
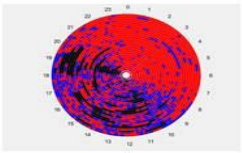


Technology to Advance Assessment & Interventions for Dementia

Jeffrey Kaye
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NIA - Layton Aging & Alzheimer's Disease Center
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Contemporary Assessment

"How long have you been here? She seems to be trying to remember. *Three weeks*. What is this? I show her a pencil. *A pen*. A purse, key, diary and cigar are identified correctly. ... When objects are shown to her, she does not remember after a short time which objects have been shown..."

--- A. Alzheimer, Nov. 6, 1901

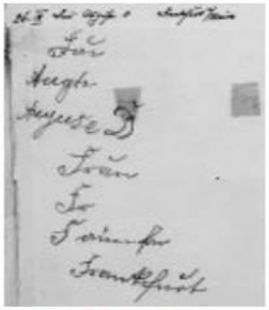
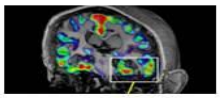


Figure 2: **Auguste D's handwriting**

Still crazy after all these years...

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

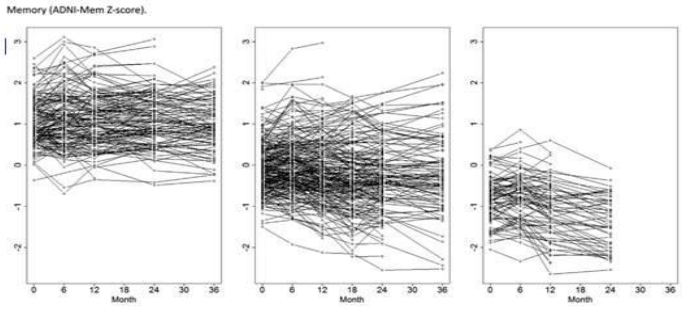
Might be a problem...



'Objective' Testing

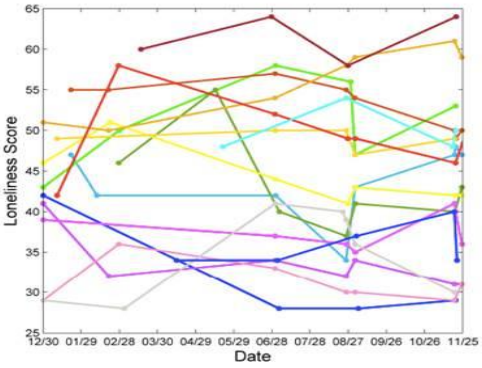
Clinic – History Taking

Detecting Meaningful Change



High variability in cognitive tests
-- ADNI Memory Composite
Dodge et. al., 2014

High variability in self-report measures
-- UCLA Loneliness Scale
Austin et al., 2016



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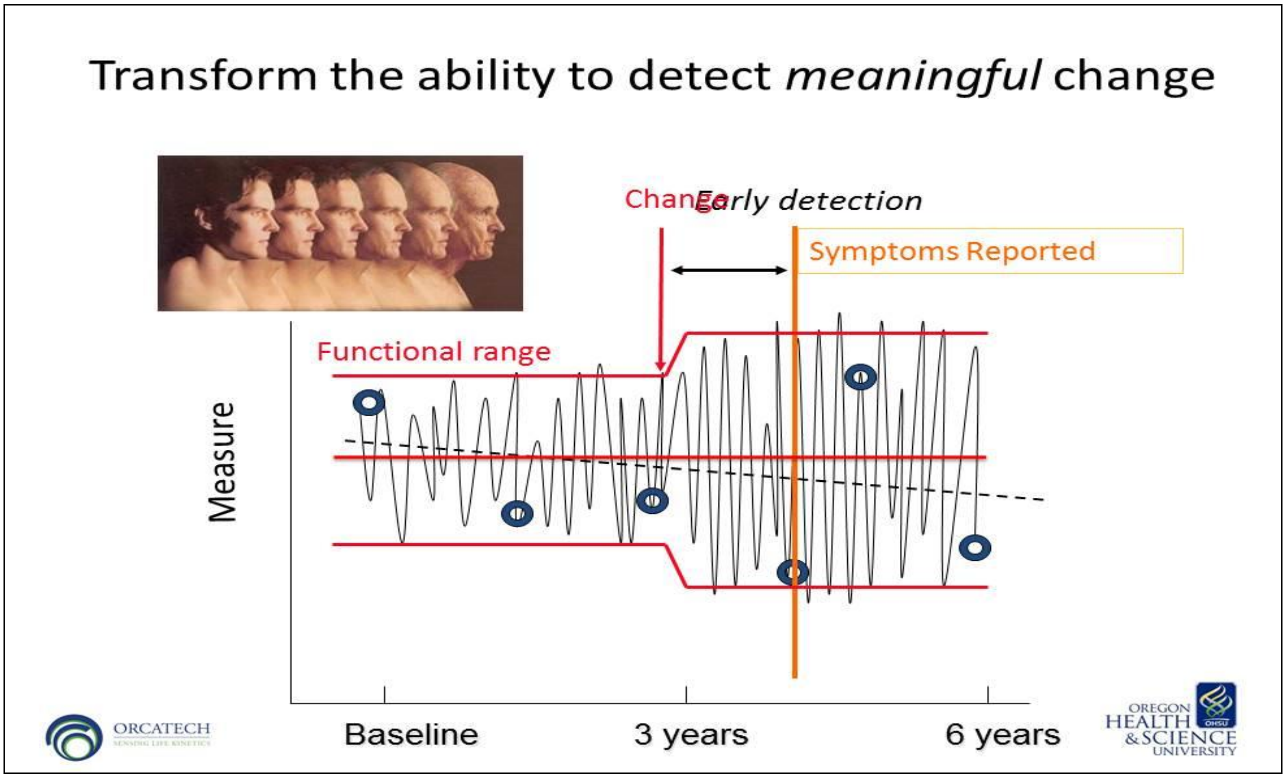
The way it should be…

- Home-based
- Multi-domain
- Holistic
- Real-time
- Continuous
- Objective
- Unobtrusive
- Ambient

Pervasive Computing Technologies

- Transform the ability to detect *meaningful* change
- Increase the *speed or efficiency* of clinical trials and dementia research in general
- Provide *new fundamental insights* into human biology and behavior


