BMJ Open Multicohort cross-sectional study of cognitive and behavioural digital biomarkers in neurodegeneration: the Living Lab Study protocol

Mark Crook-Rumsey , ^{1,2} Sarah J C Daniels, ^{2,3} Subati Abulikemu, ^{2,3} Helen Lai, ^{2,3} Adrien Rapeaux, ^{2,4} Charalambos Hadjipanayi, ^{2,4} Eyal Soreq, ^{2,3} Lucia M Li, ^{2,3} James Bashford, Julian Jeyasingh-Jacob, James Bashford, Julian Jeyasingh-Jacob, James Bashford, Damion Lambert, Spannian Weil, Adam Hampshire, Javid J Sharp, J Sharp, Javid J Sharp, J Shlomi Haar (1) 2,3

To cite: Crook-Rumsev M. Daniels SJC, Abulikemu S, et al. Multicohort crosssectional study of cognitive and behavioural digital biomarkers in neurodegeneration: the Living Lab Study protocol. BMJ Open 2023;13:e072094. doi:10.1136/ bmjopen-2023-072094

Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi. org/10.1136/bmjopen-2023-072094).

Received 23 January 2023 Accepted 24 July 2023



@ Author(s) (or their employer(s)) 2023. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by

For numbered affiliations see end of article.

Correspondence to

Dr Mark Crook-Rumsey: mark.crook-rumsey@ukdri.ac. uk and Dr Shlomi Haar; s.haar@imperial.ac.uk

ABSTRACT

Introduction and aims Digital biomarkers can provide a cost-effective, objective and robust measure for neurological disease progression, changes in care needs and the effect of interventions. Motor function, physiology and behaviour can provide informative measures of neurological conditions and neurodegenerative decline. New digital technologies present an opportunity to provide remote, high-frequency monitoring of patients from within their homes. The purpose of the living lab study is to develop novel digital biomarkers of functional impairment in those living with neurodegenerative disease (NDD) and neurological conditions.

Methods and analysis The Living Lab study is a crosssectional observational study of cognition and behaviour in people living with NDDs and other, non-degenerative neurological conditions. Patients (n≥25 for each patient group) with dementia, Parkinson's disease, amyotrophic lateral sclerosis, mild cognitive impairment, traumatic brain injury and stroke along with controls (n≥60) will be pragmatically recruited. Patients will carry out activities of daily living and functional assessments within the Living Lab. The Living Lab is an apartment-laboratory containing a functional kitchen, bathroom, bed and living area to provide a controlled environment to develop novel digital biomarkers. The Living Lab provides an important intermediary stage between the conventional laboratory and the home. Multiple passive environmental sensors, internet-enabled medical devices, wearables and electroencephalography (EEG) will be used to characterise functional impairments of NDDs and non-NDD conditions. We will also relate these digital technology measures to clinical and cognitive outcomes.

Ethics and dissemination Ethical approvals have been granted by the Imperial College Research Ethics Committee (reference number: 21IC6992). Results from the study will be disseminated at conferences and within peer-reviewed journals.

INTRODUCTION

Neurodegenerative disorders (NDDs) and neurological conditions constitute a major global challenge. Dementia is a prevailing NDD,

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The comprehensive collection of multimodal physiological, behavioural and cognitive data to create novel, quantifiable digital biomarkers of functional/ cognitive decline for a range of neurodegenerative disorders and neurological conditions is a strength of this study.
- ⇒ The Living Lab study offers a unique opportunity to simulate a home-like environment and activities while maintaining the rigour and replicability of a laboratory environment. The Living Lab therefore provides an important intermediary stage between the laboratory and home.
- ⇒ New insights gained from this study can be immediately applied to the ongoing Minder remote home monitoring projects of neurodegenerative disease (NDD) and non-NDD conditions.
- ⇒ A limitation of this study is its cross-sectional design. It will be important to validate the biomarkers developed and identified within this study in longitudinal studies of neurodegenerative disease.
- ⇒ Inclusion of diverse NDD and non-NDD populations enhances the versatility of our digital biomarkers, although it may present a limitation by requiring larger sample sizes to model specific clinical characteristics.

affecting approximately 850000 people in the UK, 57 million globally and is expected to rise to 152 million by 2050.² Parkinson's disease (PD) is the second most common NDD manifesting severe cognitive and mobility problems. In 2016 6.1 million people had PD globally.³ The increasing prevalence of other NDDs, such as amyotrophic lateral sclerosis (ALS), mild cognitive impairment (MCI) and neurological conditions at high risk of developing NDD, such as traumatic brain injury (TBI) and stroke also contribute to the burden of disease.



