Full/long title of study	Social Cognition and Functioning In Alzheimer's Dementia study
Short title	SOCIAL study
Version and date of protocol	Draft Version 1.2, 26/05/2023
Sponsor:	University College London (UCL)
Sponsor reference number:	157181
Funder (s):	Wellcome Trust (222932/Z/21/Z)
IRAS Number:	313873
Clinicaltrials.gov no:	
UCL Data Protection Number:	Z6364106/2023/02/10 health research

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PROTOCOL VERSION HISTORY

Version Stage	Versions Number	Version Date	Protocol updated & finalised by;	Reasons for Update
Current	1.2	26/05/2023	Dr Andrew Sommerlad	After REC meeting
Previous	1.1	05/05/2023	Dr Andrew Sommerlad	After initial REC review
	1.0	24/04/2023	Dr Andrew Sommerlad	For REC submission
	Draft 0.2	20/03/2023	Dr Andrew Sommerlad	Draft after sponsor review
	Draft 0.1	25/02/2023	Dr Andrew Sommerlad	Draft before sponsor review

DECLARATIONS

The undersigned confirm that the following protocol has been agreed and accepted and that the investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the U.K. Policy Framework for Health and Social Care Research 2017 (3rd edition) (as amended thereafter), the EU General Data Protection Regulation (2016/679) and the UK Data Protection Act (2018), Sponsor SOPs and applicable Trust policies and legal frameworks.

I (investigator) agree to ensure that the confidential information contained in this document will not be used for any other purposes other than the evaluation or conduct of the research investigation without the prior written consent of the Sponsor.

I (investigator) agree to ensure that no research activity or recruitment will commence at participating research sites until the appropriate regulatory approvals and NHS confirmations of Capacity and Capability have been issued, and Sponsor green light confirmed.

I (investigator) also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest, accurate and transparent account of the study will be given. Any deviations from the study as planned in this protocol will be explained and reported accordingly.

Chief Investigator:

Signature: .....  **..... Date. 26/05/2023**

Print Name (in full): ..... Andrew Sommerlad

Position: ...Chief Investigator / Associate Professor and Consultant Psychiatrist

On behalf of the Study Sponsor:

Signature: ..... Date. 26/05/2023

Print Name (in full): .....Pushpsen Joshi.....

Position: .....

STUDY SUMMARY

IDENTIFIERS	
IRAS Number	313873
REC Reference No.	23/WA/0157
Sponsor Reference No.	157181
Other research reference number(s) (if applicable)	UCL Data Protection number: Z6364106/2023/02/10 health research
Full (Scientific) title	Social Cognition and Functioning In Alzheimer's Dementia study
Health condition(s) or problem(s) studied	Alzheimer's dementia
Study Type i.e. Cohort etc.	Cohort
Target sample size	414 (207 people with Alzheimer's disease and 207 family/friend informants)
STUDY TIMELINES	
Study Duration/length	36 months
Expected Start Date	1st May 2023
End of Study definition and anticipated date	Completion of longitudinal data collection (30th April 2026)
Key Study milestones	Study submission First patient recruitment Last patient recruitment Completion of follow-up data collection
FUNDING & OTHER	
Funding	Wellcome Trust (222932/Z/21/Z)
KEY STUDY CONTACTS	
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Funder(s)	Wellcome Trust

KEY ROLES AND RESPONSIBILITIES

SPONSOR: The sponsor is responsible for ensuring before a study begins that arrangements are in place for the research team to access resources and support to deliver the research as proposed and allocate responsibilities for the management, monitoring and reporting of the research. The Sponsor also must be satisfied there is agreement on appropriate arrangements to record, report and review significant developments as the research proceeds, and approve any modifications to the design.

FUNDER: The funder is the entity that will provide the funds (financial support) for the conduction of the study. Funders are expected to provide assistance to any enquiry, audit or investigation related to the funded work.

CHIEF INVESTIGATOR (CI): The person who takes overall responsibility for the design, conduct and reporting of a study. If the study involves researchers at more than once site, the CI takes on the primary responsibility whether he/she is an investigator at any particular site.

The CI role is to complete and to ensure that all relevant regulatory approvals and confirmations of NHS Capacity and Capability are in place before the study begins. Ensure arrangements are in place for good study conduct, robust monitoring and reporting, including prompt reporting of incidents, this includes putting in place adequate training for study staff to conduct the study as per the protocol and relevant standards.