Transform the ability to detect *meaningful* change
Change
Early detection
Symptoms Reported
Functional range
Measure
Baseline
3 years
6 years
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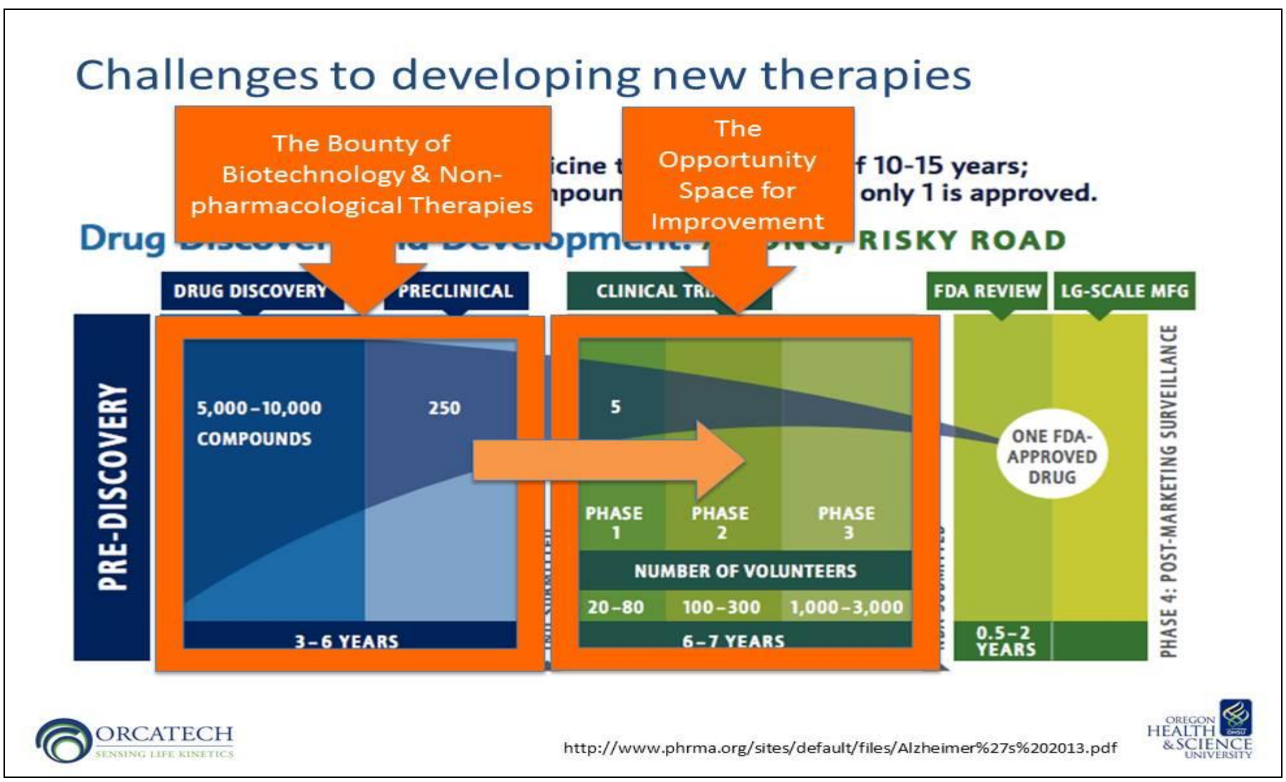
Challenges to developing new therapies
The Bounty of Biotechnology & Non-pharmacological Therapies
The Opportunity Space for Improvement
f 10-15 years;
only 1 is approved.
RISKY ROAD
DRUG DISCOVERY
PRECLINICAL
FDA REVIEW
LG-SCALE MFG
PRE-DISCOVERY
5,000–10,000 COMPOUNDS
250
5
ONE FDA-APPROVED DRUG
PHASE 1
PHASE 2
PHASE 3
NUMBER OF VOLUNTEERS
20–80
100–300
1,000–3,000
3–6 YEARS
6–7 YEARS
0.5–2 YEARS
PHASE 4: POST-MARKETING SURVEILLANCE
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http://www.phrma.org/sites/default/files/Alzheimer%27s%202013.pdf
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Increase the *speed or efficiency* of clinical trials and dementia research in general

MCI Prevention Trial – Sample Size Estimates

	Current Method	Continuous Measures	
	LM Delayed Recall*	Computer Use**	Walking Speed**
SAMPLE SIZE TO SHOW 50% EFFECT	688	10	94
SAMPLE SIZE TO SHOW 30% EFFECT	1912	26	262
SAMPLE SIZE TO SHOW 20% EFFECT	4300	58	588

- 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.

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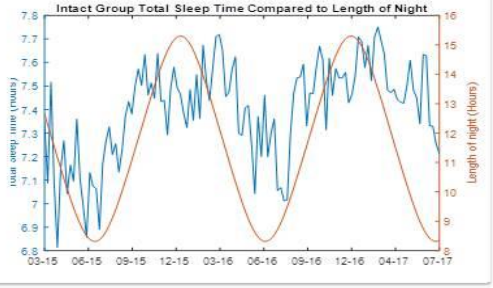
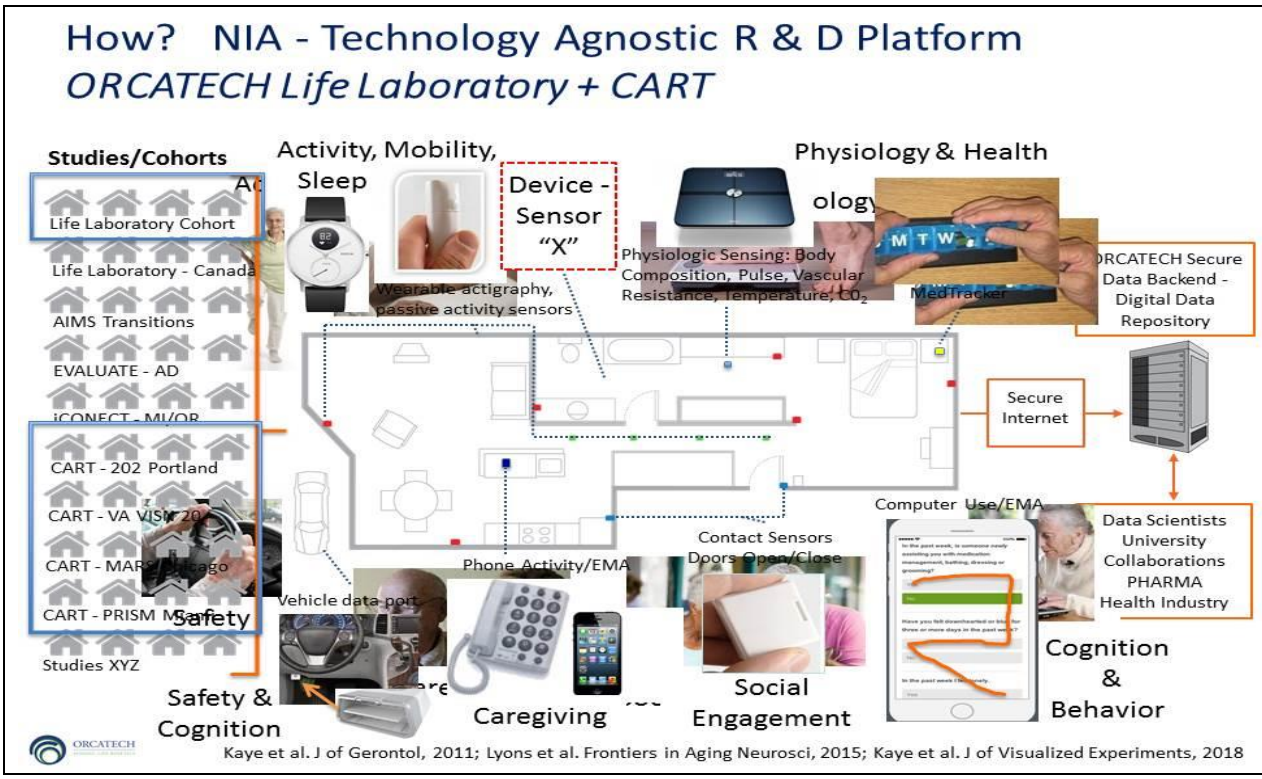
Dodge, et al., PLoS One, 2015