Biomarkers have long been proposed as an advance to diagnostic and monitoring frameworks for neurological conditions. Traditional biomarkers (eg, positron emission tomography and cerebral spinal fluid), however, are fraught with limitations. They are difficult to access, expensive, invasive or inconvenient and are problematic for taking repeated measurements. With the emergence of internet-enabled medical devices, internet-of-things (IoT) environmental sensors, portables and wearables, remote high-frequency measurements can be taken from a patient's home. It is possible to develop digital biomarkers of behaviour and cognition for people with NDDs and neurological conditions. Indeed, ongoing remote monitoring projects are demonstrating promising results within the homes of people living with dementia (PLWD) using passive-infrared sensors (PIR) to detect agitation and urinary tract infections.⁵⁶

While initial results are promising, it is evident that development is needed to expand these digital biomarkers to further capture functional impairments across other NDDs and non-NDD conditions. There is a need to understand the clinical relevance and validity of such measures. Problems facing developing digital biomarkers from home-based data include multiple occupancies, validating measures and features derived from the data. The problem is compounded by not having a reliable baseline to compare recorded activity. Individuals would likely not tolerate cameras in their homes to create reliable baselines and it is important that homebased health monitoring systems preserve an individual's privacy. However, by simulating a home environment in a controlled setting, these issues can be addressed. In this study, we will investigate emerging technologies for determining novel biomarkers of function and performance within an artificial apartment-laboratory. We will investigate the type and number of sensors that are required for creating reliable digital biomarkers of functional performance in those with NDDs which can then be integrated into ongoing Minder home monitoring projects.

Minder's home-based monitoring platform uses passive sensors including PIR sensors, door sensors and bed mats to monitor behavioural activity.^{5 6} These sensors have shown the ability to track activities, behaviour, medication adherence, cognitive stats, agitation and urinary tract infections in real time for individuals with NDDs.⁶ 8 However, since the data is primarily collected without accompanying ground truth, it is challenging to determine the accuracy and creating models for predicting and detecting behaviours in uncontrolled environments. In this study, we will investigate the relationship between passive sensors and controlled ground truth via cameras, floor sensors and current gold-standard measures of functional performance and disease assessment. This will enable us to develop technologies capable of detecting early health problems, adverse clinical events and responses to therapies from within the home.

Recent advances in ultra-wideband (UWB) RADAR have demonstrated the potential utility for remote monitoring of older adults in their homes without collecting personally identifiable information. UWB offers highly sensitive passive sensing to determine presence, breathing, heart rate, posture and movement without causing harm while using minimal power. Initial studies demonstrate that gait differences can be classified from UWB including walking with an aid or foot-drag. 10 However, studies often simulate (act-out) this behaviour rather than collect data from patients. We plan to investigate the differences in movement and physiology across different patient cohorts to define clinically relevant features that could be reliably deployed for automated monitoring.

To develop reliable ground truths for validating movement measures, we will have different angles of the laboratory recorded by Microsoft Kinect cameras to capture body joint dimensional coordinates. The use of the cameras in our study is twofold: they offer a real-time video of events for post hoc annotation and through kinematic joint data new features can be derived to extend clinical measurements of physical function.

To develop digital biomarkers that reflect behavioural and cognitive impairments, it is important that a comprehensive evaluation of cognition can be used as a reference. Here, pen-and-paper tests (Addenbrooke's cognitive examination (ACE-III)) and digital batteries (Cognitron and Cats-and-Dogs Test) 11-13 will be used to capture a range of cognitive dimensions and visuoperceptual deficits.

Electronencephalography (EEG) will be recorded during Living Lab activities and cognitive tasks. EEG measures have reliably revealed cognitive disruptions in those with NDDs¹⁴ and non-NDD conditions. ¹⁵ With the development of mobile EEG systems, free-movement real-world tasks can be examined. 16 17 We will examine the relationship between cognitive measures and real-world functional activities of daily living.

The development of internet-enabled medical devices, such as blood pressure monitors, allows for frequent remote measurements to track autonomic dysfunction. Autonomic dysfunction is present in many neurological conditions such as ALS, 18 PD, 19 Alzheimer's disease 20 and TBI.²¹ It is also associated with increased frailty in older adults, 22 which in turn increases the likelihood of adverse outcomes such as falls, a decline in mobility and delirium.²³ Through a range of IoT devices within this study, we will explore differences in autonomic dysfunction and their ability to discern differences between NDD groups from healthy older adults and in developing a composite battery of digital measures of risk and frailty.

Goals and objectives of the Living Lab study

1. To develop disease agnostic digital biomarkers of behavioural performance and cognition in adults with NDD and non-NDD conditions to track healthy ageing, deviation from healthy ageing due to neurological conditions and disease progression.



Table 1 Inclusion and exclusion criteria	
Inclusion criteria	Exclusion criteria
Persons with a neurological diagnosis	
Subjects must be aged over 16.	Additional neurological conditions that impact or the assessments being completed.
The ability to provide informed consent.	Unable to give consent for themselves.
Have sufficient functional English to allow completion of the assessment instruments.	
Diagnosis of a neurological condition such as dementia, mild cognitive impairment, amyotrophic lateral sclerosis, traumatic brain injury, Parkinson's disease or stroke.	
Controls	
Subjects must be aged over 16.	Diagnosis of a neurological condition.
The ability to provide informed consent.	Unable to give consent for themselves.
Have sufficient functional English to allow completion of the assessment instruments.	

