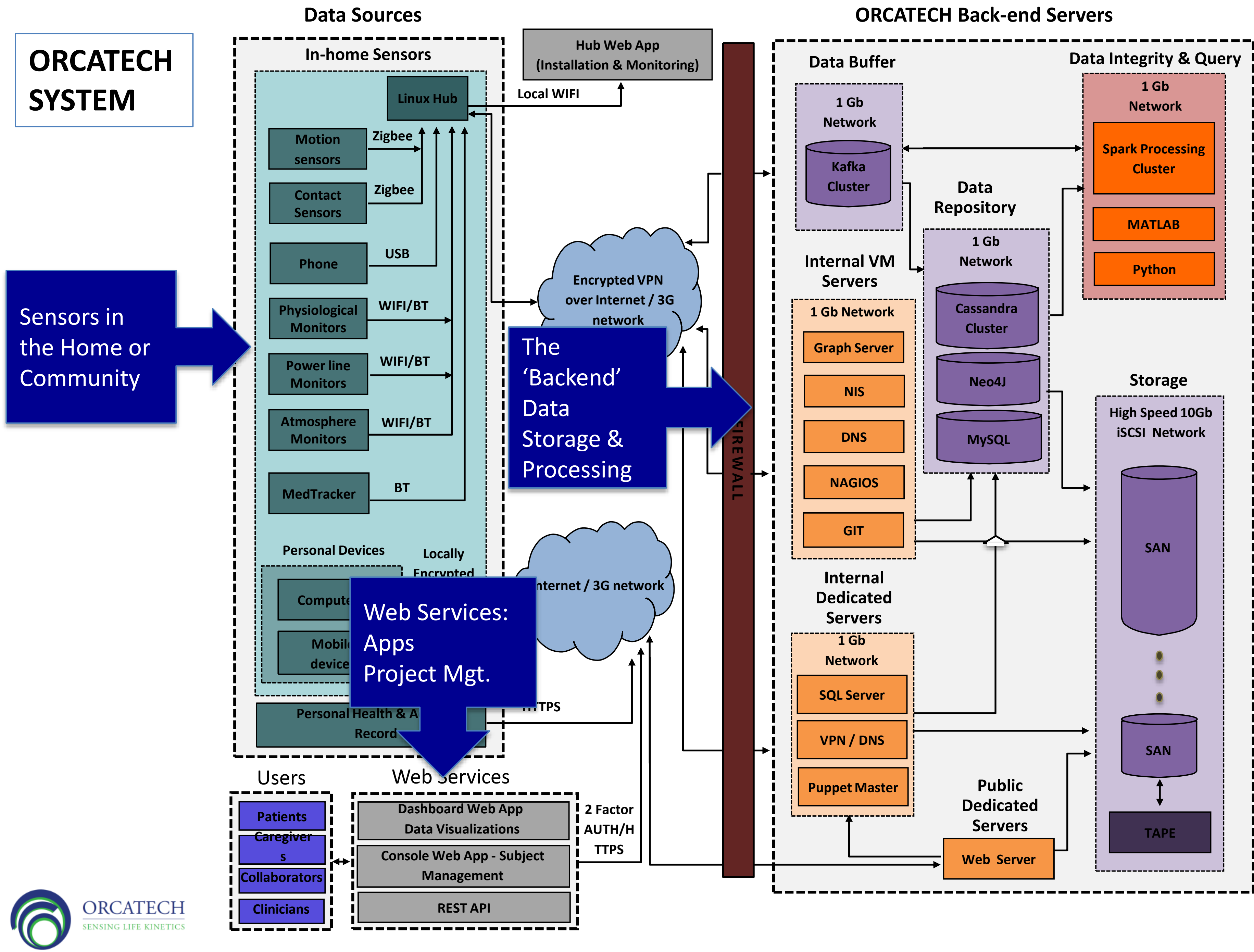
ORCATECH SYSTEM
Data Sources
ORCATECH Back-end Servers
In-home Sensors
Hub Web App (Installation & Monitoring)
Linux Hub
Local WIFI
Motion sensors
Zigbee
Contact Sensors
Zigbee
Phone
USB
Physiological Monitors
WIFI/BT
Power line Monitors
WIFI/BT
Atmosphere Monitors
WIFI/BT
MedTracker
BT
Personal Devices
Locally Encrypted
Compute
Mobile device
Personal Health & A Record
Sensors in the Home or Community
Encrypted VPN over Internet / 3G network
The 'Backend' Data Storage & Processing
nternet / 3G network
Web Services: Apps Project Mgt.
TTPS
FIREWALL
Data Buffer
1 Gb Network
Kafka Cluster
Data Integrity & Query
1 Gb Network
Spark Processing Cluster
MATLAB
Python
Data Repository
1 Gb Network
Cassandra Cluster
Neo4J
MySQL
Internal VM Servers
1 Gb Network
Graph Server
NIS
DNS
NAGIOS
GIT
Storage
High Speed 10Gb iSCSI Network
SAN
SAN
TAPE
Internal Dedicated Servers
1 Gb Network
SQL Server
VPN / DNS
Puppet Master
Public Dedicated Servers
Web Server
Users
Patients
Caregivers
Collaborators
Clinicians
Web Services
Dashboard Web App Data Visualizations
Console Web App - Subject Management
REST API
2 Factor AUTH/HTTPS
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Cognitive Function Affected by Sleep History

