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PERSPECTIVE

Digital phenotyping: An equal opportunity approach to reducing disparities in Alzheimer's disease and related dementia research

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Abstract

A rapidly aging world population is fueling a concomitant increase in Alzheimer's disease (AD) and related dementias (ADRD). Scientific inquiry, however, has largely focused on White populations in Australia, the European Union, and North America. As such, there is an incomplete understanding of AD in other populations. In this perspective, we describe research efforts and challenges of cohort studies from three regions of the world: Central America, East Africa, and East Asia. These cohorts are engaging with the Davos Alzheimer's Collaborative (DAC), a global partnership that brings

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together cohorts from around the world to advance understanding of AD. Each cohort is poised to leverage the widespread use of mobile devices to integrate digital phenotyping into current methodologies and mitigate the lack of representativeness in AD research of racial and ethnic minorities across the globe. In addition to methods that these three cohorts are already using, DAC has developed a digital phenotyping protocol that can collect ADRD-related data remotely via smartphone and/or in clinic via a tablet to generate a common data elements digital dataset that can be harmonized with additional clinical and molecular data being collected at each cohort site and when combined across cohorts and made accessible can provide a global data resource that is more racially/ethnically represented of the world population.

KEYWORDS
biomarkers, digital technologies, health disparity, minority and vulnerable populations

1 | INTRODUCTION

Rapid aging of the world population is fueling a concomitant increase in the number of people diagnosed with Alzheimer's disease (AD) and related dementias (ADRD). While public health awareness of this global ADRD problem grows, the scientific inquiry has been heavily biased toward participants who are White in Australia, the European Union, and North America (approximately 80.94%).[1] This bias in research is perpetuated through a peer-review–driven system that relies on methodological precedent in its evaluative process. The existing cycle of predefined methodology that is not tenable in most parts of the world unwittingly sustains science that is not representative of all. Moreover, even in parts of the world where the majority of ADRD research is conducted, racial and ethnic minorities remain significantly underrepresented among research participants.[2] In both cases, there is insufficient consideration of what AD research methods are broadly feasible when developing the study design in under-resourced areas. Unintentionally, these barriers manifest themselves as preventing researchers from studying diverse populations due to inclusion/exclusion criteria disproportionately affecting certain groups, history of medical/research mistrust, etc. This lack of representativeness is in stark contrast with the growing body of evidence that other ethnicities bear a disproportionate burden of ADRD and cognitive impairment compared to White individuals.[3] Moreover, unraveling the complex effects of ancestry, lifestyle, social determinants of health, and other factors on ADRD requires a global effort and engagement of diverse populations around the world.

The Davos Alzheimer's Collaborative (DAC) Global Cohort Development (GCD) program seeks to upend this seemingly interminable prejudice in ADRD research by rethinking how to be maximally inclusive. The goal is to reduce barriers to participating in research by leveraging the cost-effective and global penetration of the smartphone.[4] The multiple sensors embedded within provide data-collection tools for ADRD-related digital phenotyping at an unprecedented scale. To further increase digital phenotyping uptake, the technology platform that was selected was evaluated for feasibility in a device-agnostic framework (i.e., iPads, tablets, iPhones, Androids) and across operating systems that span back to Android 6 and iOS 14.0. Appendix B shows all digital phenotyping tasks that comprise the DAC protocol and that are deployable across all cohort sites.

Rather than following the traditional prescriptive methodology of research, DAC has focused on prioritizing understanding the complexion of the cohort through communication with the cohort's research team to determine what might fit not only their research objectives but also would be feasible within their own research infrastructure with due consideration to participant burden. This more holistic view of how to make ADRD research globally inclusive resulted in developing a data collection protocol that included not just well-accepted derived measures of interest (e.g., cognition, gait/balance, ocular scanning, etc.), but also sensor-based digital data streams that could be used to develop novel measures of cognition, mood, function, and behavior that are agnostic to age, sex, education, language/culture. The unique strategy of DAC is to harness the richness of digital data in its raw native format that can be analyzed using deep machine learning and other emerging advanced analytic methods into clinically meaningful measures that are globally applicable today and also be re-analyzed for still-to-be-determined validated measures in the future. Similar to 1948, when the Framingham Heart Study (FHS) first launched in the absence of the concept of "risk factors," any understanding that measures such as blood pressure or cholesterol could be high, or the development of linear or logistic regression, they nonetheless embarked on an initial 20-year plan to collect longitudinal data on a community-based cohort and use this data resource that led to the discovery of all the major cardiovascular risk factors known today and the development of the whole new field of preventive medicine. DAC is taking on today for ADRD what FHS took on for heart health in 1948, but does so with the immense advantage of technological capabilities (hardware, software, analytics) that were not available to FHS. DAC is further accelerating global scientific opportunity by collecting longitudinal data on a much more compressed timeline (e.g., every 3 months) and has relaxed

