

P14.3-002 - Quantification of Cognitive Impairments in Preclinical and Early Alzheimer's Disease: A Proof of Concept Study to Investigate the Feasibility, Adherence and Preliminary Clinical Validity of Remote Smartphone Based Self-Assessments of Cognition, Function, and Behavior

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The promise of remote monitoring of cognition in AD

- Subtle **cognitive changes** emerge **years prior** to clinical diagnosis of AD. This window offers a promising opportunity for preventing decline.
- **Frequent remote monitoring** of cognition enables the possibility of capturing these subtle changes in cognition in a an ecologically valid setting (e.g. recall over days)
 - More frequent measurement may also **increase signal-to-noise ratio** of remote monitoring outcomes to generate more reliable and ultimately valid measures of cognitive performance and changes over time
- **Cognitive domains** relevant for remote **monitoring in the continuum of preclinical to eAD** include:
 - Episodic long-term memory (declining first in the preclinical phase)
 - Learning, semantic memory, and executive functioning (affected in prodromal and eAD)
- A comprehensive **battery of cognitive tests** enables generation of profiles of cognitive impairment across domains. Examples of their use include to:
 - **Differentiate** dementia syndromes
 - **Enable quantification** of contribution of non-AD pathology to syndrome
 - **Quantify impairments** associated with vascular dementia

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Remote assessments of cognition and functioning in daily life (with an expected daily burden ~10 min/day^a)

ACTIVE TASKS (provisioned smartphones)								
Episodic memory	Executive functioning	Logical memory & conceptual fluency	Semantic memory	Visuospatial working memory	Psychomotor speed, attention	Gait and balance	Fine motor	Psychomotor speed, language
Gallery game 	Tilt task 	Story time 	Object features 	Find the egg 	IPS 	30-sec walk 	Speeded tapping 	Fairy-tale
SURVEYS (provisioned smartphones)				PASSIVE MONITORING (in participant's smartphone)				
Sleep quality	Mood	Social behavior	Orientation	Location & activity patterns	Gait and balance	Ambient noise	App usage	Screen usage
Sleep 	Emotions 	Social network index 	Time (Date, Day, Month) 	GPS, Bluetooth, Wi-Fi 	Accelerometer, gyroscope 	Microphone 	Application logs 	Proximity sensors

^aActual burden shown in results
AD, Alzheimer's disease; GPS, Global Positioning System; IPS, information processing speed.

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Primary objective:

- To evaluate **feasibility and adherence** to smartphone-based remote self-assessments, including user experience in participants with eAD, SCD, and healthy controls