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Clin Neuropsychol. 2015 Jan; 29(1): 53–66.
Published online 2015 Feb 2. doi: 10.1080/13854046.2015.1005139

The impact of sleep on neuropsychological performance in cognitively intact older adults using a novel in-home sensor based sleep assessment approach

Adriana Seelye,[1,2] Nora Mattek,[1,2] Diane Howieson,[1] Thomas Riley,[2,3] Katherine Wild,[1,2] and Jeffrey Kaye[1,2,3]

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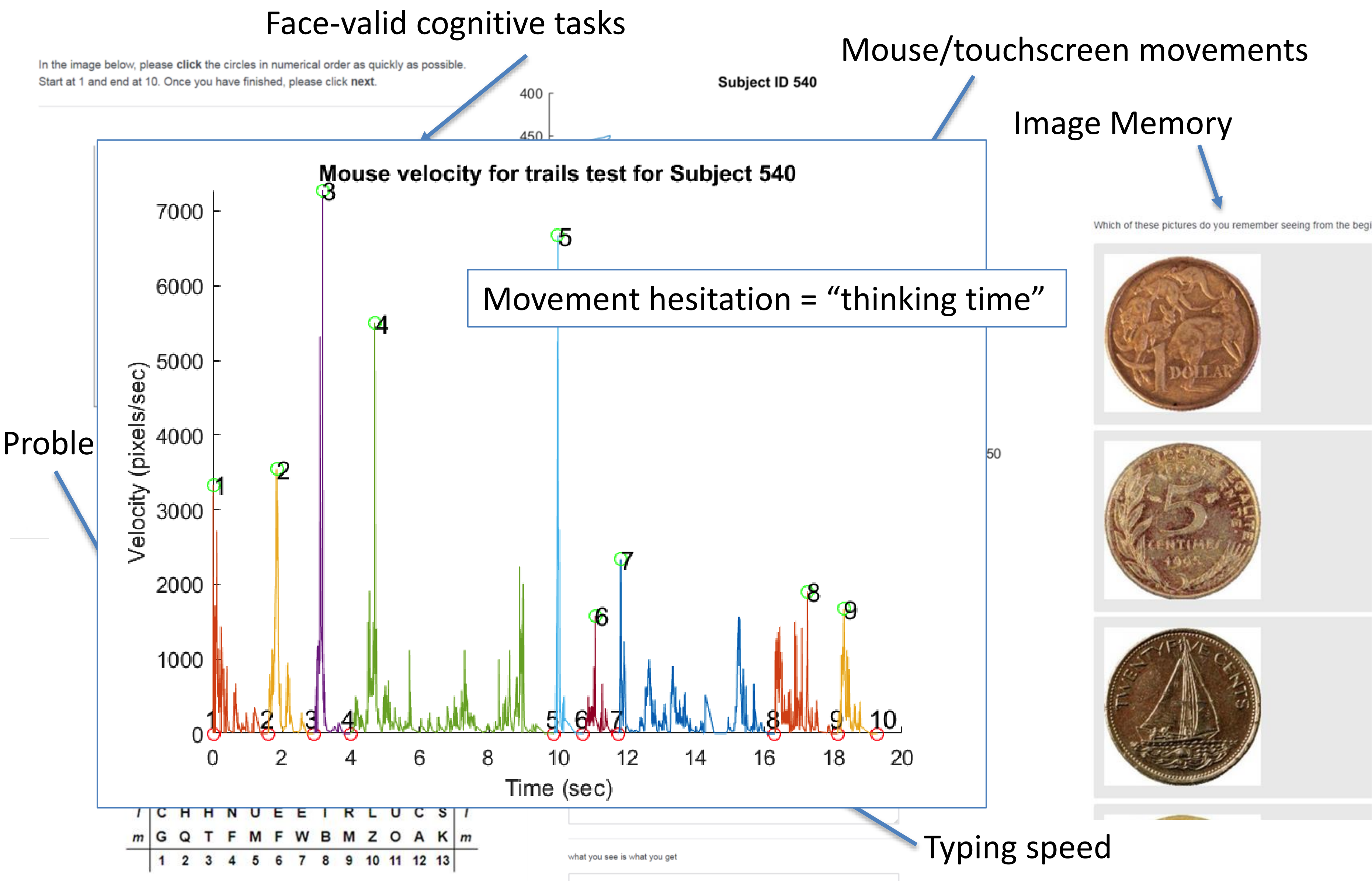
Abstract