The Chief Investigator is responsible for submission of annual reports as required. The Chief Investigator will notify the REC and JRO of the end of the study (including the reasons for premature termination, where applicable). Within one year after the end of study, the Chief Investigator will submit a final report with the results, including any publications/abstracts to the REC and JRO.

PRINCIPLE INVESTIGATOR (PI): Individually or as leader of the researchers at a site; ensuring that the study is conducted as per the approved study protocol, and report/notify the relevant parties – this includes the CI of any breaches or incidents related to the study.

KEY WORDS

Alzheimer's disease; Dementia; Social functioning; Social cognition; Theory of mind; Outcome measurement

LIST OF ABBREVIATIONS

ACE-III	Addenbrookes Cognitive Examination-III
AD	Alzheimer's disease
BADL	Bristol Scale for ADLs
CCI	Charlson Comorbidity Index
CSDD	Cornell Scale for Depression in Dementia
FTD	Fronto-temporal Dementia
IRI	Interpersonal Reactivity Index
JRO	UCLH/UCL Joint Research Office
NIHR	National Institute for Health Research
NHS	National Health Service
NPI	Neuropsychiatric Inventory
PALS	Patient Advice and Liaison Service
PI	Principal Investigator
PIS	Participant Information Sheet
PPI	Patient and Public Involvement
QOL-AD	Quality of Life in Alzheimer's Disease scale
SF-DEM	Social Functioning in Dementia Scale
TASIT-S	The Awareness of Social Inference Test short form
ToM	Theory of Mind
UCL	University College London
UCLH	University College London NHS Foundation Trust
UK	United Kingdom

CONTENTS

1 INTRODUCTION

Research Question

Is impairment in theory of mind associated with decline in social functioning in people with mild Alzheimer's disease (AD)?

Background

Impaired social functioning is a core feature of dementia and declines progressively through the disease course, but we do not currently understand the specific causes of this decline and have no effective treatments for social functioning. Social cognitive impairment, particularly impaired theory of mind, is a likely major cause of this decline and, if this is established, it could be a target for future interventions which aim to maintain social cognition.

Objectives

1. To test whether theory of mind deficits, or those in other social cognitive domains, are associated with current and subsequent level of social behaviour and functioning in Alzheimer's disease.
2. To establish the reliability and validity of novel approaches to the measurement of social behaviour and function in Alzheimer's disease

Methods

We will construct a new observational cohort study of 207 people with mild Alzheimer's disease (with 207 family/friend informants) recruited from NHS memory clinics and other sources. At baseline, we will assess social cognition using a detailed neuropsychological battery and will assess social functioning. At 4 and 8 months, participants will remotely rate their social functioning using a questionnaire and the full battery of testing will be repeated at 1 year follow-up. In a remote monitoring sub-study, up to 50 consenting participants with a mobile phone will have remote digital monitoring using a mobile phone application throughout the study duration. In a further behavioural observation sub-study, up to 50 consenting participants will have social behaviour assessed during a video-recorded semi-structured social interaction at baseline and 1 year follow-up. See figure 1 for information.

Impact

Our study will improve the understanding of the nature and consequences of social cognitive decline in people with Alzheimer's disease which will have potential to inform people with Alzheimer's disease and their family and friends to understand and adjust to their experiences. The potential for identifying social cognitive decline as a core driver of the troubling impairments in social functioning experienced by people with Alzheimer's disease, then future psychosocial interventions with efficacy in other neuropsychiatric conditions, appropriately tailored, could ameliorate the effect of social cognitive impairment. Improving measurement of the person-centred domain of social functioning for people with dementia would enable researchers and care settings to identify drivers of social functioning and test the effects of interventions with greater accuracy. Our international team has the necessary expertise and networks to maximise impact by disseminating and promoting our findings globally in research and patient-oriented settings. We will disseminate our findings in publications, conference presentations and other approaches and will make data and other outputs freely available.