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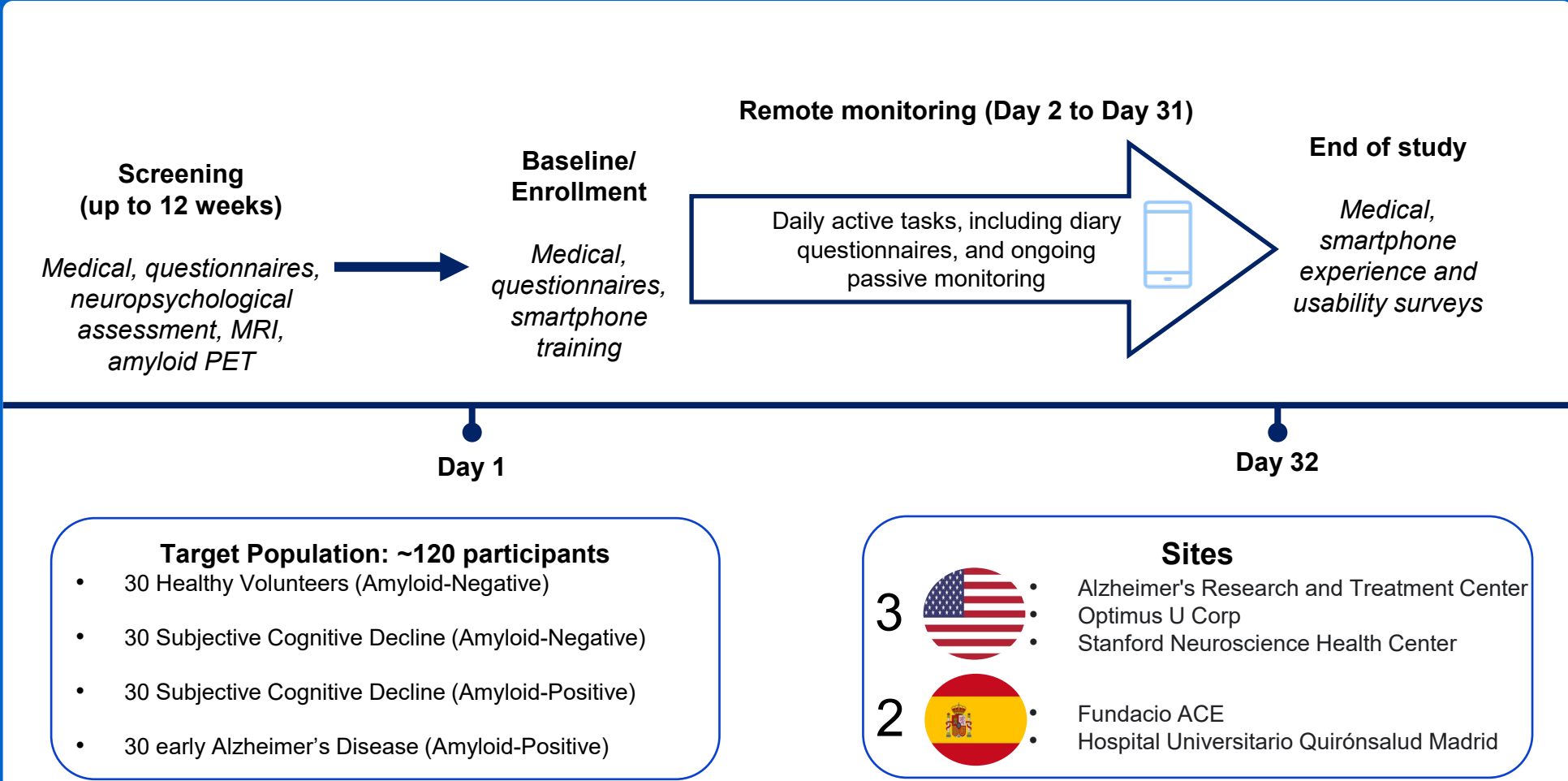
Secondary and exploratory objectives:

- To explore associations between sensor data on cognition, function, and behavior collected using smartphones and in-clinic assessments including neuropsychological tests
- To explore whether sensor data collected using smartphones are different between participants with and without cognitive impairment
- To explore associations between the clinical assessments, smartphone-based sensor data and the brain imaging read-out

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<https://www.isrctn.com/ISRCTN17035495>
MRI, magnetic resonance imaging; PET, positron emission tomography

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Key inclusion and exclusion criteria

	Healthy control	Subjective cognitive decline	Early Alzheimer's disease
Age	65 years or above		
Diagnosis	Clinical neuropsychological testing as defined by a performance not worse than one standard deviation (1 SD) below the mean , based on normative data	-	NIA-AA criteria for MCI due to AD or probable AD
CCI (on first 12 questions)	< 16	≥ 16	-
MMSE	≥ 29 (with high-school graduation) ≥ 28 (without high-school graduation)	≥ 27 (with high-school graduation) ≥ 26 (without high-school graduation)	≥ 24 (with high-school graduation) ≥ 23 (without high-school graduation)
CDR	0	0	0.5
Amyloid beta pathology (PET)	Negative	Negative (Not more than 30 participants) Positive (20 to 30 participants)	Positive
Other inclusion	<ul style="list-style-type: none"> ● Previous experience with smartphone or tablet technology ● Fluency in the language of the tests used at the study site ● Adequate visual and auditory acuity 		
Key exclusion	<ul style="list-style-type: none"> ● History or known presence of any significant neurological disorders ● History or known presence of any significant psychiatric disorders ● Current active clinically significant anxiety or depressive disorder 		

AD, Alzheimer's disease; CCI, Cognitive Change Index; CDR, Clinical dementia rating; eAD, early Alzheimer's disease; MMSE, Mini-Mental State Examination; NIA-AA, National Institute on Aging and Alzheimer's Association; PET, positron emission tomography; SD, standard deviation.