the adherence to protocol design to accommodate whatever schedule works best for each participant. For example, missing an assessment window does not exclude a participant from remaining in the study and reduces loss to follow-up. This study design aligns with the reality of any decades-long longitudinal study and is a long-used approach at FHS. Participants are invited to every examination, and future participation to follow-up of existing as well as new data collection protocols is not contingent on participation in past or current ones. Analytic methods have previously been developed to address missing data such as imputation. The frequency of the DAC data collection protocol lends itself to these missingness issues.[5,6] Numerous data harmonization approaches to account for variations in data due to difference in test instruments (e.g., different cognitive tests for the same cognitive domain, magnetic resonance imaging scanners, different blood collection, and different biosample assays for same biomarkers) are common practice.[7,8,9,10] Thus, the DAC protocol leverages the successful history of long-standing cohort studies coupled with a commitment to making these data accessible to the global research community to take on the new analytic challenges that will emerge when designing a protocol that essentially allows inclusion of anyone and removes barriers such as exclusion criteria.

Acquisition of digital sensor data through smartphones lowers barriers to entry because of its global reach, low costs, easy adaptability, and minimal dependence on highly trained personnel. Remarkably, > 6.6 billion people use smartphones globally, that is, > 83% of the worldwide population. The equalizing opportunity of digital technology is enhanced when paired with blood collection as the other major universally feasible sample collection method, enabling genomic, clinical, ADRD biomarker, and exposome profiling. Together, a digital and blood repository also creates a new data-generating resource as future advances in digital and blood processing emerge. The prospective opportunities of digital data exceed that of blood because it is a non-diluting resource and can be more readily used for continuous assessments and experimentation.

With the use of digital data in ADRD research still in its infancy and, in its native format, prolonged lifespan of use, researchers from low- and middle-resourced economies can stand equal to those from high-resourced countries. This equal opportunity science scenario can become a reality through robust decentralization of data access. DAC's commitment to inviting and engaging the international scientific community is facilitated through its collaboration with the Alzheimer's Disease Data Initiative (ADDI), a cloud-based platform that provides free access to GCD collaborating cohorts' data and analytic tools. The individual cohorts will conduct analyses on the data that they generated, providing them the opportunity to expand/initiate their footprint in the digital space. Critically, each site will maintain sovereignty over their own data to do their own analyses at the individual level using the data their cohort generated. Through the ADDI, researchers globally will be able to access aggregated data across multiple cohorts that have implemented the same/similar digital protocol. Providing the international research community this unique data resource will hopefully fuel new scientific discoveries using advanced analytic methods including identifying and validating clinically meaningful metrics from sensor-based digital data that are globally applicable.

RESEARCH IN CONTEXT

1. **Systematic review**: A PubMed search was conducted regarding digital phenotyping and Alzheimer's disease (AD) and related dementias (ADRD). Nearly all data supporting the biological framework of ADRD was collected in high-resourced settings, although cognitive impairment and ADRD are strongly affected by social determinants of health that vary across populations.
2. **Interpretation**: Leveraging the widespread use of mobile devices to track behaviors that reflect pre-symptomatic cognitive and functional decline has the potential to advance global AD research and mitigate the data gap between high- and low-resourced countries.
3. **Future directions**: Future studies in diverse populations are necessary to determine the extent to which the outcomes of digital technologies correlate with and/or complement the standard clinical measures and biological markers of cognitive and functional decline in diverse populations.