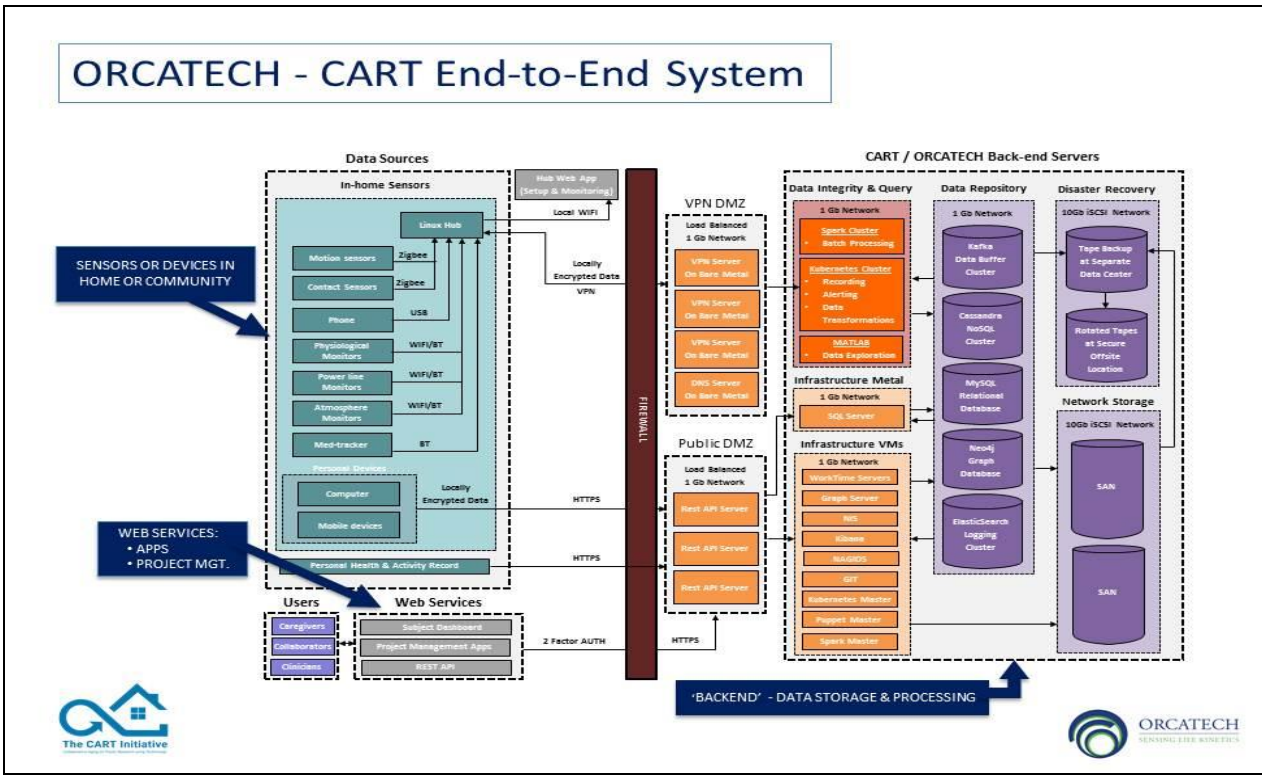
OHSU SCIENCE UNIVERSITY

Provide *new insights* into human biology and behavior

Disrupted Infradian Rhythms in MCI
Reynolds, et al., 2017



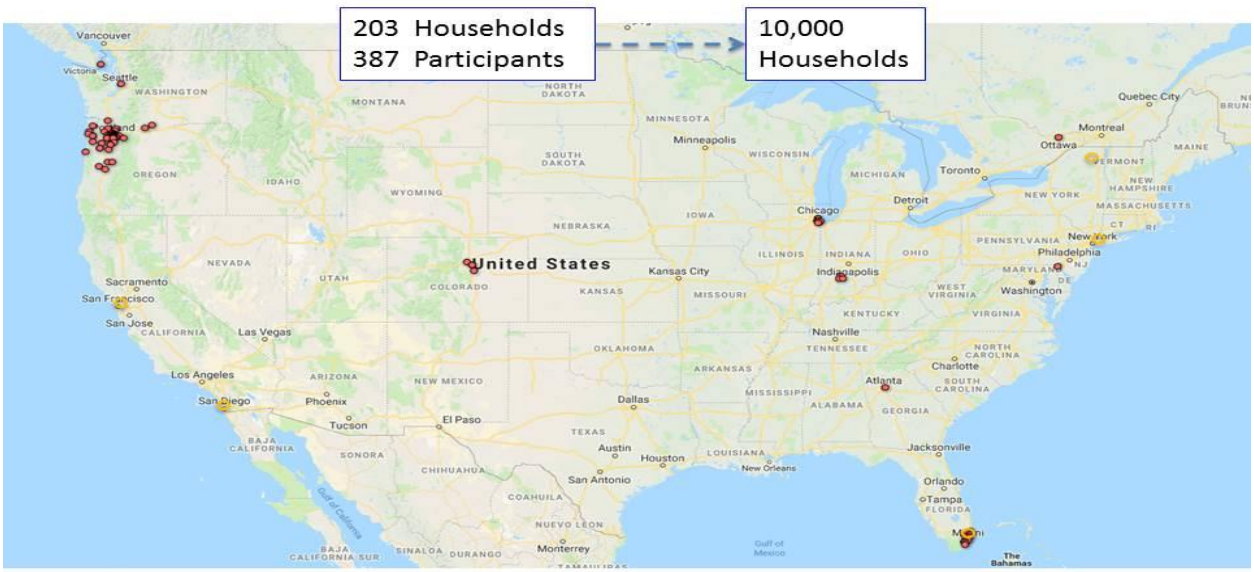

How? NIA - Technology Agnostic R & D Platform
ORCATECH Life Laboratory + CART
Studies/Cohorts
Life Laboratory Cohort
Life Laboratory - Canada
AIMS Transitions
EVALUATE - AD
CART - 202 Portland
CART - VA
CART - MAR
CART - PRISM
Studies XYZ
Activity, Mobility, Sleep
Device - Sensor "X"
Wearable actigraphy, passive activity sensors
Physiology & Health
Physiologic Sensing: Body Composition, Pulse, Vascular Resistance, Temperature, CO_2
MedTracker
ORCATECH Secure Data Backend - Digital Data Repository
Secure Internet
Computer Use/EMA
Data Scientists
University Collaborations
PHARMA
Health Industry
Contact Sensors
Doors Open/Close
Phone Activity/EMA
Vehicle data port
Safety
Safety & Cognition
Caregiving
Social Engagement
Cognition & Behavior
Kaye et al. J of Gerontol, 2011; Lyons et al. Frontiers in Aging Neurosci, 2015; Kaye et al. J of Visualized Experiments, 2018


ORCATECH - CART End-to-End System
Data Sources
In-home Sensors
SENSORS OR DEVICES IN HOME OR COMMUNITY