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Demographics

	HC	SCD negative	SCD positive	eAD	Total
N	32	31	30	30	123
Age (Median) [range]	68.5 [65 - 83]	70 [65 - 89]	72 [65 - 82]	74.5 [65 - 83]	71 [65 - 89]
Gender (M:F)	20:12	17:14	16:14	18:12	71:52
Ethnicity (Hispanic:Non Hispanic)	14:18	6:25	10:20	8:22	38:85
Race (Asian:African-American:White)	0:3:29	1:2:28	0:0:30	0:1:29	1:6:116
Language (English:Spanish)	17:15	17:14	14:16	16:14	64:59
Years of education [range]	12 [17 - 8]	15 [17 - 8]	14 [17 - 8]	13 [17 - 8]	13 [17 - 8]

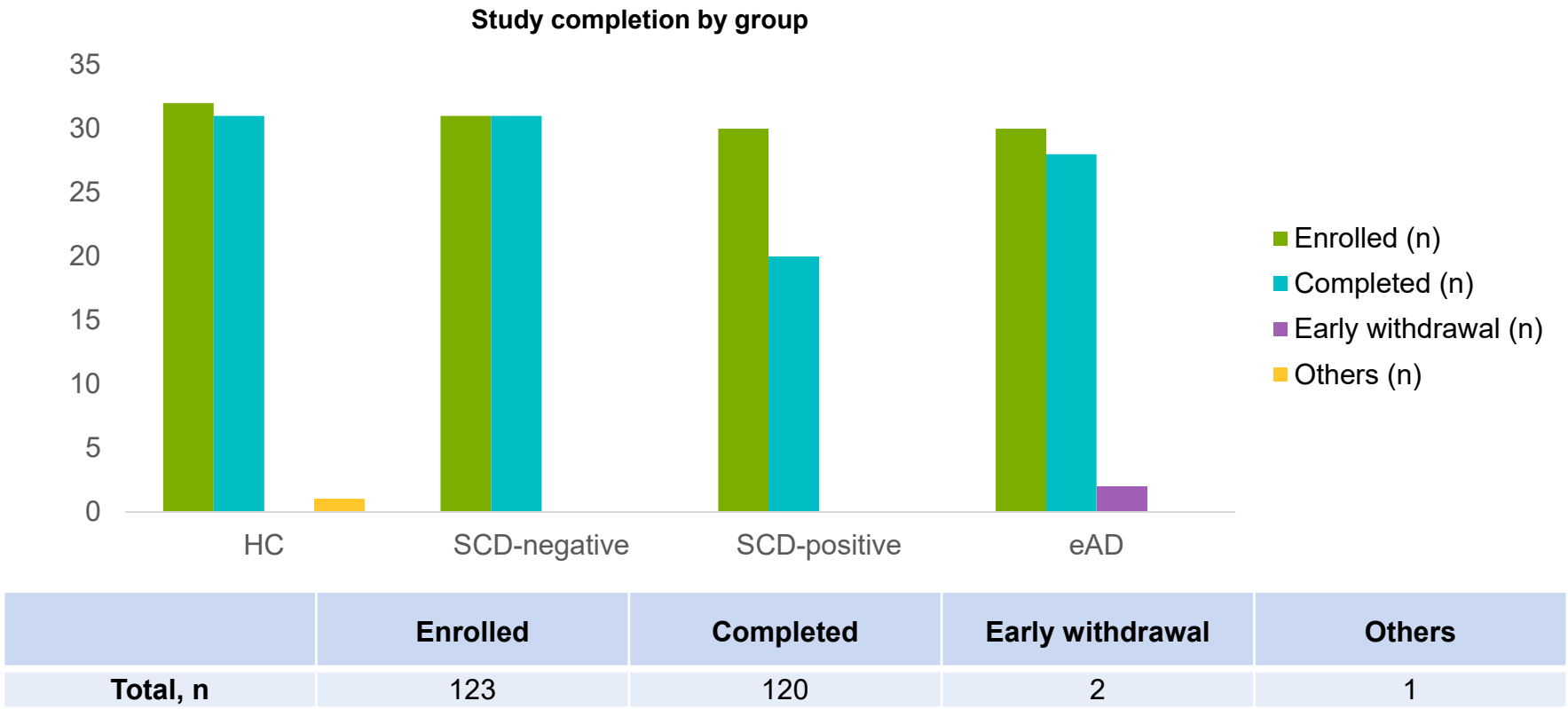
eAD, early Alzheimer's disease; HC, healthy control; SCD neg, amyloid PET-negative subjective cognitive decline; SCD pos, amyloid-positive subjective cognitive decline.