To date, the power of equal opportunity science using the GCD protocol developed around digital and blood biomarkers has attracted the interest of 25 cohorts from 19 countries. Together the cohorts represent > 230,000 people across diverse racial/ethnic origins. Importantly, each of the cohorts offers a unique perspective of ADRD health disparities within specific regions/countries, contributing to filling the gaps in our knowledge of the factors that contribute to dementia.

2 | THE PANAMA AGING RESEARCH INITIATIVE

Latin American and Caribbean (LAC) countries are experiencing unprecedented demographic and health transitions. A recent meta-analysis estimated the pooled prevalence of dementia in LAC at 10%,[11] similar to more developed regions but with a much more rapid rate of increase. According to Alzheimer's Disease International, in Central America alone, the number of people living with dementia is projected to increase more than 4.5-fold (reaching 978,000 cases) by 2050.[12] Yet despite these shifting demographics there is scarce evidence of AD risk factors and biomarker data in the region.

Panama, an upper-middle-income country in Central America, faces important challenges with respect to population aging. Despite its income classification, the health status of elderly individuals is significantly affected by low income and education levels, both of which are well-established dementia risk factors. The Panama Aging Research Initiative (PARI) is the first prospective study of age-related health factors in older Panamanians. PARI, now in its tenth year, is focused

on demographic, clinical, and genetic factors associated with cognitive impairment in adults aged ≥ 50 years, including the study of vascular, metabolic, and inflammatory factors and their relation to the timing, sequence, and trajectories of AD biomarkers. A major component of the longitudinal study is the collection of blood samples at each in-person visit and correlating changes in blood- based protein profiles with cognitive and functional changes over time. Ultimately, the aim of this research is to identify individuals at risk for dementia, or rule out individuals not at risk, a screening approach well suited to primary care settings.

To date, PARI has identified various risk factors associated with dementia and cognitive impairment in elderly Panamanians of diverse backgrounds, including advanced age, low educational levels, depressive symptoms, and apolipoprotein E (*APOE*) ε4 expression. From 2012 to 2013, the first wave of participants aged ≥ 65 years were recruited from the largest national public hospital based in the capital city of Panama.[13] In a subsample of these individuals who underwent consensus diagnosis, *APOE* ε4 carriers were 5.1 times (95% confidence interval [CI]: 2.5–12.5) more likely to have cognitive impairment (mild cognitive impairment [MCI]/AD combined) relative to *APOE* ε4 non-carriers.[14] In addition, cerebrospinal fluid (CSF) samples were collected from individuals diagnosed with MCI, AD, or vascular dementia, and cut-offs were established that support the use of biomarkers to differentially diagnose AD from MCI and non-AD dementias in clinical settings. From 2016 to 2017, a second wave of community-dwelling participants was recruited, aged ≥ 60 years, and blood-based biomarker profiles were compared to three cohorts in the United States.[15,16] The pooled data had excellent diagnostic accuracy and positive and negative predictive power for both MCI and AD.[17] These collaborations also led to the first biobank of plasma, serum, and DNA samples that are essential steps toward determining the long-term predictive power of blood-based biomarkers in AD.

There are significant challenges to conducting cohort aging studies in Panama, including scarce research funding available to carry out this type of work. As longitudinal studies are costly, PARI relies heavily on an unpaid, transient student workforce to conduct clinical and neuropsychological assessments. Other challenges include a highly heterogeneous genetic admixture and social determinants of health among study participants, both of which require large samples to tease out their potential impact on dementia risk. However, although participant recruitment is costly, older individuals are eager to participate in research studies focused on age-related cognitive impairment, and enrollment is limited only by the human resources available to collect data.

In this regard, PARI has begun to leverage the high per capita levels of mobile phone use in Panama across racial and ethnic groups. A tablet-based battery of screening questionnaires, cognitive exercises, and functional tests is currently in development for pilot testing in a sample of participants who self-identify as smartphone users with access to wireless networks. Wearable devices will track sleep and activity patterns on a continuous basis. Digital data will be compared to self-report questionnaires and assessments and parameters of fluid biological markers. The hypothesis is that digital data can capture subtle changes in performance that may signal the earliest transitions in health status and predict changes in outcomes. Mobile technologies have the potential to reveal novel and innovative relations among health variables to improve measurements of functional decline related to early AD.