- 2. Determine whether individual or composite sensor configurations can predict patients' clinical scores and differentiate them from controls.
- 3. To develop sensitive biomarkers that will interface with the ongoing UK Dementia Research Institute's (UK DRI) Minder studies of home-based digital biomarkers in NDDs and NDD conditions.

METHODS AND ANALYSIS Study design

The Living Lab study is a cross-sectional, observational study that will be conducted by the UK DRI, Care Research & Technology Centre (CR&T) based at Imperial College London, London, UK. Pragmatically recruited patients via the authors' networks will have one of the following diagnoses: ALS, dementia, MCI, TBI, PD or stroke. Adults without NDD or neurological conditions will be recruited as controls. The inclusion of younger adults will allow for the exploration of age-related digital biomarkers against aged controls. Participants will come to the Living Lab for a one-time visit to complete a range of cognitive and behavioural activities.

Patient recruitment

Patients will be recruited via word-of-mouth or online advertisements distributed through disease-associated organisations. Individuals that meet the inclusion and exclusion criteria (table 1) will be given written and verbal information about the study and invited to participate.

Participants will be reminded that participation will not affect their clinical care.

Sample size

Power analyses were performed to determine the required participant numbers using an α =0.05 and power=95%. Sample sizes were calculated using expected group differences in the Short Physical Performance Battery (SPPB) and ACE-III for those with expected physical impairments (ie, ALS and PD) and those with expected cognitive impairments (ie, dementia and TBI).

We estimate a minimum of six patients and seven healthy controls (HC) are required to determine physical differences between a physically impaired NDD group for the SPPB. We calculate 17 participants per group for non-physically impaired NDD conditions are required. A previous kinematic SPPB sit-to-stand study used 25 participants with subacute stroke and 17 HC.²⁴ To determine effects of ageing, 26 younger adults (≤30 years old) and 26 older adults will be required.

We estimate that seven patients and seven controls will be required to determine cognitive differences between an NDD group with expected cognitive impairments (eg, dementia) and a HC group for the ACE-III based on Pott's *et al* reliability of the ACE-III. Previous research evaluating technology-derived behavioural performance differences have used 20 participants to determine differences between cognitively impaired individuals and controls. Previous research impaired individuals and controls.

To ensure statistical power for the prediction of potential digital biomarkers on clinically validated scales, we will follow the recommended sample size suggestion of n≥25 for performing regression analyses.²⁷

For the recruitment of controls, we will follow recommendations made for multiarm multistage trials that use a common control group without compromising statistical power. Optimal allocation to the control group is approximately \sqrt{K} : one patient allocated to the control group for every one patient allocated to an experimental treatment, where K is the number of treatments. Using K here as the number of NDD cohorts, we can calculate an optimal number of controls with $\sqrt{6} \times 25$ (patients per cohort). Therefore, approximately 61 healthy older adult controls will be recruited for the study. Subsets of age/sex-matched controls can then be derived from this data set to match the patient groups.

Living Lab description

The Living Lab is a 32 m² space designed to mimic residential living (figure 1A). It is designed in a studio apartment layout containing a fully functional domestic kitchen (including a hob, dishwasher, fridge, freezer, microwave, kettle and toaster), dining area, sitting room, a bed and bathroom. The studio is furnished with domestic utensils, pans and kitchen appliances, allowing for the performance of functional tasks such as meal preparation and cleaning.

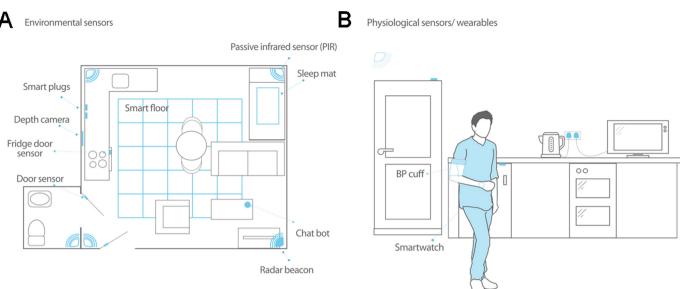


Figure 1 Living Lab layout. (A) Top view illustration of the Living Lab set-up. (B) Illustration of the physiological and wearable sensors. BP=blood pressure.