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97.5% feasibility (120 out of 123 participants successfully completed the study)



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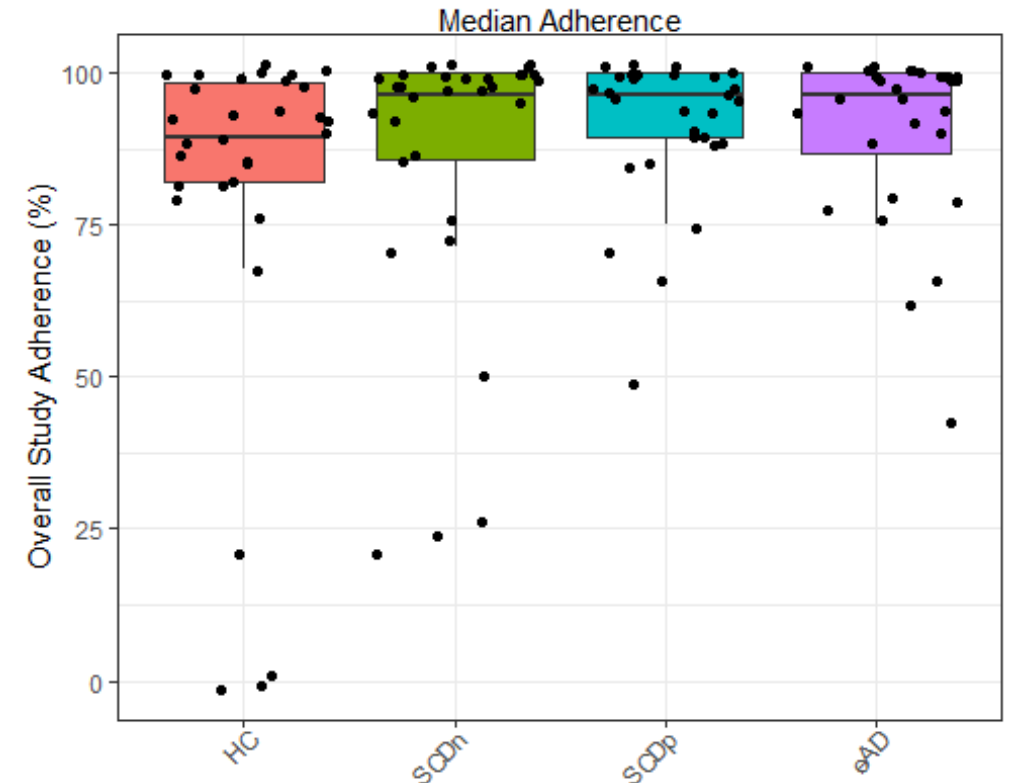
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96.4% median adherence observed across all cohorts within the 28-day remote monitoring period

- Overall adherence is the proportion of remote study days on which participants completed at least one planned task relative to the number of remote study days with planned active testing (i.e. 28 days)
- Good adherence was observed, even in eAD participants
- Adherence is comparable across all cohorts