Go to:

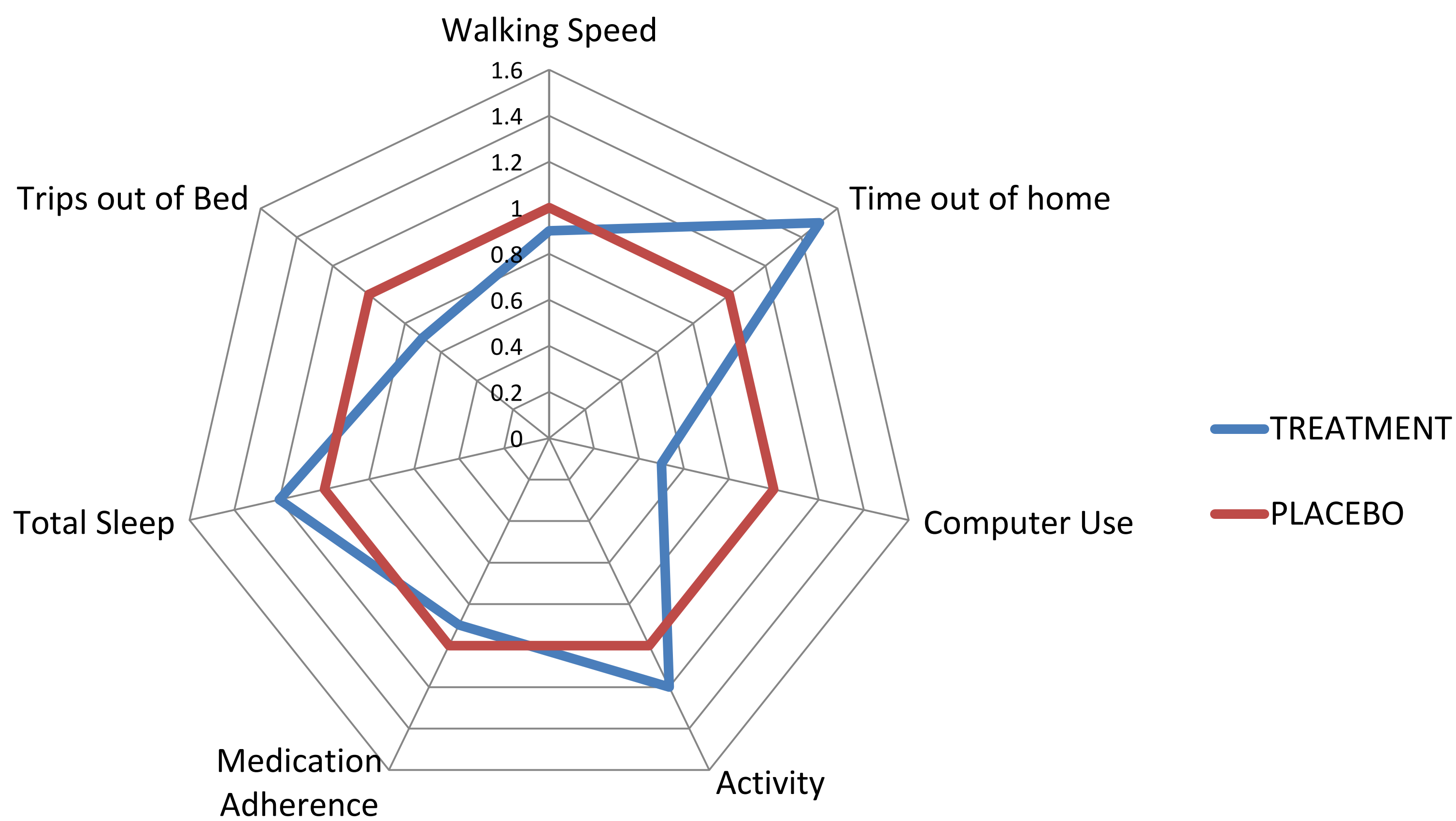
The relationship between recent episodes of poor sleep and cognitive testing performance in healthy cognitively intact older adults is not well understood. In this exploratory study, we examined the impact of recent sleep disturbance, sleep duration, and sleep variability on cognitive performance in 63 cognitively intact older adults using a novel unobtrusive in-home sensor based sleep assessment methodology. Specifically, we examined the impact of sleep the *night prior*, the *week prior*, and the *month prior* to a neuropsychological evaluation on cognitive performance. Results showed that mildly disturbed sleep the week prior and month prior to cognitive testing was associated with reduced