Passive devices

Environmental sensors

Unobtrusive environmental sensors are fitted within the laboratory for detailed behavioural monitoring (figure 1). Technologies include PIRs, door sensors, smart plugs and a Withings Bed Mat, all of which provide low-cost continuous monitoring of activity. PIRs, door sensors and smart plugs all provide a binary output based on movement, opening/closing a door and using an appliance, respectively. In this study, the bed mat will only record heart rate and respiration during the 3 min of lying in a supine position. When environmental sensors are combined, they can provide rich insights into home-based activities and have previously been used to predict night-time wandering, falls and infections in PLWD.³⁰ A related project run by the UKDRI CR&T, called the Minder study, currently has these devices deployed in the homes of PLWD. Insights gained from the current protocol can be retrospectively analysed with the longitudinal data from patients' homes.

Ultra-wideband RADAR

In addition to the environmental sensors, low-cost networked UWB developed at Imperial College London³¹ will record all the Living Lab tasks illustrated in figure 2. The UWB samples at 500 Hz and mitigates privacy concerns as it does not collect personally identifiable data (ie, video or sound). It is low power and has no adverse effects on the body. Three UWB devices will be placed on the laboratory's walls to provide ample coverage of the Living Lab.

RGBD cameras

Microsoft Azure Kinect development kit cameras will record all tasks completed in the Living Lab. Six Kinect depth sensors are positioned around the walls of the Living Lab to mitigate occlusion problems and increase coverage. The Kinect sensors use the time-of-flight principle to augment a two-dimensional pixel grid by adding distance to each pixel. Deep learning and convolutional neural network-based body tracking software development kit (SDK), allow tracking of multiple people simultaneously and capturing three-dimensional coordinates of 32 body joints. Multiple joint data skeletons can be merged to compute and evaluate kinematic profiles of gait patterns, pose symmetry and centre of mass. One Kinect camera will additionally record regular video as a reference for events within the Living Lab.

Active devices

Wearables

Participants will be fitted with a ScanWatch (Withings, Land-Issy-les, Moulineaux, France) and Movisens Move 4 devices on the left and right wrists. The ScanWatch will provide a measure of blood oxygen saturation, the number of steps and heart rate which is automatically sampled every 10 min.

The Move 4 is a triaxial accelerator which records movement at 64 Hz with a dynamic range of ± 16 G's (1 G represents gravitational acceleration at $9.8\,\mathrm{m/s^2}$). These will record continuously throughout the entirety of the study.

Blood pressure and heart rate

Blood pressure will be measured using the BPM Core wireless blood pressure cuff (Withings, Land-Issy-les, Moulineaux, France). The BPM Core is an automated wireless upper arm sphygmomanometer with an integrated display. Participants will be instructed on how to use the device. Participants will be asked to take the first reading after lying in a supine position on the bed for 3 min. After the supine reading, participants will then be asked to stand. While in the standing position, participants will take a further three blood pressure recordings at 1 min,

Living lab protocol

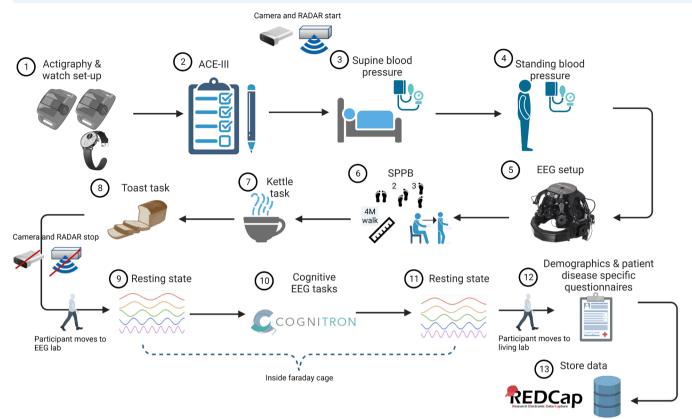


Figure 2 Graphical illustration of the Living Lab protocol. ACE-III=Addenbrooke's cognitive examination; SPPB=Short Physical Performance Battery; EEG=electroencephalography.

3 min and 5 min. Data are automatically uploaded to the Minder home monitoring platform via Wi-Fi.³²

EEG

EEG will be recorded using a 21-channel DSI-24 EEG (Wearable Sensing, California, USA), which is a quick set-up dry-electrode system. The DSI-24 will record wirelessly while the functional tasks are completed within the Living Lab allowing participants to move freely. EEG for the resting-state and cognitive tasks will be completed within a Faraday cage, sound attenuated EEG laboratory adjacent to the Living Lab with a wired connection.

Living Lab tasks

After consent, participants will complete activities in the Living Lab as illustrated in figure 2. Participants will complete the tasks in sequence but can omit steps if they are unwilling/unable. While the PIR and floor sensors record continuously, UWB and cameras will only be activated after the wearable devices have been fitted, the cognitive examination has been completed and the participant has been fitted with the blood pressure device. The following section describes each of the Living Lab protocol tasks. Where possible, the researcher remains outside of the laboratory to avoid data contamination and communicates with the participant via an Amazon Echo.