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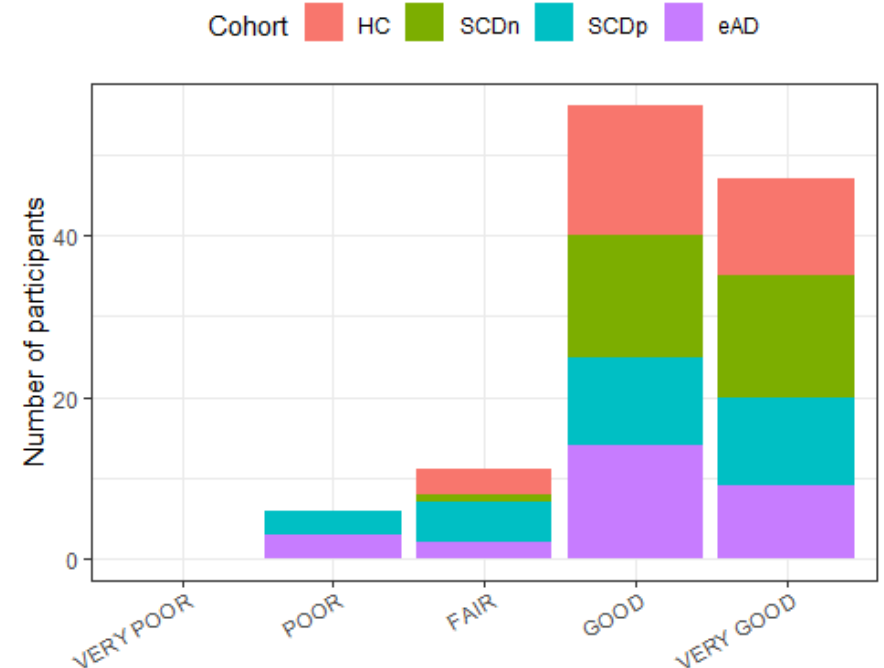
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85.8% rated their user experience as good or very good

- All participants provided their feedback on app usability by participating in a user experience survey at the end of study
- ~86% of respondents rated their experience as good or very good in using the study smartphone and the assessment app

How would you rate your overall experience with the Digital POC study application and phone?



eAD, early Alzheimer's disease; HC, healthy control; POC, proof-of-concept; SCD neg, amyloid PET-negative subjective cognitive decline; SCD pos, amyloid-positive subjective cognitive decline.

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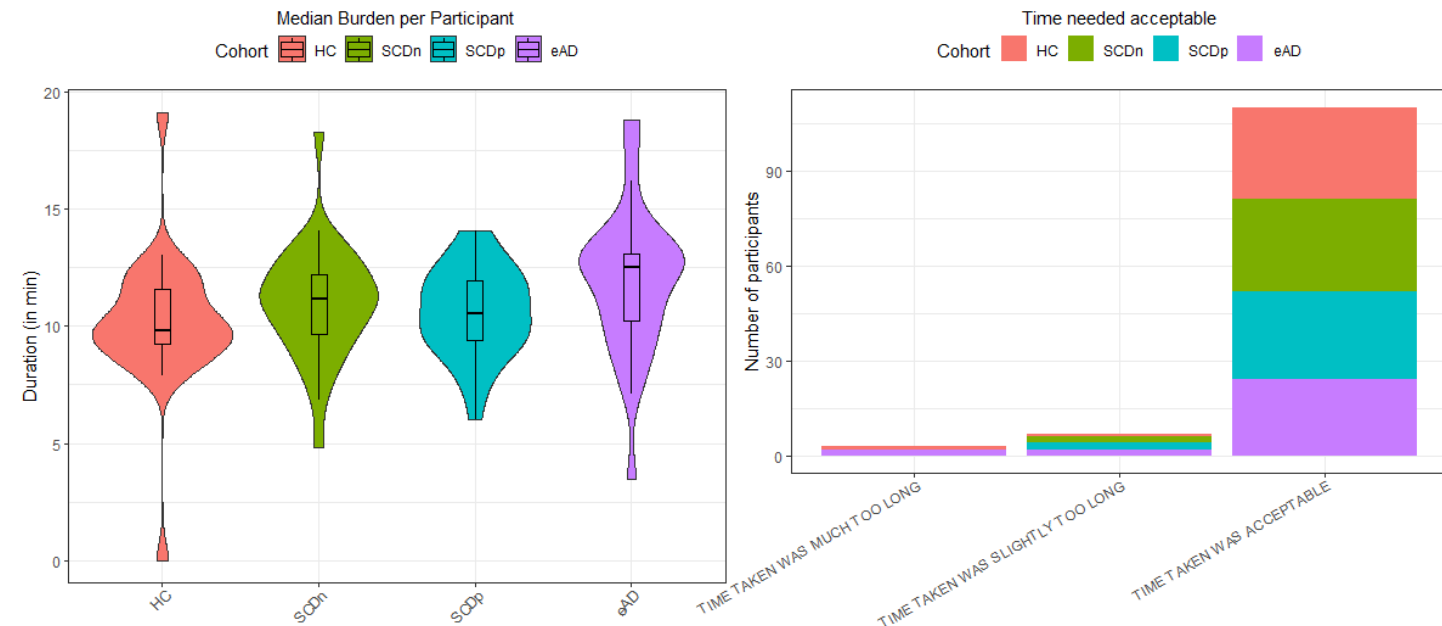
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On average, participants spent 10.9 minutes a day performing the remote assessments; the majority rated their perceived burden to be acceptable