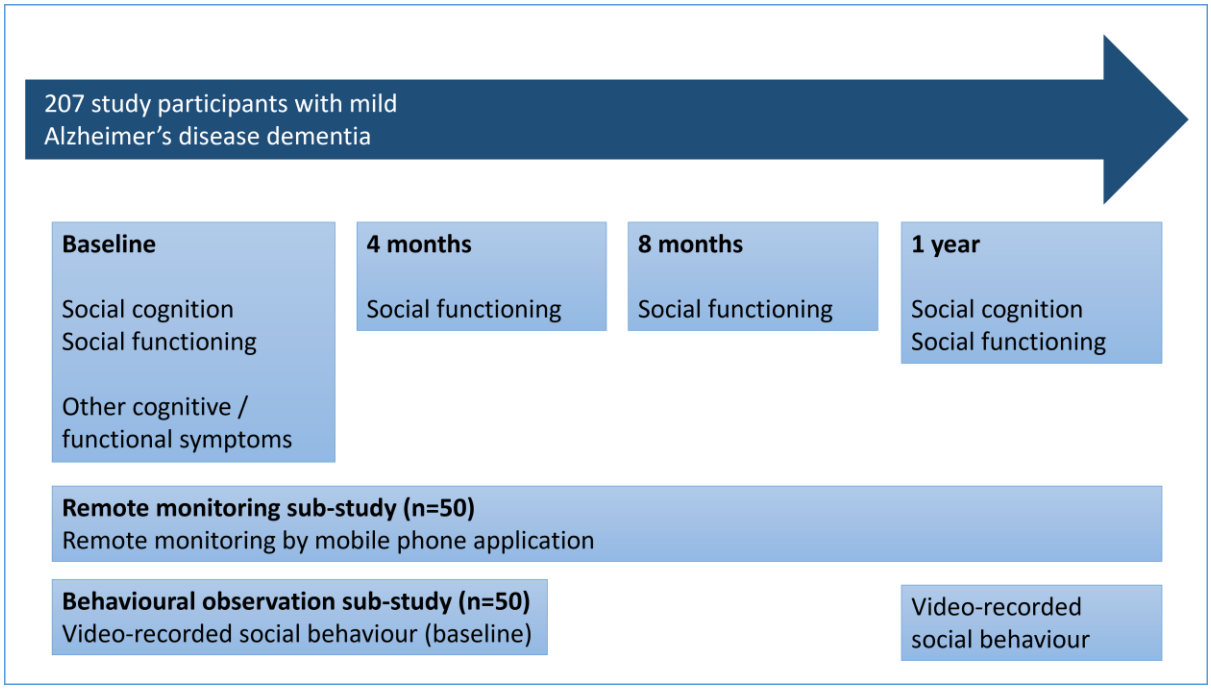

Figure 1. Schematic of proposed study flow for participants in SOCIAL study.

2 BACKGROUND AND RATIONALE

Evidence of decline in social functioning, defined as how individuals interact in society and their own personal environment [1], is a diagnostic criterion for dementia [2], meaning that it is characteristic of the condition. Decline in functioning may precede dementia diagnosis by several years [3] and continues during disease progression with worse social functioning in those with more severe dementia (figure 2) [4]. These impairments are highly distressing to people with dementia and can have a hugely damaging effect on relationships with their families [5]. Developing dementia is the greatest fear for UK older adults [6] and the resultant loss of enjoyment in previous activities and impaired social relationships are particular concerns [7]. Concerns about social functioning in dementia have been deepened by the COVID-19 pandemic due to the impact of social isolation on mental and cognitive health. Having more frequent social contact with others is beneficial for people who do not have dementia as it confers better cognitive function and lower dementia risk [8] and there is now concern about the adverse consequences of social isolation on people with dementia in care homes [9].