Participants will complete the ACE-III.³³ The ACE-III is a brief assessment of five cognitive domains: attention, memory, verbal fluency, language and visuospatial abilities. It is a commonly used clinical tool which contains 24 questions administered by the researcher. The total score is out of 100, where higher scores indicate better cognitive function.

SPPB

The SPPB is a routine measure of physical performance, often administered to hospital patients, nursing home residents and community-dwelling adults.34-36 The SPPB is comprised of three 10s balance tests with feet side-byside, semi-tandem or full-tandem, a timed 4-metre walk at the participant's usual walking pace, which is repeated thrice and a timed five times repeated sit-to-stand test. The SPPB will be delivered via the SPPB Guide application.³⁷

Kettle task

The kettle task³⁸ is a brief performance-based test that evaluates an activity of daily living. It requires a participant to prepare two different hot beverages. All items required to make the beverages are presented on a tray for the participant along with distractor items. The task has demonstrated good inter-rater reliability and

Toast task

The toast task is an adapted version of Clinical Task Instructions S-AD09 from Queensland Health: Assess meal preparation and provide basic/bridging intervention. ⁴¹ Participants will be asked if they feel comfortable and willing to make two slices of margarine/jam on toast. If the participant agrees, they will be told where all the items are within the laboratory. Once confirmed that the participant has understood, they will begin the task from a seated start on the bed and will finish with two slices of toast sitting at the table. The participants will be asked to perform this task twice.

EEG lab tasks

Resting-state

Two 2min recordings of eyes-open and eyes-closed resting-state activity will be recorded before and after the cognitive tasks are completed while participants are comfortably seated.

Cognitive tasks

Six tasks from the Cognitron platform^{11 12} will be used to assess a spectrum of cognition during EEG recording and will be presented in a Chrome browser. The Cognitron will be used due to the non-language cognitive tests, its adaptive difficulty scaling and because it is manageable for older adults and patients with MCI/motor difficulties to complete. It also offers massive normative comparison data. The tasks include two-dimensional Mental Rotations (dimensional manipulation), Blocks (two-dimensional spatial problem solving), Paired Associate Learning (working memory), Motor Control (reaction time) and Object Memory (episodic memory). Object memory will be tested twice: once at the beginning ('immediate') of the cognitive task session and once at the end ('delayed'), with an interval of approximately 20 min.

Visual processing and structural retinal changes are associated with a higher risk of more rapid development of dementia in PD^{42} but it is unclear if this is applicable to other neurological conditions. The Cats-and-Dogs Click or tap here to enter text task will be administered to explore whether deficits in higher visual function are a useful measure of dementia risk.

Demographics and activities of daily living

Demographic information will include age, sex, handedness, education, ethnicity, medications and time since diagnosis. Participants are asked to complete the validated EuroQol 5-dimension 5-level (EQ-5D-5L) questionnaire. The EQ-5D-5L evaluates the participant's quality of life based on five factors: mobility, self-care, usual activities, pain or discomfort and anxiety/depression. Participants respond on a 5-point scale ranging from no problems to extreme problems. Participants will also complete the Bristol Activities of Daily Living questionnaire to measure average functional performance

on basic everyday tasks. Responses are given on a 4-point scale from independent to total dependence.

Disease-specific questionnaires

Participants may also be asked to complete questionnaires specific to their disease or condition to provide detail on their general function/disease severity. For example, individuals with ALS will complete the ALS Functional Rating Scale-Revised. These questionnaires will be used to further validate the developed biomarker's specificity to the aspects of each neurological condition.

Analysis plan

We will report descriptive data and demographics with numbers and percentages for categorical data. Means and SD will be reported for continuous data but medians and IQRs will be used for skewed distributions.

Kinematic data from Kinect cameras will be used to explore the differences in posture, balance and gait dysfunction by extracting features from the recorded 32-joint data. T-tests and Mann-Whitney U tests will be used for comparisons of the derived features between HCs and people with NDDs with normal or non-normal distributions, respectively. Relationships between derived features and measures of physical, cognitive ability and clinical measures will be evaluated using generalised linear models. The functional tests of the SPPB will be explored along with the kettle and toast tasks.

For UWB validation, we will explore the following derived features from the data: breathing, heart rate, postural steadiness, gait, sit-to-stand sequences and balance. For breathing and heart rate analyses, measurements will be taken from the movements of the chest during periods of rest (ie, sitting and lying). Postural steadiness will be analysed during periods of standing (eg, standing blood pressure measurements). Gait, sit-to-stand sequences and balance will be analysed from the SPPB. Features will be used for analyses of functional performance, group comparisons and questionnaire predictions using generalised linear models.

Wearables from both wrists will be analysed for all the tasks in the Living Lab (steps 2–8, figure 2). Each of the tasks will be explored independently. Analysis of variance will be used to compare individuals with NDD/neurological conditions with HCs while accounting for the left and right wrist-worn devices. Generalised linear models will be used to assess the relationship between wearables, physical performance, cognitive performance and disease-specific questionnaires.