WEB SERVICES:
• APPS
• PROJECT MGT.
Users
Web Services
VPN DMZ
Public DMZ
FIREWALL
CART / ORCATECH Back-end Servers
Data Integrity & Query
Data Repository
Disaster Recovery
Infrastructure Metal
Infrastructure VMs
Network Storage
'BACKEND' - DATA STORAGE & PROCESSING
The CART Initiative
ORCATECH

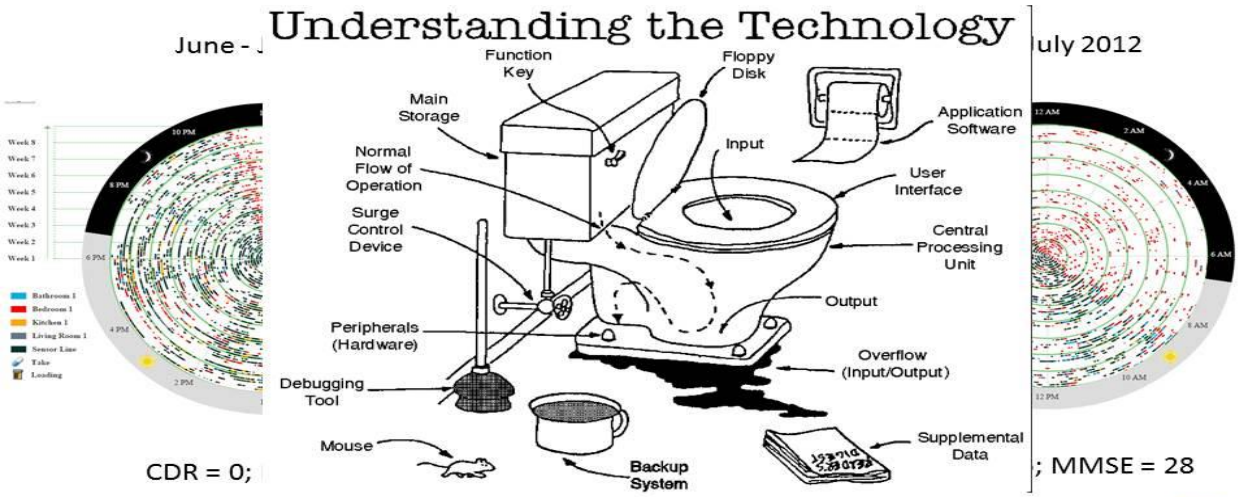
CART - *Collaborative Aging Research Using Technology* www.carthome.org

- Established to address needed research capability for evidence building (facilitated by technology) in aging research.
- Goal: Design and implement a scalable, disseminated technology system ('platform') for more effective aging research, ultimately deployable to 10,000+ homes
- *Focus on diversity, technology agnosticism, "future-proofing", use case flexibility, sustainability, facilitating secure data sharing.*
- Interagency U2C (U2CAG054397) with NIH (NIA, NIBIB, NCI, NINDS, NINR, NCATS, OBSSR,) and VA
- Research Team: PI, Jeffrey Kaye, ORCATECH/Oregon Health & Science University; Nina Silverberg, NIA; Collaborators: Intel, U. Miami, Cornell, Rush, OSU, U. Penn, VA VISN 20

CART + ORCATECH Sites/Homes in U.S. and Canada



Assessments - *Examples*



June - J

uly 2012

CDR = 0;