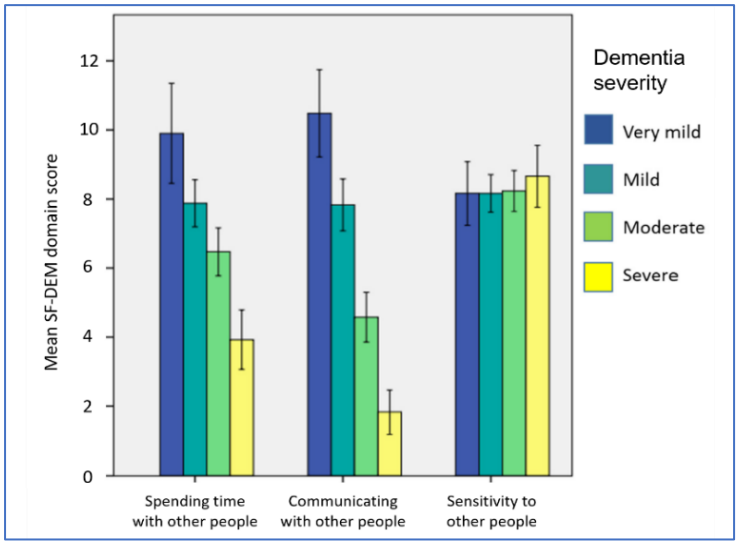

Figure 2. Social functioning domain scores by dementia severity

Therefore, impaired social behaviour and functioning as a result of dementia is a public health concern and is highly distressing for people affected. These impairments occur prior to dementia and continue throughout the disease-course. There is little evidence on what causes social functioning impairment but social cognition deficits, particularly related to theory of mind, are likely crucial drivers. The effect of social cognition deficits on social functioning impairment will therefore be the focus of this study and we will examine this relationship in people with dementia caused by Alzheimer's disease (AD), as this is the commonest form of dementia and social functioning in under-studied in this condition.

Successful social cognition requires processing of social information and signals from others and formulation of suitable responses. Deficits in social cognition, e.g., difficulty attributing mental states to others (theory of mind), difficulty recognising their emotions, and lack of empathy are a likely cause of social functioning decline in AD. People with mild and moderate AD have theory of mind (ToM) deficits [10-12]. A study of 16 people with AD indicated a specific pattern of deterioration in ToM following backwards developmental steps typical of the acquisition of theory of mind ability, where simple ToM levels are preserved but more complex levels are impaired [13]. People with AD have particular difficulty in tasks relying on detecting second order ToM i.e., predicting what another person is thinking about someone else's thoughts/feelings. These difficulties are distinct from other cognitive impairments so do not simply reflect poor memory [14, 15]. Other social cognitive domains including emotion recognition [16] and empathy [17] are also impaired. However, previous studies have been small and, crucially, the relevance of social cognitive impairments to clinical presentation and function of people with AD is unknown.

No previous studies have examined the longitudinal association between objectively-measured social cognition and functioning. Two studies suggested a link, but were limited by imprecise measurement. One cross-sectional study found emotion recognition deficits correlating with social behavioural difficulties in an atypical hospitalised population with care staff completing ratings [18]. A longitudinal study reported that social cognition contributed to functional decline [15], but assessed social cognition using six questions with unproved validity. Other suggestive evidence includes a study of UK adults [19] finding that understanding others' perspective declined with age, as in other studies [20], and was associated with social contact frequency, suggesting that ToM decline reflects neurodegeneration and affects social functioning. This study will therefore aim to clarify whether theory of mind deficits drive social function impairments in AD.

This study will also aim to improve measurement of social functioning in dementia. Most previous social functioning research has used questionnaires, whereby the person with dementia or their relative rates the frequency of participation in social activities. These tools are appropriate when

validated in the target populations [21] but have limitations, which this study will improve on using novel and innovative approaches to assess quantity and quality of social functioning. Firstly, questionnaires may lack detail on the quality of social functioning as they often do not ask about the engagement of the person with dementia. This was supported in the preparatory patient and public involvement work for this study as a discussion group of dementia family carers stated that the quality of social relationships was adversely affected. This study will therefore modify an approach used in frontotemporal dementia (FTD) of observing and rating the quality of social behaviour [22].

Second, questionnaires are susceptible to recall bias, particularly in people with dementia, so we will remotely assess social functioning using smartphones, as used in other neuropsychiatric conditions [23], using an existing 'passive sensing' platform [24].

3 AIM(S) AND OBJECTIVES

The overall aim of this study is to test the hypothesis that impairment in theory of mind is responsible for social behaviour and functioning decline in people with AD.

3.1 Primary Objective

- Examine the association between theory of mind impairment in Alzheimer's disease with decline in social functioning and relationships

3.2 Secondary Objectives

- Investigate whether deficits in other social cognitive domains is associated with social functioning decline.
- Establish, in sub-studies of participants, the acceptability, reliability and validity of novel approaches to assess social behaviour through observation, and social functioning using a remote digital monitoring app.