Blood pressure and heart rate differences will be assessed between patient groups and HCs using analyses of variance across each of the measurements. Comparisons between supine to standing ratios will be calculated to examine orthostatic hypotension.

EEG data will be analysed individually for each of the LivingLab and SPPB tasks. We will analyse the power in different frequency bands along with their ratios. For each task, changes in the beta band (13–30 Hz) will be

analysed in relation to movement. For resting-state analyses frequency spectrum (ie, alpha, beta, theta, delta) analyses will be performed. For each of the Cognitron tasks, frequency and event-related analyses will be analysed. Comparison between neurological condition groups and HCs will be made with two-sample t-tests. EEG scores will be used in correlational analyses aspects of the functional Living Lab tasks to understand relationships of cognition. EEG measures will be used in generalised linear models for the prediction of disease-specific questionnaire scores and functional performance scores.

It is important to note the possible limitations of using a diverse cohort of diseases. Our study has sufficient participants to develop biomarkers for unique features such as balance in functional performance or attention in cognitive performance. However, the possible heterogeneity of patients' disease characteristics might make developing biomarkers difficult for specific characterisation of disease stages. In such instances, we may need to recruit additional participants to answer questions specific to a disease.

Data management

Data and related documentation will be retained for 10 years after the study concludes in line with ethical obligations. This will provide sufficient time for analyses to be performed and for future analyses to be conducted on the data as new methods are developed.

Patient demographic and questionnaires, including ACE-III scores and SPPB scores, will be collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Imperial College London. 46 47 REDCap is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for data integration and interoperability.

Data recorded from UWB, Kinect cameras, wearables and EEG devices will be uploaded to a Research Data Store at Imperial College London without personally identifiable information. This is a secure storage service only accessible by the Imperial College London network. Personally identifiable information from the reference camera will be stored on a separate data store located at the Data Science Institute, Imperial College London, only accessible by the research team. Data will follow a modified Brain Imaging Data Structure (BIDS) format.⁴⁸ BIDS is a standardised method for organising neuroimaging files and data that can be easily interpreted by other researchers. We will use a similar format and naming convention for the data collected to easily identify and analyse the multimodal data collected.

Custom-made software will be used to add labels and annotations to the events that occur within the Living

Lab. This will provide the ability to extract events of interest to evaluate the study aims.

ETHICS AND DISSEMINATION

Ethical considerations

The relevant ethical approvals have been granted by the Imperial College Research Ethics Committee (21IC6992) and the Imperial College Research Governance and Integrity Team. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

Our study poses minimal risk to participants and will not affect their privacy, be invasive or restrictive. There is a risk that participants may lose balance during the balance tasks of the SPPB. Participants will only be asked to attempt the balance task if they feel confident. Risks are mitigated by the researcher being present and close to the participant to provide support while they attempt the task as instructed within the SPPB instructions.

The primary ethical consideration is the time it takes to complete the protocol which is approximately 2.5–3 hours. As the study contains both physical and cognitive components, some participants may find this tiring. Participants will be reminded that they can decide not to do a particular task or conclude the study at any point.

Dissemination

The results of this study will be presented at scientific meetings and international conferences, and published in peer-reviewed journals. Data will be shared with approved researchers to conduct further analyses and provide further insights for developing digital biomarkers for NDD and neurological conditions.

Patient and public involvement

Patients and the public are involved in the early stages of projects at the UKDRI CR&T Centre at Imperial College London. Design teams have run co-design workshops with Minder Champions to define the direction of work that takes place within the centre. Prototypes along with the Minder platform are designed in conjunction with patients and their carers to interact and develop new technologies with the patient in mind.

Author affiliations

¹UK Dementia Research Institute, Basic and Clinical Neuroscience, King's College London, London, UK

²UK Dementia Research Institute, Care Research and Technology Centre, Imperial College London, London, UK

³Department of Brain Sciences, Imperial College London, London, UK ⁴Department of Electrical and Electronic Engineering, Imperial College London,

⁵University of Surrey, United Kingdom Dementia Research Institute, Guildford, UK ⁶National Hospital for Neurology and Neurosurgery, UCLH, London, UK

Twitter Mark Crook-Rumsey @CrookRumsey, Charalambos Hadjipanayi @c_ hadjipanayi, Dragos C Gruia @DragosCGruia and Shlomi Haar @HaarShlomi

Acknowledgements MC-R is supported by the UK DRI Cross-Centre Postdoctoral Programme. SH is supported by the Edmond and Lily Safra Fellowship. RSM is supported by the Wellcome Clinical Research Career Development Fellowship (205167/Z/16/Z). The project is also supported by the UK DRI, Care Research & Technology Centre. We would like to thank the participants and their careers for volunteering their time to participate in the Living Lab study.