3 | THE IDENTIFICATION AND INTERVENTION FOR DEMENTIA IN ELDERLY AFRICANS STUDY, TANZANIA

It is becoming more apparent that the majority of people living with dementia worldwide live in low- and middle-income countries (LMICs) including sub-Saharan Africa and that the majority of older persons also live in LMIC. Demographic transition continues in Africa though rates of population ageing are slower than in some other regions. Despite this, the limited epidemiological data on dementia in sub-Saharan Africa indicates that prevalence may be increasing, contrasting with recent decreases observed in high-income countries. This is, of course, a concerning trend.

Despite this, African dementia prevalence estimates remain low (≈ 5%), and incidence data are extremely limited. In a 2022 review, only four dementia incidence studies were identified, none of which originated in East Africa.[18,19] The lack of available data is likely to be due at least in part to lack of validated cognitive and functional assessment tools for dementia appropriate for use in cross-cultural African settings. Additional challenges are lack of access to neuroimaging, biomarker, and genetic studies, and few appropriately trained specialist personnel, all of which pose challenges in dementia diagnosis.

Tanzania is a country of 61.5 million people in East Africa which graduated to lower-middle-income status in 2020, reflecting economic growth. Several epidemiological studies of dementia and cognitive impairment have been conducted in the Hai demographic surveillance site within Kilimanjaro, Northern Tanzania since 2010. Hai is a rural area, with a high proportion of subsistence farmers and an area of low migration, with natural boundaries. Additionally, due to an impressive initiative of the 1990s, the Adult Morbidity and Mortality Project (AMMP), there is well-established infrastructure for conducting epidemiological work.

Households are organized into 10-household cells, each with an elected leader (*balozi*) who reports to the village chairperson. In addition, the AMMP project villages have an "enumerator" system by which individuals are appointed to act as enumerators, under the supervision of the district medical officer, to conduct some public and primary health functions and recruit and assess individuals within their village for approved research. The *balozi* and enumerator systems provide a stable structure for conducting population censuses and epidemiological studies.

The first two-phase community door-to-door epidemiological study of dementia was completed in 2009 and 2010. The study revealed that age-adjusted prevalence of dementia by Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria in rural Tanzania was 6.4% (95% CI 4.9–7.9) in individuals aged ≥ 70 years.[20] This

study was repeated using similar but not identical, two-phase methodology in 2019 using DSM-5 dementia diagnosis criteria as part of a related subsequent study, the National Institute for Health and Care Research–funded Dementia Prevention and Enhanced Care (DePEC) study. The age-adjusted prevalence of dementia was 4.6% (95% CI 2.9–6.4) in those aged ≥ 60 years and 8.9% (95% CI 6.1–11.8) in those aged ≥ 70 years. Prevalence rates increased significantly with age, but this was a non-significant increase compared to 2009 and 2010. In terms of dementia subtype, 41% of cases were vascular dementia (VAD), a higher proportion than expected, and 48.7% were AD dementia.[21] In the repeat 2019 prevalence study, AD and mixed AD/VAD represented the majority of cases, and despite limitations in methodology, this was initial evidence of an increase in AD compared to VAD.[22]

Experiences from the 2010 study highlighted the need for appropriate cognitive measures for dementia screening that are useful in low-literacy settings. This study used as a screening measure the Community Screening Instrument for Dementia (CSI-D), initially developed for use in cross-cultural and low-literacy settings and used widely in LMIC settings by the 10/66 collaboration. There was a significant difference in CSI-D scores between males 27.7 (interquartile range [IQR] 25.7 to 29.4) and females (median 25.7 IQR 22.7 to 28.0). After adjusting for the effect of age, illiteracy and lack of formal education were significantly associated with "probable dementia" by CSI-D, whereas no association was found between DSM-IV dementia diagnosis in those with and without formal education.[23] Similarly, apparent prevalence of dementia using the 10/66 cross-cultural protocol was ≈ 20% compared to 6.4% by DSM-IV criteria.[20] Among this rural low-literate population, existing "low-literacy" measures used in other settings were still educationally biased and not clinically useful in identifying those with dementia. Similarly, a minimally adapted version of the Mini-Mental State Examination (MMSE), one of the most widely used tools worldwide, demonstrated that among low-literacy elders, median MMSE score was 19/30 (moderate dementia range) even though most individuals obtaining this score remained socially functional.[24]