working memory on cognitive evaluation. One night of mild sleep disturbance was not associated with decreased cognitive performance the next day. Sleep duration was unrelated to cognition. In-home, unobtrusive sensor monitoring technologies provide a novel method for objective, long-term, and continuous assessment of sleep behavior and other everyday activities that might contribute to decreased or variable cognitive performance in healthy older adults.

Cognition: Online (Computer/Internet-based) Testing

Survey for Memory, Attention, and Response Time (SMART)



Behavioral/Functional Fingerprinting by Treatment Status



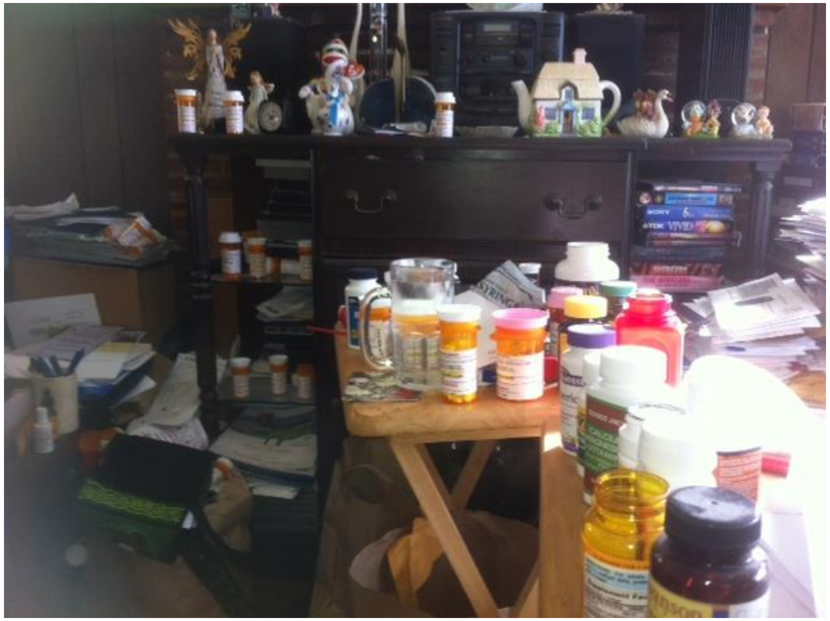
Values are odds ratios. 1 is the reference value, and is 'normalized' to placebo.