; MMSE = 28

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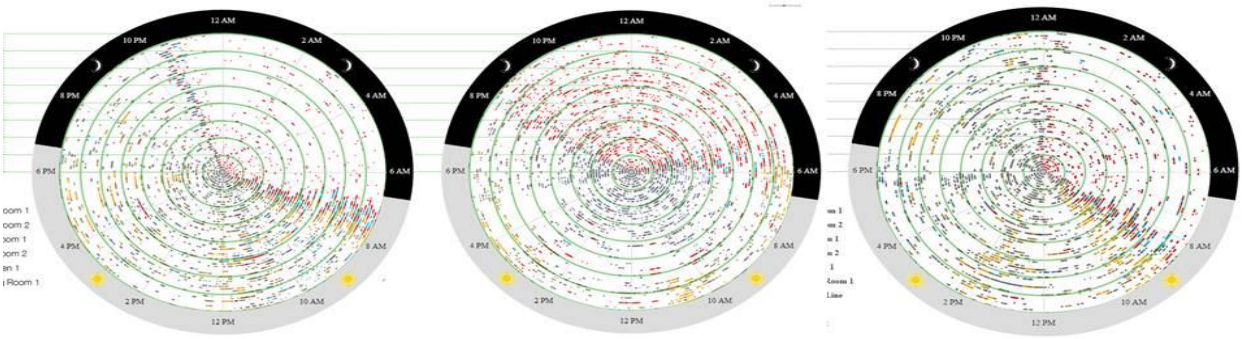
Developing PD and Tx Response

FEB-MAR 2011

SEPT-OCT 2012

SEPT-OCT 2013



Healthy

Diagnosed with Parkinson's Disease

Treatment with Sinemet

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Physical Activity and Mobility Behaviors

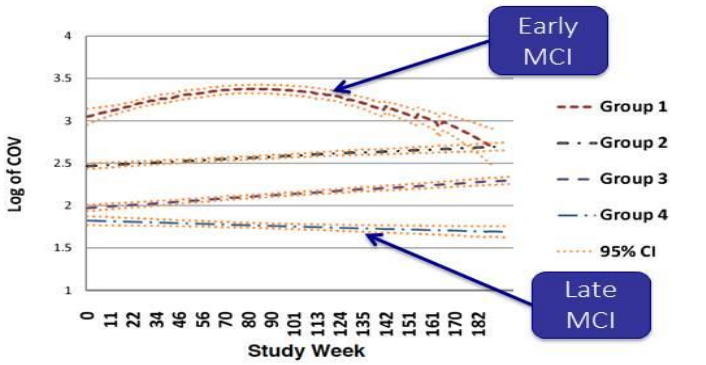
Room activity distributions differentiating MCI vs not MCI

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)

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

Trajectories of gait speed over time



Dodge, et al. Neurology, 2012

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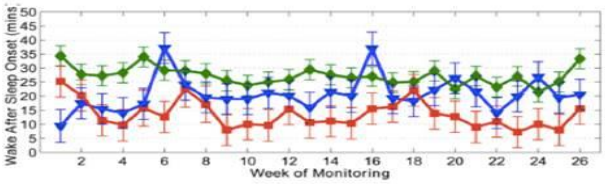
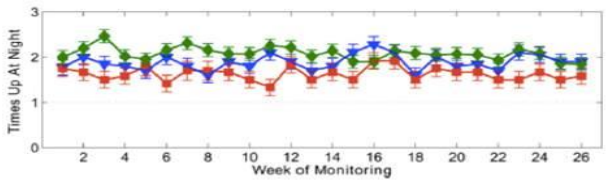
Chronobiological Behavior

Normal -
NA-MCI -
A-MCI -



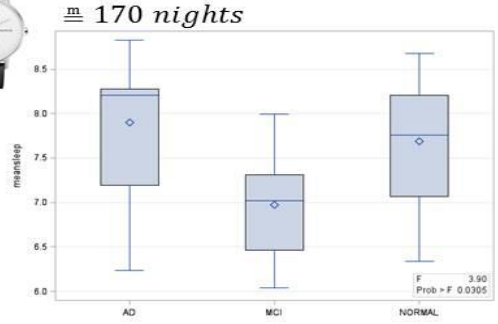


Hayes, et al. Alzheimer Dis Assoc Disord. 2014
Hayes, et al. IEEE Eng Med Biol Soc, 2010

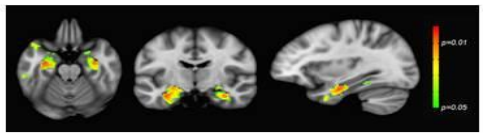
No Differences Between Groups in Self-Report Measures

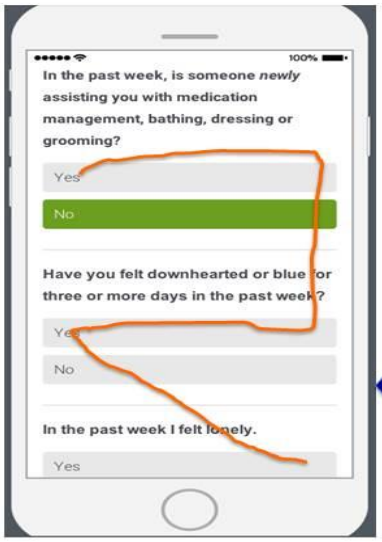
Self-Report Measure	Intact	aMCI	naMCI	P value
Subjective Daytime Sleepiness	1.8 ± 0.2	1.5 ± 0.3	2.0 ± 0.3	0.69
Subjective Insomnia	1.3 ± 0.2	0.8 ± 0.3	1.6 ± 0.3	0.21
Subjective Restlessness	1.0 ± 0.1	0.4 ± 0.3	0.7 ± 0.2	0.34
Times up at night	1.1 ± 0.1	1.0 ± 0.3	1.0 ± 0.2	0.77

≙ 170 *nights*



Cognition, Behavior, Motor Function: Computer Use





Some Self-Report Data is Necessary

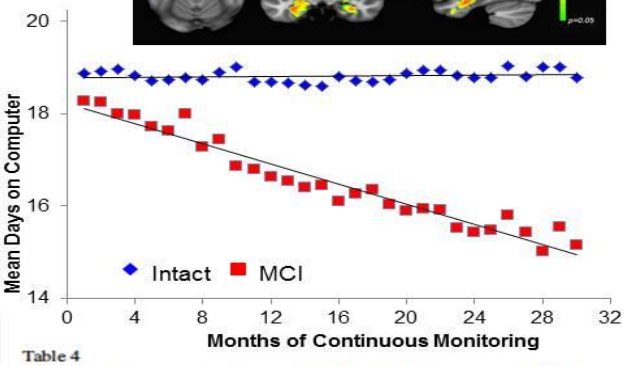


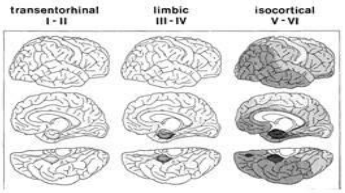
Table 4
Associations between cognitive status and mouse movement variability derived from one week of data