4 STUDY DESIGN & METHODS OF DATA COLLECTION

This is a multi-site observational cohort study. We will recruit 207 people with mild Alzheimer's disease and, for each, a family member or friend who has contact with the participant at least weekly as an informant (hereafter referred to as a family informant), from National Health Service (NHS) memory clinics and other services. These NHS services will identify potential study participants and provide them with information about the study. Interested participants will be contacted by the study team, based at University College London (UCL) or in the relevant National Institute for Health Research (NIHR) Clinical Research Networks (CRNs). The researchers will answer questions about the study and obtain informed consent to participation.

All participants will be recruited and followed-up for one year. Data will be collected in face-to-face interviews with researchers at baseline and one year follow-up either at an NHS or university site or at the participants' own home, depending on their choice. Data can be collected remotely in case of further COVID-19 or other pandemic restrictions. In these interviews, participants will give information about their socio-demographic characteristics, and complete standardised tests of social cognitive abilities and validated questionnaires about dementia symptoms. A subgroup of consenting participants will have a social interaction with their family informant videotaped at baseline and 1 year. At 4 and 8 months, data will be collected solely from the family informant remotely via video call where a questionnaire about social functioning will be completed. In addition, another subgroup of consenting participants who have a smartphone will have a mobile phone application installed to collect data about their telephone call and text message frequency, and geolocation.

5 STUDY SCHEDULE

5.1 Main SOCIAL study

Screening

Potentially eligible participants identified by NHS sites will be provided with a brief introduction to the study and will be asked screening questions to ensure eligibility. If they show continued interest, they will be provided by hand, post or email with a participant information sheet (PIS) (for person with Alzheimer's dementia and for informant). At least 24 hours later, the research team will contact the participant to answer questions and ask about their willingness to participate in the study. A meeting will then be arranged with participants who express a wish to take part.

Baseline meeting

At this meeting, to be held in person at a university or NHS office, the participant's home, or virtually via Microsoft Teams, depending on participant preference and any COVID-19 related restrictions (face-to-face rather than virtual prioritised), we will obtain consent and collect baseline data. Once all participants' questions have been answered, they will be asked to sign the consent form which will be provided on paper or electronically depending on interview format, and they will be provided with a copy of this for their records.

Once the consent form is signed, we will collect sociodemographic information about the person with Alzheimer's dementia and their friend or family informant using the *Demographic Data Collection Form*, including: age, sex, first language, ethnicity, marital status, education level, employment/occupation information. The dyadic relationship between participants will be ascertained, and we will ask how long since dementia was diagnosed. We will then collect social cognition and functioning data and data about other dementia symptoms. This will in total take around 60-75 minutes for the person with Alzheimer's dementia and 30-40 minutes for the friend/family informant. Participants can have a break during this or can continue testing on a separate occasion if required.

The following information will be collected:

Person with dementia: (60-75 minutes, in-person or virtually if required)

1. Sociodemographic information (e.g., age, sex, first language, marital status, ethnicity, education, dementia subtype) (5 minutes)
2. Social Functioning in Dementia (SF-DEM) Scale (5 minutes).

   SF-DEM [21] is a validated scale for assessing social functioning in people with dementia of any severity. The scale consists of 20 questions answered on Likert scales, such as:

   - Thinking about the past month, how often have you seen friends or family in your own home?
   - Thinking about the past month, how often have you contacted friends or family by phone or computer?

   The scale generates scores in three social functioning domains: time spent with other people, communicating with other people and sensitivity to other people.

3. Interpersonal Reactivity Index (IRI) (9 minutes).

   The IRI [25] is a widely-used and validated scale for assessing four different dimensions of empathy: the empathic concern for others, tendency to see others' perspectives, personal distress response to others' suffering, and empathy for fictional characters. It comprises 28 questions which ask participants to rate their agreement with statements about empathic feelings on a Likert scale. Examples of these are:

- I often have tender, concerned feelings for people less fortunate than me
- When I'm upset at someone, I usually try to "put myself in his shoes" for a while

4. The Awareness of Social Inference Test short form (TASIT-S) (30 minutes)

TASIT-S [26] is a task-based assessment of key domains of social cognition, including emotion recognition, and theory of mind. It has been validated and used extensively in people with dementia, including delivered remotely. The task (figure 3), lasting around 30 minutes in our pilot testing, contains three parts in which the participants are presented with short videos of professional actors.