EVALUATE - AD

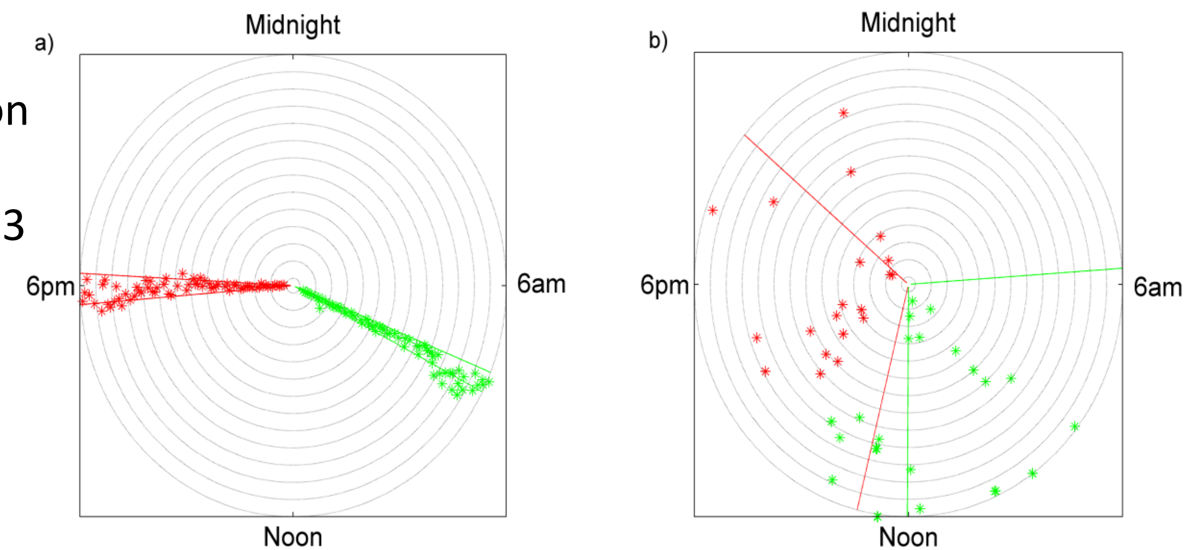
Ecologically Valid, Ambient, Longitudinal and Unbiased Assessment of Treatment Efficacy in Alzheimer's Disease

- Longitudinal naturalistic observational cohort study spanning up to 18 months
- Goal: Establish Digital Biomarkers that are sensitive to clinical change associated with conventional AD TXs
- ORCATECH platform
- Sixty subjects: 30 patients/30 care partners (30 households)
- NIA / Merck Funding

