Building an evidence library of digital measurement technologies to accelerate endpoint development in Alzheimer's Disease and related dementias clinical trials

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DATAcc
Digital Health Measurement Collaborative Community
by DiMe
ALZHEIMER'S DISEASE & RELATED DEMENTIAS
Digital Measures Development

Current problem

- Interest in digital health technologies (DHTs) for clinical research[1] has exponentially increased.
- In the **Alzheimer's Diseases and related dementias (ADRD)** field, researchers are focused on DHT-centered measurement in parallel with a growing R&D effort to identify therapeutic drug candidates[2]
- After many years of inconsistent results and failed attempts, regulatory authorities have now approved some AD-specific therapeutic agents[3,4]
- Such progress presents new perspectives and challenges for accurately identifying and assessing candidates within clinical protocols
- Researchers require fit for purpose measurement tools, creating a prime opportunity for DHTs to play a strategic role
- **There exists a need to aggregate & advance DHTs for diagnosing and assessing within ADRD populations**

Study overview

Study aim

To produce a dynamic, open-source library, hosted and maintained by DATAcc, to provide an overview of the landscape of ADRD-relevant DHTs with their corresponding uses and evidence

Approach

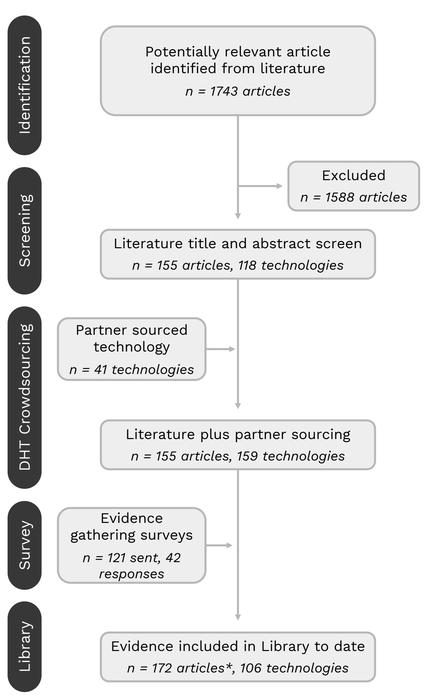
A focused search of peer-reviewed literature combined with outreach to the DHT development community

Methods

Literature scoping & community outreach

1. Focused literature search:
   We developed search terms to identify ADRD related digital health technology and deployed them in PubMed, Embase, and APAPsycInfo. We aggregated and deduplicated the results in reference management software Zotero.
1. Data screening/extraction:
   Two reviewers screened the identified articles for relevance, co-reviewing a random sample of 100 articles to insure harmony on inclusion/exclusion standards. This screening process led to the selection of relevant articles from which we identified the initial list of DHTs.
1. Community sourcing:
   DiMe project partners reviewed the list of identified DHTs and offered additional qualifying technologies. We contacted creators of identified DHTs (where feasible) and provided them a Qualtrics survey link to return supporting evidence.

Recovered Evidence Flow Diagram



**This includes respondent-submitted conference and poster and oral presentation materials, and documentation of regulatory approvals*

Methods, cont.