Despite challenges in resources and infrastructure, the Identification and Intervention for Dementia in Elderly Africans (IDEA) collaboration was able to develop simple cognitive and functional screening measures and validate these for use in clinical and community settings, for both dementia and delirium. Using the data from the original 2010 epidemiological prevalence study, the IDEA brief six-item screen was developed,[25,26] in addition to a new culturally appropriate functional assessment measure with local stakeholders.[27] Normative values for measures of verbal learning/episodic memory and category fluency by age and education level in both Tanzania (east Africa) and Nigeria (west Africa) were also established, allowing identification of MCI and facilitating dementia diagnosis in individuals with higher levels of education.[28]

Although IDEA and related studies in the same area were able to inform on dementia subtypes to some extent, based on clinical neurological assessment, clinical criteria, and a restricted set of neuroimaging data, these data are limited by the lack of biomarkers and resources and access to imaging for all participants. This is an important consideration when recruiting for future interventional studies, as well as considering the issue of equitable access to and representation of research data in rural African populations.

The IDEA screen was developed into a software application that can be delivered on tablet devices and charged using solar power in rural and remote areas. This allows quality control, monitoring of data, and access to prompt support and clarification of queries from data collectors. Tablet-based administration of cognitive screening was an accurate and feasible method of assessment in this setting.[29] Currently, accurate screening measures for identification of frank dementia in Tanzania are available, but there is an ongoing need for measures of early cognitive decline and sensitive measures of cognitive change. Accurate data on dementia subtypes are needed to inform future interventional initiatives.

Ongoing challenges to conducting dementia research work in Tanzania are mainly of resources and infrastructure. Although clinical studies can often be completed at relatively low cost, even modest costs can be out of reach of local clinicians and service providers interested in completing this work. Mobile phone use is widespread in sub-Saharan Africa, although smartphone use remains limited in rural elders, a situation that is likely to change rapidly with decreasing costs of devices and data. There is a real need for capacity building in research including clinical and research skills, grant writing, and financial management as well as support to develop culturally appropriate tools to enable local clinical researchers and patient advocates to apply for and independently lead studies without consistent need for high-income partners, a potential ongoing source of inequity.

4 | THE TAIWAN TAIPEI MEDICAL UNIVERSITY–SHUANG HO HOSPITAL COHORT

Alzheimer's Disease International estimates that the number of people with dementia will increase from 23 million (2015) to almost 71 million by 2050 in the Asia Pacific region.[30] However, nearly all genetic analyses have been primarily conducted on White populations of Western European origin, making it difficult to understand the early stages of AD in other populations.[31] Taiwan, one of the most densely populated countries in the world, is showing increased prevalence of dementia. Current data indicate that approximately 312,166 individuals of the 23 million population have been affected by dementia, with numbers expected to rise in the future.

Taipei Medical University (TMU)–Shuang Ho Hospital cohort has been recruited from one of the largest hospitals located in New Taipei City focused on the study of AD in the Taiwanese population. Started in 2015, this cohort has collected robust clinical measures (i.e., cardiovascular risk factors, *APOE*, AD blood-based biomarkers, cognition, etc.) on 1866 participants. Additionally, TMU is implementing a digital phenotyping protocol that will collect measures of cognition via a smartphone such as voice data, gait and balance measured in a 2- to 3-minute task, and various cognitive screeners assessing different domains. Given the prevalence of the smartphone in Taiwan, the longitudinal data can be collected on a more compressed timeline (e.g., multiple times in a year) and generate more granular measures that can detect subtle changes

more readily, a key element in an insidious onset disease such as AD and ADRD.