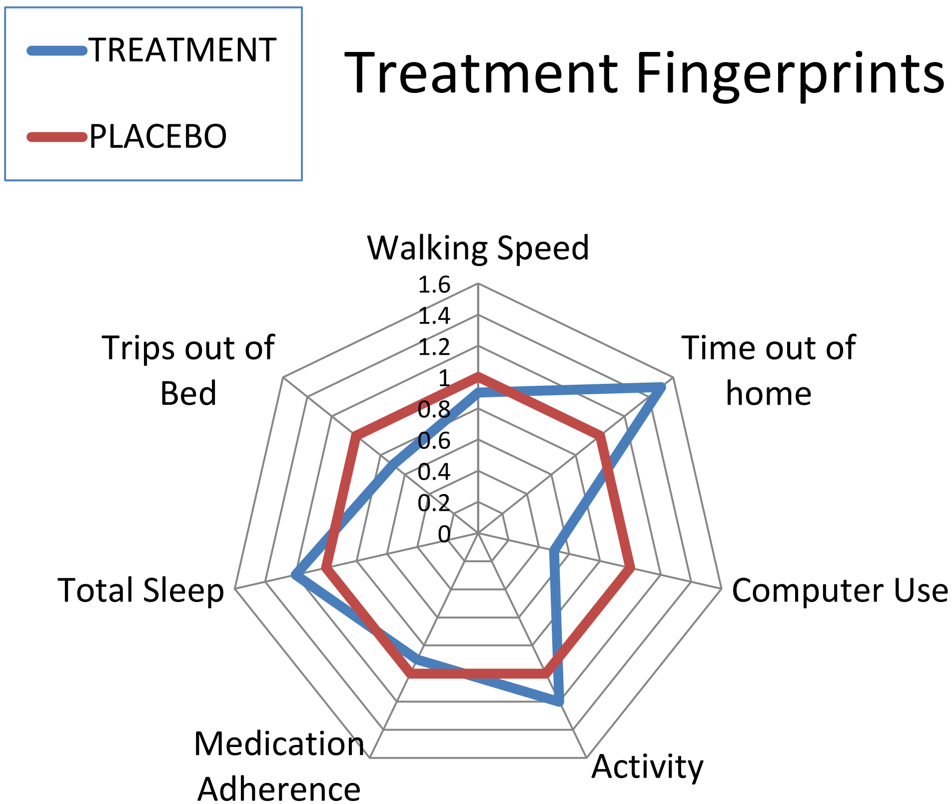
Core Functions & Measures	Sensors or Devices Used	Conventional Assessment Measures
Physical Capacity/Personal Mobility Total daily activity, number of room transitions, median weekly walking speed from multiple daily walks, daily steps, time out of home	PIR motion sensors and contact sensors; Actigraphy	Walking speed (with stopwatch). Self-report of activity from OADC Personal & Family History Questionnaire (Paffenbarger scale, e.g., *estimate hours per day you spent in low activity*)
Sleep/Nighttime behavior Time of awakening, time spent in bed at night, wake after sleep onset, times up at night, and sleep latency	PIR motion sensors; Actigraphy	Pittsburgh Sleep Quality Index and Sleep Disturbance Symptom Questionnaire (OADC Personal & Family History Questionnaire)
Physiologic Health Daily BMI, pulse, arterial resistance	Biofunction Scale (AM pulse, art. resistance); Actigraph pulse	Vital signs (height, weight, pulse)
Medication Adherence Percentage of doses missed in a 7-day period, relative to prescribed schedule.	MedTracker Electronic Pillbox	Self-report of adherence to medication taking regimen (visual-analogue scale: ranging from zero to 100%)
Socialization/Engagement Time out of home, time alone or with spouse, phone call patterns, on-line computer activity (email, social network sites)	PIR motion sensors, contact sensors, actigraphy, personal computer, phone monitors	Self-report of 8 social activities from OADC Personal & Family History Questionnaire (e.g., how often do you have visitors: rarely/never, daily, weekly, monthly. yearly)
Cognitive Function Time to complete on-line tasks (e.g., weekly PHAR), mouse movements, prospective memory for medication, AM weighing protocol.	Personal computer or tablet, MedTracker, Biofunction scale.	Z-score composite of UDS cognitive battery; ADAS-cog 13 score.
Community Mobility – Driving Time and distance driving, hard braking, hard accelerations, most frequent locations out of home	Home sensors (exit door contact sensors); Automobile data port telematic sensor	FAQ rating of ability: *Traveling out of neighborhood, driving, arranging to take buses*
Health & Life Events On-line self-report: ER, doctor, hospital visits, home visitors, mood, pain, loneliness, falls, injuries, change in home space, home assistance received, change in medications	Personal computer or tablet (On-line reporting)	Mood: Geriatric Depression Scale (15 item) and Neuro- Psychiatric Inventory (NPI); Self-report of health events from OADC Personal & Family History Questionnaire
Care Partner Engagement Time alone/time with cognitively impaired partner; time in bathroom together	PIR motion sensors, contact sensors, actigraphy	Zarit Caregiver Burden scale – ZBI-12



Circular plots of medication taking patterns from two individuals over the same 3 month period.