Library creation

Record ID	Model	Manufacturer	Technology Type	Form Factor	Wear Location	Specific Therapeutic a...	Evidence Value	Health Concept	Outcome Measured	Population	Sample (n)	Evidence Reported
MODEL Altoida DNS Count 6	Filled 100%											
5 4	Altoida DNS	Altoida	Ambient	Smartphone or tablet	Not applicable	ADRD: MCI AD ADRD: AD	Meier, I. B., Buegler, M., H...	Neurocognitive Physical	Longitudinal trajectory ris...	Two experiments (Study ...	29/496	Analytical Validation Clini
6 5	Altoida DNS	Altoida	Ambient	Smartphone or tablet	Not applicable	ADRD: Prodromal deme...	Harms, R. L., Ferrari, A.,...	Neurocognitive	Augmented reality tasks a...	Middle-aged cognitively ...	130	Analytical Validation NICI
7 7	Altoida DNS	Altoida	Ambient	Smartphone or tablet	Not applicable	ADRD: Preclinical deme...	Muurling, M., de Boer, C.,...	Neurocognitive	Functional domain profile...	Data will be collected in 1...	220	Analytical Validation Clini
8 8	Altoida DNS	Altoida	Ambient	Smartphone or tablet	Not applicable	ADRD: MCI (NOS)	Sood, M., Harms, R., Bügl...	Neurocognitive	Hand micro-movements™...	58 cognitively normal and...	148	Analytical Validation Clini
9 132	Altoida DNS	Altoida	Ambient	Smartphone or tablet	Not applicable	ADRD: PD ADRD: Prodro	Tarnanas, I., Vlamos, P., &...	Neurocognitive Physical	hand micro-movements, ...	788 subjects combined fr...		Analytical Validation Use
135	Altoida DNS	Altoida	Ambient	Smartphone or tablet	Not applicable	ADRD: MCI AD ADRD: AD	Seixas, A. A., Rajabli, F., P...	Neurocognitive Physical	Reaction time, speed, att...	Two experiments (Study ...		Analytical Validation Use
MODEL Altoida iADL task Count 1	Filled 100%											
11 137	Altoida iADL task	Altoida	Ambient	Smartphone or tablet	Not applicable	ADRD: MCI AD ADRD: AD	Tarnanas, I., Tsolaki, A.,...	Neurocognitive Activities	Medium-to-high cognitiv...	215 subjects: 71 with nor...		Cost of implementation
MODEL Altoida Neuro Motor In Count 1	Filled 100%											
12 136	Altoida Neuro Motor Index	Altoida	Ambient	Smartphone or tablet	Not applicable	ADRD: Preclinical deme...	Buegler, M., Harms, R. L.,...	Neurocognitive Physical	Medium-to-high cognitiv...	Study A was a semi-natur...		Analytical Validation Clini
MODEL Ambulatory Research Count 2	Filled 100%											
13 9	Ambulatory Research in C...	Cognitive Technology Res...	Ambient	Smartphone or tablet	Not applicable	ADRD: MCI (NOS)	Wilks, H., Aschenbrenner,...	Neurocognitive	Assessment of Cognition ...	Older adults (aged 61–94...	169	Clinical Validation
14 10	Ambulatory Research in C...	Cognitive Technology Res...	Ambient	Smartphone or tablet	Not applicable	ADRD: MCI (NOS)	Nicosia, J., Aschenbrenn...	Neurocognitive	Assessment of Cognition ...	Cognitively normal older ...	268	Analytical Validation Use
MODEL Amsterdam Instrumen Count 1	Filled 100%											
15 11	Amsterdam Instrumental ...	Alzheimer Center VU Uni...	Ambient	Smartphone or tablet	Not applicable	ADRD: Preclinical deme...	Muurling, M., de Boer, C.,...	Activities of daily living	Activities of daily living sc...	Data will be collected in 1...	220	Clinical Validation
MODEL Automatic Speech Rec Count 1	Filled 100%											
16 13	Automatic Speech Recog...	Tóth, L., Hoffmann, I., Go...	Ambient	Smartphone or tablet	Not applicable	ADRD: MCI (NOS)	Tóth, L., Hoffmann, I., Go...	Neurocognitive	Acousitc features includin...	38 healthy controls and 4...	86	Use as a prognostic or ...

- We compiled the results of the literature analysis and community sourcing into an online library database featuring individual DHTs with their corresponding evidence
- The library offers information such as the name and creator of a technology, the type of technology it represents with its accompanying form factor, and relevant evidence
- We label evidence based on health concepts within the ADRD clinical space that the technology is intended to address
- Each evidence value provides links to peer-reviewed literature or publicly hosted data
- We include publication descriptions of outcome measures and sample characteristics to indicate the types of research and populations where technologies have been evaluated
- Lastly, we tag evidence according to the study type or category by which it is reported, such as verification, analytical validation, clinical validation, usability/feasibility, etc.

Results

Populations represented

- Our results feature a wide **spectrum of ADRD populations**, including Lewy Body, Vascular dementias, Frontotemporal dementias, and all severities of Alzheimer's disease
- To date, the most prevalently reported clinical populations are **Mild Cognitive Impairment, not otherwise specified (NOS)** and **Alzheimer's Disease Dementia, NOS**

Technology types, form factors, and health concepts

- **Wearables** represent 32% of included technologies, while **non-wearables** (**ambient, environmental, and software/app**) DHTs represent 61%
- **Smartphones/tablets** are most common form factor (42%), followed by **strap or brace** (19%), then **contactless** (6%)
- **Neurocognition** represents the largest health concept of measurement (51% of evidence). **Physical activity** is second largest, with 42% of evidence. **Sleep** is third, featuring 12% of evidence.

V3[5] and other evidence standards in action

- A majority (69%) of the evidence reports **clinical validation** within ADRD populations
- 34% of evidence reports **analytical validation**
- 19% of the evidence reports demonstrating **usability or feasibility** within ADRD populations

Discussion

- **We created an open-source evidence library of tech for ADRD research which is sortable and searchable**
- Our review of the sourced evidence shows the use of the V3 framework - mainly clinical validity - is prevalent in the ADRD technology space
- The dominance of software-based measurement of cognition underscores the clinical relevance of cognitive function in this population. **It provides an accessible modality for assessing a range of cognitive variables in clinical research, both in laboratory and real-world settings**
- Though many ADRD populations are identified, the largest are Mild Cognitive Impairment, NOS, and AD Dementia, NOS, posing challenges when using evidence to support future uses of a technology product
- In line with the **EVIDENCE checklist**[6] authors should aim to specify the **exact ADRD** population under assessment
- The library will be hosted on the DATAcc website and undergo cyclical updates
- **Users will be able to continually submit evidence** to the library to help crowdsource information, keeping the resource up to date and adding existing DHTs for which we have not yet received evidence
- **We hope this research will aid the development and selection of digital endpoints in clinical trials**

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References and acknowledgements

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