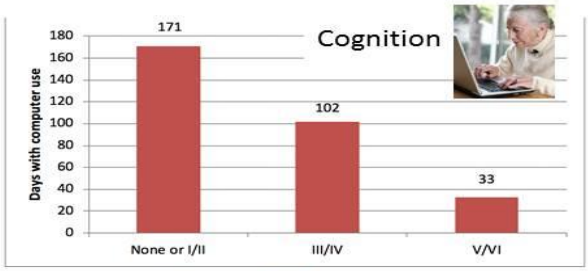
	Outcome, movement curvature (IQR_K)		Outcome, time spent idling (IQR_Idle)	
Covariate	Coefficient	*P* value	Coefficient	*P* value
MCI (reference: cognitively intact group)	0.013	.008**	386.8	.04*
Age (y)	−0.001	.03*	−15.0	.31
Education (y)	0.002	.05	−12.4	.70

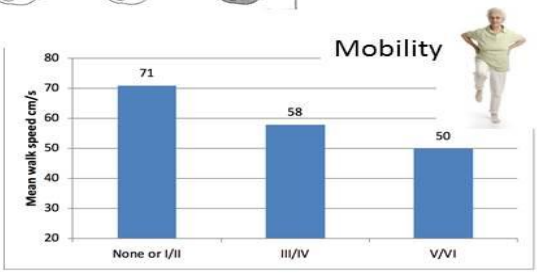
Abbreviations: IQR, interquartile range; MCI, mild cognitive impairment.
NOTE. *$P < .05$, **$P < .01$.

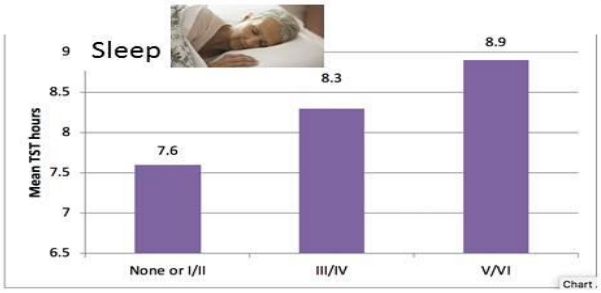
Kaye, et al. Alzheimers Dement. 2014; Silbert et al., Alzheimers Dement, 2015; Seelye et al. Alzheimers Dement.: Diagnosis, Assessment & Disease Monitoring, 2015; Seelye et al. Alzheimer's Disease & Assoc. Disorders, 2015; Seelye et al., Alzheimer & Dementia, 2018

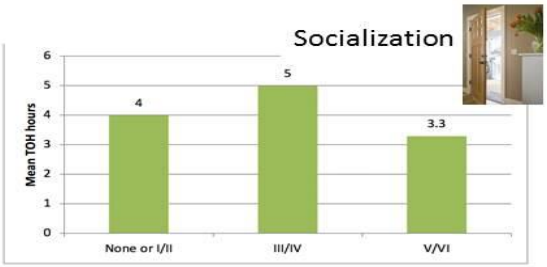
Digital biomarkers and Braak Score



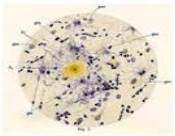


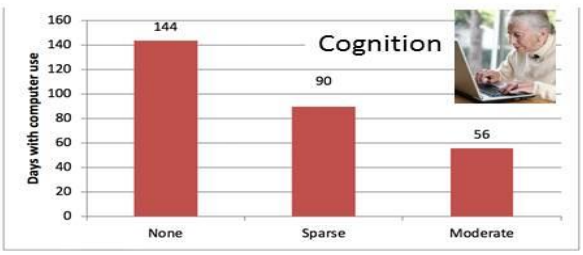


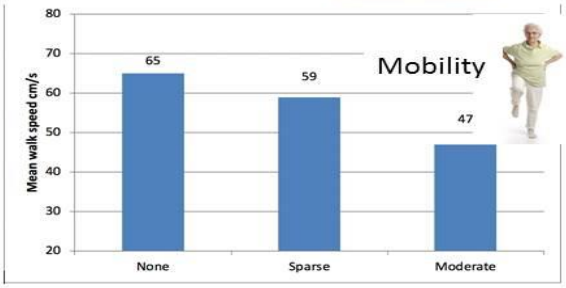


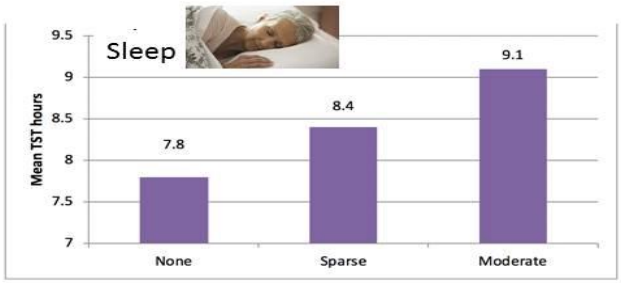


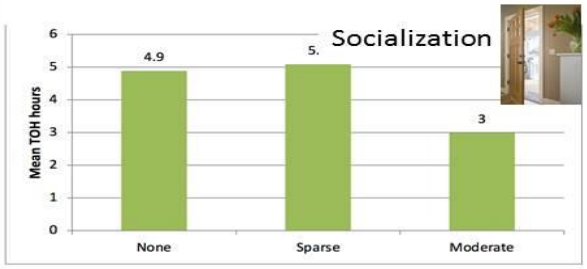
Digital biomarkers and Plaque Score





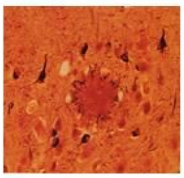


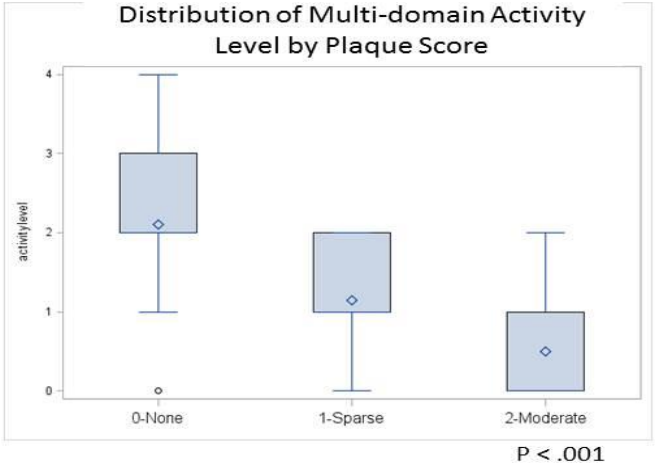




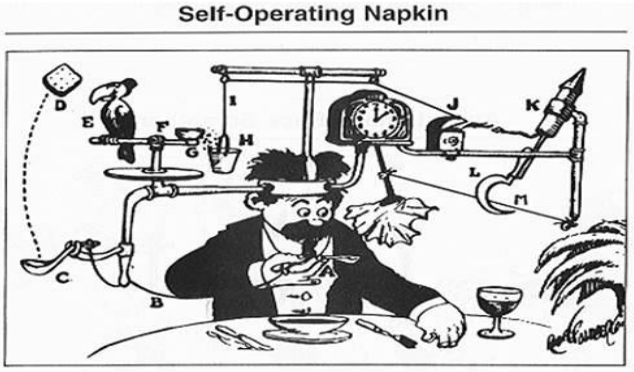
Digital functional activity composite relative to plaque score