- Healthy controls spent less time (9.79+/-3 minutes) in comparison with eAD (12.5+/-3.11 minutes) who took more time to complete the schedule of assessments

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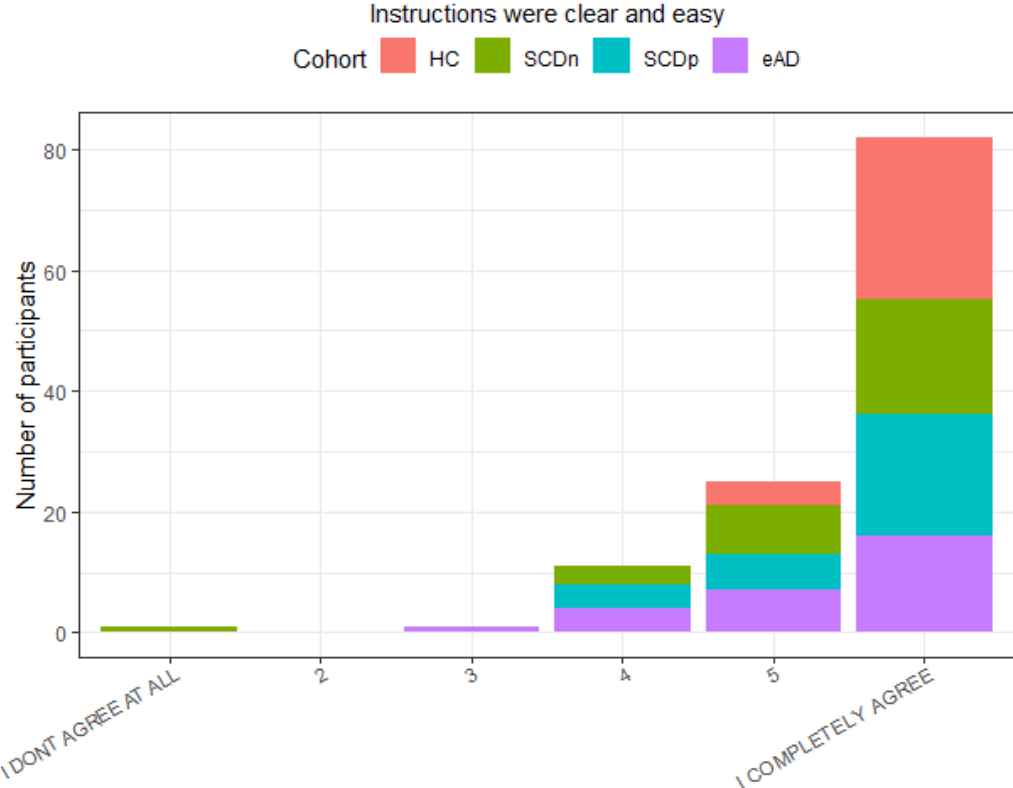
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More than 89% of the participants agreed that the task instructions were clear and easy to follow

- 107 participants rated ≥ 5 (i.e. 6 being "I completely agree") signifying the task instructions were clear and easy to read
- No significant differences observed across different cohorts



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Remote monitoring of cognition holds promise to provide denser, more ecologically valid measures of cognitive functioning (e.g. recall over days), with a very broad reach

Feasibility, acceptance, and adherence are fundamental metrics in the development of a remote monitoring solution for the AD continuum

Primary results from this proof-of-concept study show excellent feasibility, acceptable adherence, and good user experience for the suite of digital assessments presented here in healthy volunteers, subjective cognitive decline, and early AD individuals

Further analysis on the psychometric properties of the individual tasks will be presented later in the year

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