In addition, a subset of 400 participants will contribute to validation studies of digital phenotypes using well-accepted cognitively related assessments such as the Clinical Dementia Rating, Cookie Theft Picture Description (CTPD), and Gait–Balance. These tests are paired with digital technologies including use of Tobii pro nano and the software OpenFace to analyze eye tracking during the CTPD administration and OpenPose for obtaining digital measures from Gait–Balance tests. Validation of the digital measures can then be translated into digital tasks delivered via smartphone/device using the multiple sensors embedded in the smartphone (i.e., accelerometer, microphone, gyroscope, etc.) to allow for scalable data collection that can detect cognitive decline with increased prognostic and diagnostic accuracy, even in the context of heterogeneity of individual time point measures (see Appendix A). These data will be stored as a digital biobank so that future research can leverage this repository to further science.

5 | CONCLUSIONS

The increase in life expectancy globally has led to a higher prevalence of dementia, but research on risk and preventive factors of dementia has been conducted largely in White populations in developed countries. A large body of research has shown that cognitive impairment and ADRD do not affect all communities equally. Even within developed countries, dementia risk and prevalence have been found to vary by sex, race and ethnicity,[32,33] geographic location,[34] and neighborhood characteristics.[35] AD diagnosis reliant on CSF, structural and molecular biomarkers, and the evidence supporting this approach was generated from studies with mostly White participants.[2] As such, there is an incomplete understanding of the way AD impacts diverse populations.

The DAC program aims to leverage the widespread use of digital technologies across the globe and examine the potential of mobile phones and wearable sensors to acquire insight into everyday life activities, behaviors, and habits in real time and in a more accurate way than self-report techniques. In this regard, applying digital technologies to data collection tools has the potential to facilitate the assessment of functional decline in cohort studies examining cognitive and functional impairment and progression to AD in low-resourced settings.

An important goal of AD research is to identify measures that reflect subtle cognitive and/or functional decline before the frank onset of symptoms. Digital biomarkers may assist in this goal by providing accurate and continuous monitoring of behavioral change. This is important for identifying populations at risk before the onset of symptoms, particularly because different populations, even within countries, will likely have different trajectories of functional decline. Validating measures to track functional decline also enables an assessment of the health disparities that exist in AD trajectories. Furthermore, mobile technologies are widespread, far less expensive, and less invasive compared to standard methods for measuring prognostic AD biomarkers, such as positron emission tomography scans or lumbar puncture, which are costly, invasive, and unavailable in many countries, and therefore highly limited in terms of their capacity to identify at-risk groups in low-resourced settings.

Digital phenotyping, together with clinical and other cognitive and behavioral measures, has the potential to advance AD research in low-resourced settings by considering the experience of research participants in their natural environment. Digital technologies could facilitate data collection over time by tracking pre-symptomatic functional decline in more accurate ways by not having to rely on participant self-report. For example, wearable devices are suitable to monitor sleeping patterns and physical activity, two major drivers of AD, because they can assess these behaviors in real-world contexts, and therefore carry the promise of providing greater ecological validity and sensitivity than conventional self-report measures.

The number of ADRD cohort studies applying digital phenotyping to conventional markers in LMIC is limited, so it remains unclear which outcomes have the most consistent association with cognitive and functional decline. If mobile tools are widely adopted as scientific measurement tools for dementia research, there is much that can be tested regarding the reliability, sensitivity, and specificity of numerous sensors, such as global positioning systems, accelerometer, and the microphone, that will inform the data as it is currently being collected. Specifically, an important question across all populations is how accurately these applications can detect the earliest symptoms of functional decline in preclinical AD. Thus, global research is necessary to determine the extent to which the outcomes of digital technologies correlate with and/or complement the standard clinical measures and biological markers of cognitive and functional decline in diverse populations.