Contributors MC-R, SJCD, HL, AR, ES, LML, JB, JJ-J, DL, RW, AH, DJS and SH all contributed to the design, intellectual content and approved the final version. DCG designed and implemented the Cognitron and approved the final manuscript. SA designed and implemented the Kinect cameras software, built custom software for annotation and approved the final manuscript. HC designed and implemented the ultra-wideband radar and approved the final manuscript.

Funding There is no direct funding for this study.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iDs

Mark Crook-Rumsey http://orcid.org/0000-0003-3031-3502 Dragos C Gruia http://orcid.org/0000-0003-0979-0953 Shlomi Haar http://orcid.org/0000-0003-2213-6585

REFERENCES

- 1 Dorsey ER, Elbaz A, Nichols E. Global, regional, and national burden of Parkinson's disease, 1990–2016: a systematic analysis for the global burden of disease study 2016. *Lancet Neurol* 2018;17:939–53.
- Nichols E, Steinmetz JD, Vollset SE. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the global burden of disease study 2019. *Lancet Public Health* 2022;7:e105–25.
- 3 Feigin VL, Nichols E, Alam T. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the global burden of disease study 2016. *Lancet Neurol* 2019;18:459–80.
- 4 Park Y, Go T-H, Hong SH, et al. Digital biomarkers in living LABS for vulnerable and susceptible individuals: an integrative literature review. Yonsei Med J 2022;63:S43–55.
- 5 Rezvani R, Kouchaki S, Nilforooshan R, et al. Analysing behavioural changes in people with dementia using In-Home monitoring Technologies. Alzheimer's & Dementia 2021;17:e052181. 10.1002/ alz.052181 Available: https://onlinelibrary.wiley.com/toc/15525279/ 17/S11
- 6 Honglin L, Roonak R, Magdalena AK, et al. An attention model to analyse the risk of agitation and urinary tract infections in people with dementia. arXiv 2021.
- 7 McNeill A, Briggs P, Pywell J, et al. Functional privacy concerns of older adults about pervasive health-monitoring systems. PETRA '17; Island of Rhodes Greece.New York, NY, USA, June 21, 2017:96–102
- 8 Lyons BE, Austin D, Seelye A, et al. Pervasive computing technologies to continuously assess Alzheimer's disease progression and intervention efficacy. Front Aging Neurosci 2015;7:232.
- 9 Hämäläinen M, Mucchi L, Caputo S, et al. Ultra-Wideband radarbased indoor activity monitoring for elderly care. Sensors (Basel) 2021:21:3158
- 10 Zhou J, Wang Y, Tong J, et al. Ultra wide band radar gait recognition based on slow-time Segmentation. J Zhejiang University (Engineering Science) 2020;54:283–90.
- 11 Hampshire A. Great british intelligence test protocol. 2020.
- 12 Usher I, Hellyer P, Lee KS, et al. "It's not rocket science" and "it's not brain Surgery"—"It'Sa walk in the park": prospective comparative study". BMJ 2021;375:e067883.
- 13 Weil RS, Pappa K, Schade RN, et al. The Cats-And-Dogs test: a tool to identify Visuoperceptual deficits in Parkinson's disease. Mov Disord 2017;32:1789–90.