Transforming Clinical Trials with High Frequency, Objective, Continuous Data: *"Big Data" for Each Subject*



- Meaningful, ecologically valid, and integrated outcomes
- Reduce required sample size and/or time to identify meaningful change.
- Reduce exposure to harm (fewer needed/ fewer exposed)
- More precise estimates of the trajectory of change; allow for *intra-individual* predictions.
- Provide the opportunity to substantially improve efficiency and inform go/no-go decisions of trials.

Digital Biomarkers in ADCS PEACE-AD RCT: Prazocin for Agitation in AD RCT: BMDs in Agitation

Digital Agitation Assessment -
Wrist-worn devices with long battery life, H_2O-proof and pulse measurement. Activity levels monitored continuously during entire 12-week titration study using wrist actigraphy. Continuous monitoring critical as study employs a flexible dose titration schedule, and the use of rescue medication for agitation (lorazepam).

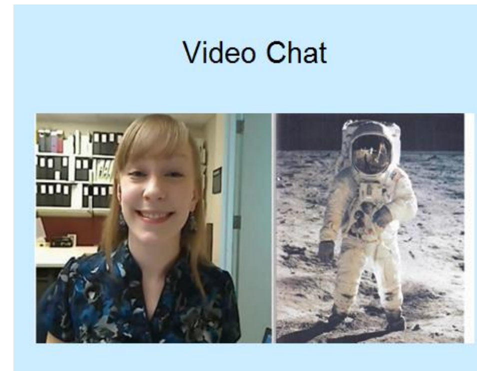
Outcome measures -
Motor activity (total activity counts/steps over a 24 hour period (MA_{24}), and the 12 hour period from 6 PM to 6 AM for each wk (MA_{12}), for the 12 wk study. Percent change in total activity counts at wk 1 (pre-TX) compared to wk 12 (post-TX) will be calculated (DMA_{24} and DMA_{12}).

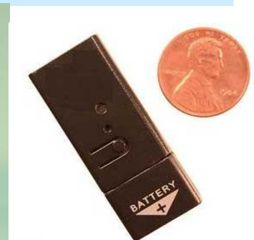
Exploratory analyses -
Value of heart rate with movement metrics, activity counts in subjects receiving lorazepam and in those discontinuing prazosin. Sleep disruption/continuity.

The "Social Engagement Study" (H. Dodge, PI)

Active, Frequent Assessments & Interventions Can be Delivered Everyday - *an RCT to Increase Social Interaction in MCI Using Home-based Technologies*

- 6 week RCT of daily 30 min video chats using Internet connected personal computers with a webcam vs. weekly brief phone interview
- N = 86; 80.5 ± 6.8 years; MCI & Normal Cognition
- 89% of all possible sessions completed; Exceptional adherence – *no drop-out*

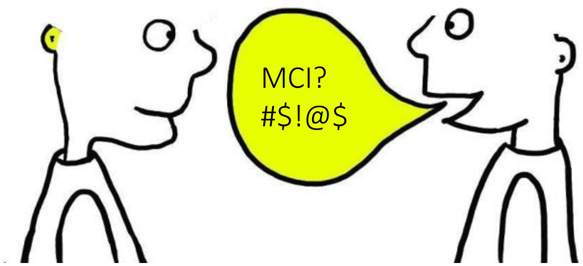




Dodge et al. Alzheimer's & Dementia: Translational Research & Clinical Interventions, 2015
Dodge et al., Current Alzheimer's Disease, 2015

Computer Use:

Social Markers of Cognitive Function



- MCI participants generate a greater proportion of words (2985 vs. 2423 words on average) out of the total number of words during the conversation sessions (controlling for age, gender, interviewer and time of assessment; p=0.03).
- Logistic regression models showed the ROC AUC of identifying MCI (vs. normals) was 0.71 (95% Confidence Interval: 0.54 – 0.89) when average proportion of word counts spoken by subjects was included in the model.