6 | LIMITATIONS

The vision of a globally represented data resource fueled by digital technologies faces significant barriers in reality. Variations in mobile devices, such as older and newer models, will generate digital data streams of different quality/fidelity that will require development of harmonization methods. Internet connectivity is not uniform and will lead to non-random missing data. Also, there will be a time lag between acquisition of digital data and the emergence of digital metrics that are truly age, sex, education, language/culture agnostic and thus will remain reliant on derived digital measures that are highly correlated with existing known measures that were developed on biased data and perpetuate the current problem of biased findings. Further, the lifecycle for any technology is short and the current DAC protocol will need to be continuously revised and updated. The long-term strategic plan is to create methods that can readily adopt locally developed technologies and testing methods that can nonetheless be harmonized across cohorts and result in a significant paradigmatic shift in how large-scale epidemiological research is conducted to achieve true global representation.

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CONFLICT OF INTEREST STATEMENT

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CONSENT STATEMENT

All participants/patients provided their written informed consent to participate in these studies.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX A

Summary of Davos Alzheimer's Collaborative cohorts and digital technologies used locally

Cohort	Sample size	Sex distribution (% female)	Education, years, mean (range)	Ethnicity	Biological markers	Digital technologies used	Metrics collected through digital technologies	Challenges
PARI, community cohort	*N* = 469[a]	76.3%	15.9 (3–34)	Hispanic	Blood-based inflammatory and AD-associated markers, *APOE* genotyping, CSF markers	Mobile phones, tablets	Anxiety, depression, sleep quality (self-report active data); heart rate, sleep tracker, distance traveled (passive data)	Unequal access to wireless capability, heterogeneous genetic admixture, variable levels of mobile phone literacy
SHH cohort	*N* = 1866	57.5%		Taiwanese	Blood-based genetic test and *APOE* genotyping,	Mobile phones	Gait, voice, eye tracking	
IDEA community longitudinal cohort	*N* = 327	56.9% female	24.5% Illiterate/no education 25.1% completed primary school (7 years education)	Tanzanian	None. Blood biomarkers now feasible locally	None at baseline, but subsequent App-based cognitive assessment using tablets	Cognitive outcomes	Prior to tablet feasibility study, village health workers needed orientation to digital data collection. Use of solar chargers due to unreliable electricity. Need to travel to access WIFI signal to upload data

[a]Enrollment is ongoing.

Abbreviations: *APOE*, apolipoprotein E; CSF, cerebrospinal fluid; IDEA, Identification and Intervention for Dementia in Elderly Africans; PARI, Panama Aging Research Initiative; SHH, Shuang Ho Hospital.

APPENDIX B

Summary of Davos Alzheimer's Collaborative digital data collection protocol to be incorporated at each site

Testing location	Hardware	Assessments	Modalities	Domains measured	Time (in minutes)	Challenges
In clinic	iPad	DCTclock	Drawing	Executive functioning, visuospatial abilities, motor planning, and attention	3 min	Orientation to digital data collection
		Questionnaire	Questionnaire	Cognitive functioning, various details on COVID infection including number of infections, diagnosis history, severity, etc.	2–4 min	

(Continues)

Testing location	Hardware	Assessments	Modalities	Domains measured	Time (in minutes)	Challenges
Remote	Smartphone—bring your own device	Gait & balance	Walking	Motor skills, balance, postural control, and dual tasking	6 min	Variable levels of access to wireless capability and phone literacy
		Complex picture description	Voice	Executive function, language conceptualization, and processing, including syntax and semantics	1 min	
		Go no go	Screen based	Response inhibition	3 min	
		Code substitution	Screen based	Working memory involving frontoparietal and cortical function	4 min	
		Simple reaction time	Screen based	Pure reaction time	3 min	
		Match to sample	Screen based	Integration of sensory processing with memory	4 min	
		Complex picture description recall	Voice	Executive function, language conceptualization, and processing, including syntax and semantics	1 min	
		Spatial processing	Screen based	Working memory involving exclusively parietal functions	3 min	
		Procedural reaction time	Screen based	Accuracy, reaction time, impulsivity, executive functioning, decision-making	3 min	
		Open-ended questions	Voice	Orientation in time and place, procedural memory, and generic memory	3 min	
		Category naming	Voice	Verbal fluency and executive functioning	1 min	
		Sleep questionnaire	Questionnaire	Sleep quality, sleep patterns, sleep disturbances, impact on cognitive functioning	1 min	

Abbreviations: DCTclock, digital Clock Drawing Test; min, minutes.