- 14 McMackin R, Muthuraman M, Groppa S, et al. Measuring network disruption in neurodegenerative diseases: new approaches using signal analysis. J Neurol Neurosurg Psychiatry 2019;90:1011–20.
- 15 Lewine JD, Plis S, Ulloa A, et al. Quantitative EEG biomarkers for mild traumatic brain injury. J Clin Neurophysiol 2019;36:298–305.
- 16 Haar S, Faisal AA. Brain activity reveals multiple motor-learning mechanisms in a real-world task. Front Hum Neurosci 2020;14:354.
- 17 Rito Lima I, Haar S, Di Grassi L, et al. Neurobehavioural signatures in race car driving: a case study. Sci Rep 2020;10:1–9.
- 18 Weise D, Menze I, Metelmann MCF, et al. Multimodal assessment of autonomic dysfunction in Amyotrophic lateral sclerosis. Eur J Neurol 2022;29:715–23.
- 19 Chen Z, Li G, Liu J. Autonomic dysfunction in Parkinson's disease: implications for pathophysiology, diagnosis, and treatment. *Neurobiol Dis* 2020;134:104700.
- 20 Femminella GD, Rengo G, Komici K, et al. Autonomic dysfunction in Alzheimer's disease: tools for assessment and review of the literature. J Alzheimers Dis 2014;42:369–77.
- 21 Khalid F, Yang GL, McGuire JL, et al. Autonomic dysfunction following traumatic brain injury: Translational insights. Neurosurg Focus 2019;47:2019.8.FOCUS19517.
- 22 Masoli JAH, Delgado J. Blood pressure, frailty and dementia. Exp Gerontol 2021;155:S0531-5565(21)00339-9.
- 23 Clegg A, Young J, lliffe S, et al. Frailty in elderly people. The Lancet 2013;381:752–62.
- 24 Mao YR, Wu XQ, Zhao JL, et al. The crucial changes of sit-tostand phases in subacute stroke survivors identified by movement decomposition analysis. Front Neurol 2018;9:185.
- 25 Potts C, Richardson J, Bond RB, et al. Reliability of Addenbrooke's cognitive examination III in differentiating between dementia, mild cognitive impairment and older adults who have not reported cognitive problems. Eur J Ageing 2022;19:495–507.
- 26 Stringer G, Couth S, Brown LJE, et al. Can you detect early dementia from an email? A proof of principle study of daily computer use to detect cognitive and functional decline. Int J Geriatr Psychiatry 2018;33:867–74.
- 27 Jenkins DG, Quintana-Ascencio PF. A solution to minimum sample size for Regressions. PLoS One 2020;15:e0229345.
- 28 Wason J, Magirr D, Law M, et al. Some recommendations for multiarm multi-stage trials. Stat Methods Med Res 2016;25:716–27.
- 29 Dunnett CW. A multiple comparison procedure for comparing several treatments with a control. *Journal of the American Statistical* Association 1955;50:1096–121.
- 30 Enshaeifar S, Zoha A, Skillman S, et al. Machine learning methods for detecting urinary tract infection and analysing daily living activities in people with dementia. PLoS One 2019;14:e0209909.
- 31 Bannon A, Rapeaux A, Constandinou TG. Tiresias: A low-cost networked UWB radar system for in-home monitoring of dementia patients. *Annu Int Conf IEEE Eng Med Biol Soc* 2021;2021:7068–72.
- 32 Enshaeifar S, Barnaghi P, Skillman S, et al. A Digital platform for remote Healthcare monitoring. WWW '20; Taipei Taiwan.New York, NY, USA, April 20, 2020:203–6
- 33 Hsieh S, Schubert S, Hoon C, et al. Validation of the Addenbrooke's cognitive examination III in Frontotemporal dementia and Alzheimer's disease. Dement Geriatr Cogn Disord 2013;36:242–50.
- 34 Freiberger E, de Vreede P, Schoene D, et al. Performance-based physical function in older community-dwelling persons: a systematic review of instruments. Age Ageing 2012;41:712–21.
- 35 Pavasini R, Guralnik J, Brown JC, et al. Short physical performance battery and all-cause mortality: systematic review and meta-analysis. BMC Med 2016;14:215:215...
- 36 Fisher S, Ottenbacher KJ, Goodwin JS, et al. Short physical performance battery in hospitalized older adults. Aging Clin Exp Res 2009;21:445–52.
- 37 Ronai P, Gallo PM. The short physical performance battery (assessment. ACSM's Health and Fitness Journal 2019;23:52–6.
- 38 Hartman-Maeir A, Armon N, Katz N. Kettle test protocol. Jerusalem: School of Occupational Therapy, Hadassah and Hebrew University of Jerusalem, 2005.
- 39 Hartman-Maeir A, Harel H, Katz N. Kettle test—A brief measure of cognitive functional performance: Reliability and validity in stroke rehabilitation. Am J Occup Ther 2009;63:592–9.
- 40 Hartman-Maeir A, Katz N, Armon N. "Validity of a cognitive– functional observation (the "kettle test") in an elderly sample with suspected dementia', in Israeli society for occupational therapy annual conference". Haifa, 2004
- 41 Queensland Health. S-Ad08: assess meal preparation and provide basic/bridging intervention, clinical task instruction: skill shared task. 2018. Available: https://www.health.qld.gov.au/__data/assets/pdf_ file/0020/711722/S-AD08.pdf



- 42 Leyland L-A, Bremner FD, Mahmood R, et al. Visual tests predict dementia risk in Parkinson disease. *Neurol Clin Pract* 2020;10:29–39.
- 43 Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L. Qual Life Res 2011;20:1727–36.
- 44 Bucks RS, Ashworth DL, Wilcock GK, et al. Assessment of activities of daily living in dementia: development of the Bristol activities of daily living scale. Age Ageing 1996;25:113–20.
- 45 Cedarbaum JM, Stambler N, Malta E, et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. J Neurol Sci 1999;169:13–21.
- 46 Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (Redcap)—A Metadata-driven methodology and Workflow process for providing Translational research Informatics support. J Biomed Inform 2009;42:377–81.
- 47 Harris PA, Taylor R, Minor BL, *et al*. The Redcap consortium: building an international community of software platform partners. *J Biomed Inform* 2019;95:S1532-0464(19)30126-1.
- 48 Gorgolewski KJ, Auer T, Calhoun VD, et al. The brain imaging data structure, a format for organizing and describing outputs of neuroimaging experiments. Sci Data 2016;3:160044.