LIWC cat.	Communication	Swear	Anger	Fillers	Family
Avg. num. in MCI	46.4	7.14	37	101.5	31.14
Avg. num. in intact	38.7	4.8	49.8	141.6	41.8
p-value	0.002	0.005	0.054	0.067	0.08

Table 4: Average number of words grouped into LIWC categories

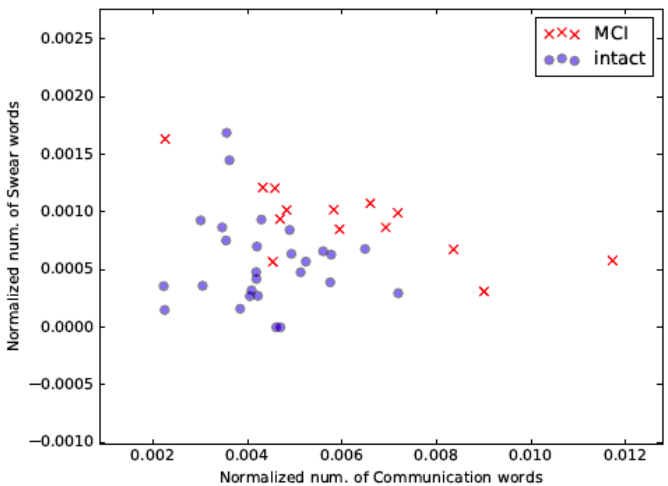
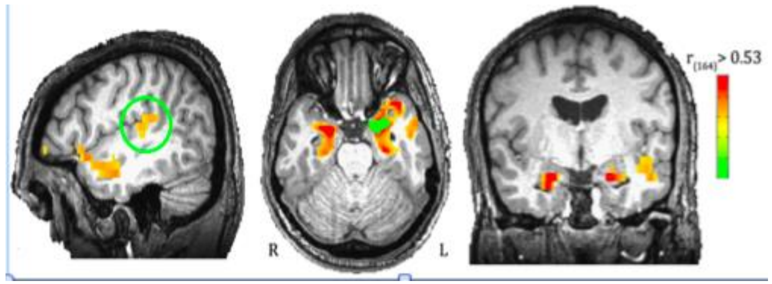


Figure 1: scatter-plot of features derived from Communication and Swear word categories

Dodge et al. Current Alzheimer Res. 2015
Asgari et al. Alzheimer's & Dementia: Translational Research & Clinical Interventions, 2017

I-CONECT: *Internet-based Conversational Engagement Clinical Trials* (PI: Dodge NIA R01AG051628; NIA R56AG056102)



Isolated 80+ yrs, 50% African American

OHSU

MCI n=90 → TX n=45; Control n=45

Healthy n=90 → TX n=45; Control n=45

UNIVERSITY OF MICHIGAN

MCI n=90 → TX n=45; Control n=45

Healthy n=90 → TX n=45; Control n=45

TX: Video Chat, 4 times/week: 6 months, 2 times/ week: 6 months
Control: 1/wk phone check. Novel Outcome Measures: MedTracker memory, Conversational Speech & Language Quantification; vMRI, DTI, fMRI

Considerations for pervasive computing and remote sensing in longitudinal research

Some Advantages -

- More frequent (continuous) assessment (vs. episodic, sparsely spaced query)
- More objective data
- More ecologically valid
- More reliable data (e.g., reduce rater biases)
- Greater analytic insight - integration (value of uniformly time-stamped data across multiple domains); greater time domain precision

Considerations for pervasive computing and remote sensing in longitudinal research

Some Challenges -

- If obtrusive, requires technology acceptance
- Technology deployment and related scalability
- Technology advances/changes – hard to “future-proof”
- Data handling
- Data security and privacy