Digital Composite = Mobility + Cognition + Sleep + Socialization





Technologies advancing dementia intervention research - *Examples*



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Ambient Independence Measures (AIMS) for Guiding Care Transitions (R01AG042191)

During the three years of study – *low staff engagement*:

- 11/26 consented staff members logged in at least once to the activity dashboard.
- Staff "page views", that is, number of pages of data looked at, ranged from 4-211 over the duration of data collection.
- Mean seconds spent on a particular page view was 36 (range, 1-750)
- Across 5 monthly email surveys, response rate of 31% (23/73).

Ambient Independence Measures Guiding Care Transitions

Bottom Line:

- Technology worked well with unique metrics acting both as assessment *and* intervention
- Inconclusive results – despite high engagement and enthusiasm at entry and booster sessions, inadequate engagement of staff across 7 communities
- Care system designed for crisis intervention
- *Realizing proactive action on trend data is an unmet need*

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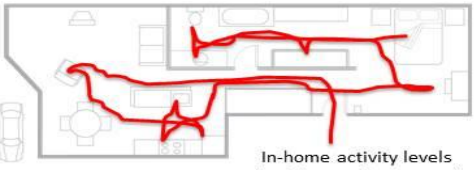
Objective in-home monitoring to identify meaningful behaviours changing during a loneliness intervention

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

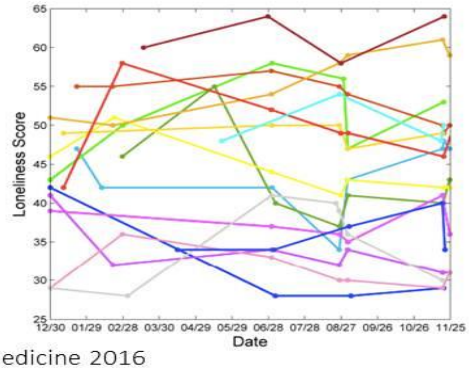
Computer use (time on computer; computer sessions)

Time spent outside home

Phone use (time on phone; number of calls

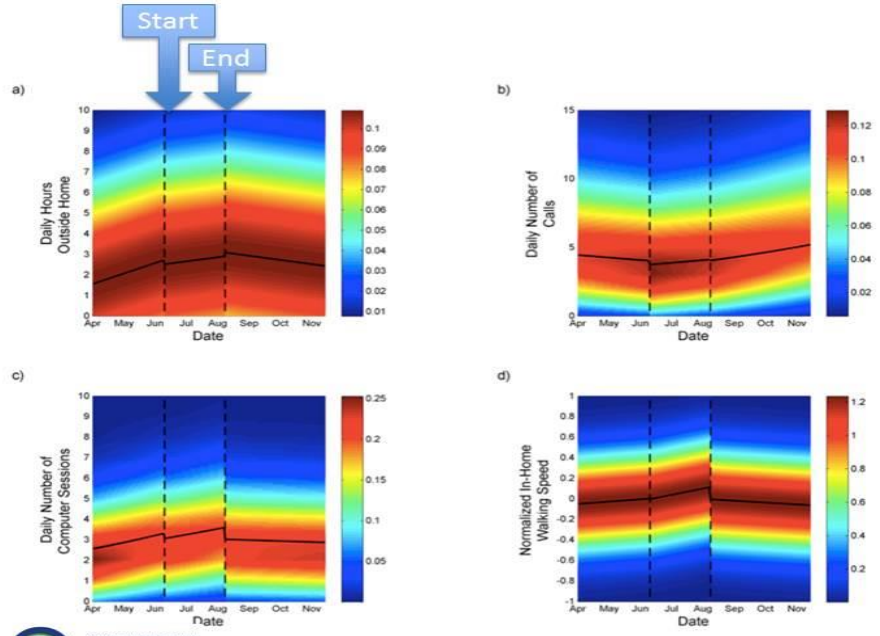


In-home activity levels (mobility, walking speed)



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, $p<0.01$)
- ↑ Walking speed over time ($\beta = 0.002$, $p<0.01$).
- ↑ Total phone calls, after intervention (IRR=1.003, $p<0.01$)

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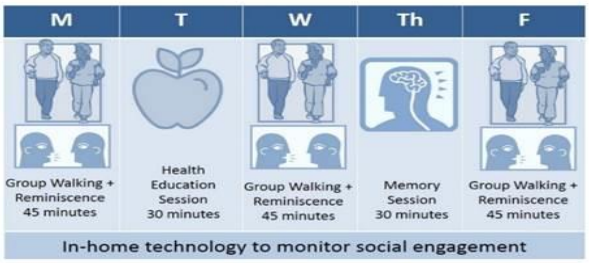
Austin, et al. 2018

Multi-modal Brain Health Program - SHARP: Sharing History through Active Reminiscence and Photo-imagery



PI: Raina Croff; NIA: P30AG008017, P30AG024978, and Alzheimer's Association

Croff R, et al. The Gerontologist, 2018.

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

Active, Frequent Assessments & Interventions 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 Res. & Clinical Interventions, 2015
Dodge et al., Current Alzheimer's Disease, 2015

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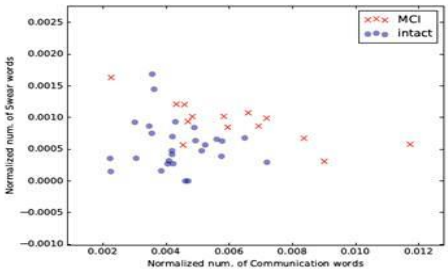
Computer Use:
Social Markers of Cognitive Function

- *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 (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

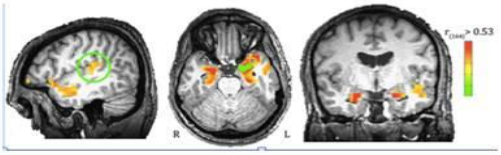
Table 4: Average number of words grouped into LIWC categories



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 R01AG056102)

- Isolated 80+ yrs
- 50% African American



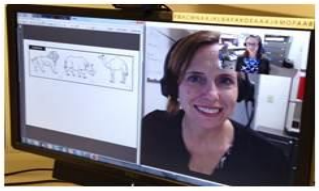
MCI n=180 — TX n=45 / Control n=45

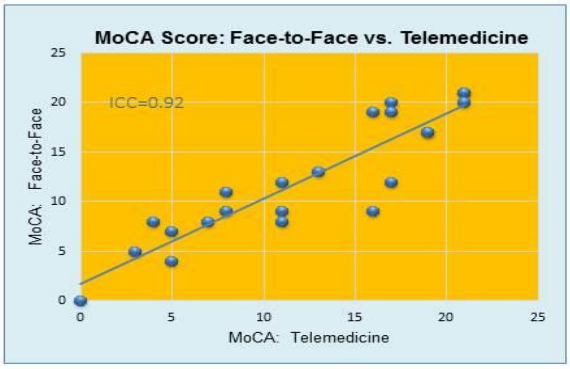
Healthy n=180 — TX n=45 / Control n=45

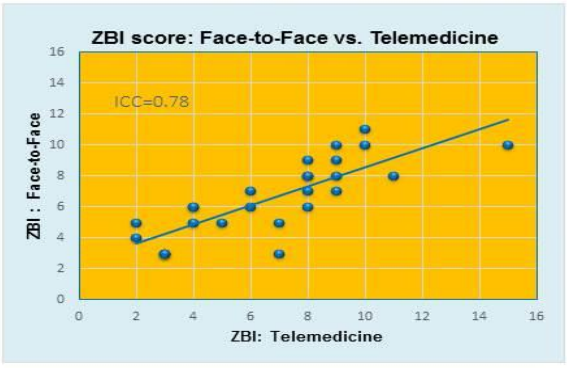
X: Video Chat, 4 times/week: 6 months, 2 times/ week: 6 months
Control: 1/wk phone check. Novel Outcome Measures: MedTracker memory, Conversational Speech & Language Quantification; vMRI, DTI, fMRI

Teledementia Care: *Direct to Home Assessment & Care*

- Alzheimer's Care via Telemedicine -- Establishing the Reliability of Telemedicine-based Measures
- STAR-C Adapted Telemedicine Intervention







Lindauer et al. Dementia Care Comes Home: Patient and Caregiver Assessment via Telemedicine. Gerontologist, 2017.

EVALUATE - AD

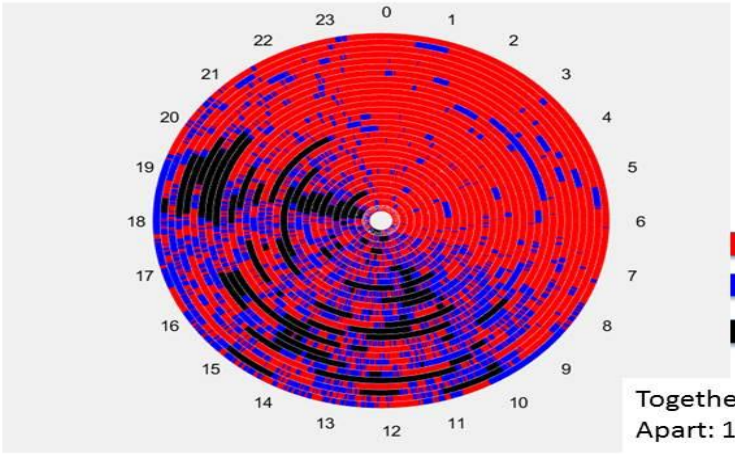
Ecologically Valid, Ambient, Longitudinal and Unbiased Assessment of Treatment Efficacy in Alzheimer's Disease

- Longitudinal naturalistic observational cohort study spanning up to 18 months
- Goal: *New Trial Paradigm* - 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

Week	0	13	26	39	52	65	78
Visit Type	Screening	Online	Phone	Online	M12	Online	M18
Consent	X						
Personal & Family History Questionnaire	X				X		X
MMSE	X				X		X
ISAAC Technology Use Survey	X				X		X
Tech & Computer Experience and Proficiency Questionnaires	X				X		
Geriatric Depression Scale Short Form (GDS-SF)	X				X		X
Zarit Burden Interview (ZBI-12)	X	X	X	X	X	X	X
Functional Assessment Questionnaire (FAQ)	X	X	X	X	X	X	X
Neuropsychiatric Inventory Questionnaire (NPI-Q)	X	X	X	X	X	X	X
Pittsburgh Sleep Quality Assessment (PSQA)	X				X		X
ORCATECH Health & Life Activity Form	Weekly for duration of study						
Caregiving: *Time out of home/Time alone in home/Time in same room with partner/Time together in bathroom*	Assessed continuously						
Physical capacity/ Mobility: *Total daily activity/Mobility/Step count/Walking speed/Time in locations*	Assessed continuously						
Sleep: *Time up/Time In Bed/Times Up at Night/Restlessness/Sleep Duration*	Assessed daily						

EVALUATE – AD

Couples & Caregiving Analysis: Time spent together



Together
Separate
Out of Home

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

ORCATECH SENSING LIFE KINETICS

Reynolds et al., 2017 unpublished
Thomas et al., AAIC 2017

OREGON HEALTH & SCIENCE UNIVERSITY

Digital Biomarkers in Later Stage Dementia Interventions

ADCS PEACE-AD RCT: Prazocin for Agitation in AD RCT (Pis: Peskind & Raskin; Lim, Reynolds, Kaye)

Digital Agitation Assessment -
Activity levels monitored continuously during entire 12-wk titration study using wrist actigraphy. Continuous monitoring critical as study employs a flexible dose titration schedule, and the use of rescue medication.

MODERATE - Monitoring Dementia-related Agitation using Technology-assisted Evaluations -
Multiple sensors used to examine the effects of environment on dementia-associated behaviors.

Thank you!

Please Collaborate – *Your Research Here!*

The CART Initiative

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