The first part includes 10 items that display the actors acting out scripts. The participants will be asked to identify the emotion the main character is exhibiting by selecting one of six emotions (happiness, surprise, fear, anger, sadness, and disgust), based on their facial expression, tone of voice and body language.

The second part includes nine conversations enacted in either a sincere manner (four items) or a sarcastic manner (five items) and participants are required to judge whether the actors in the scenes are sincere. The third part also includes nine conversations that display either sarcasm (four items) or lying (five items). For each item in parts two and three participants are asked to choose an answer (Yes, No, or Don't know) to four questions about the speaker's intentions in each video.

Each part has a practice question so if participants are unable to complete this, then the test can be abandoned, and the participant can move on to the next section.

Figure 3. TASIT-short task structure. Participants will be presented with short videos of professional actors. In part 1 (left) the participants will be asked to choose the correct emotion displayed by an actor. In part 2 and 3 (right) they will be asked a number of yes/ no/ I don't know questions about the thoughts, intentions and the inferred meaning from the actors' remarks.

5. Addenbrookes Cognitive Examination-III (ACE-III) (15 minutes)

The ACE-III [27] is a validated test of cognitive function for people with Alzheimer's dementia consisting of subdomains testing attention, verbal fluency, language, verbal memory and visuospatial function. If a previous ACE-III score completed within two months is available (from routine clinical practice) then we will ask for the date, total score and sub-scores, and not repeat the test.

6. Quality of Life in Alzheimer's Disease scale (QOL-AD) (10 minutes)

QOL-AD [28] is a validated disease-specific scale assessing quality of life in people with Alzheimer's dementia comprising 13 items (physical health, energy, mood, living situation, memory, family, marriage, friends, self as a whole, ability to do chores, ability to do things for fun, money and life as a whole), rated on Likert scale from poor (1) to excellent (4), for a total score of 13–52, with higher scores indicating better QoL.

Friend/family informant: (35-45 minutes, in-person or virtually if required)

1. Sociodemographic information (e.g., age, sex, first language, marital status, ethnicity, education) (5 minutes)
2. SF-DEM scale – carer-rated (5 minutes)

   The carer-rated version of SF-DEM [21] asks 20 questions about the social functioning of the person with dementia.

3. Neuropsychiatric Inventory (NPI) (10 minutes)

   The NPI [29] assesses 12 neuropsychiatric symptoms of the person with dementia through questions, sub-questions, and ratings of frequency and severity of each symptom. It is a valid and reliable scale assessing a range of dementia symptoms.

4. Cornell Scale for Depression in Dementia (CSDD) (10 minutes)

   CSDD [30] asks the family or friend informant to rate the severity of 19 symptoms of depression in the person with dementia during the preceding week against a Likert scale (absent (0), mild (1), severe (2). This generates ratings of symptoms in five domains: mood-related signs, behavioural disturbance, physical signs cyclic functions, and ideational disturbance and an overall score describing the likelihood of depression.

5. Bristol Scale for ADLs (BADL) (5 minutes)

   The BADL scale [31] assesses 25 activities of daily living and completed by professional or family carer, taking around 5 minutes. It is valid and sensitive to change and can be used in clinical practice or research settings including clinical trials.

6. Revised Self-monitoring Scale (RSMS) (5 minutes)
   The RSMS [32] is a 13 item questionnaire designed to measure an individual with dementia's awareness of social behaviour and sensitivity to subtle emotional expressions during face-to-face interaction. Each item is rated by a participant's informant on a 6-point scale, ranging from 'certainly, always false' (0 points) to 'certainly, always true' (6 points). Two sub-scores of the RSMS can be calculated: socioemotional expressiveness reflecting the ability to understand subtle social cues in others (max score 30), and modification of self-presentation reflecting the ability to change one's behaviour when it is inappropriate for the current social situation (max score 35) [33].
7. Charlson Comorbidity Index (CCI) (5 minutes)

   The CCI [34] is the most widely-used measure of physical ill-health/multimorbidity which is validated in general populations. It comprises questions about 18 medical illnesses which can be completed based on an informant's knowledge.

These data including social cognition tasks, social functioning questionnaires and other dementia symptom questionnaires will be computerised using Gorilla Experiment Builder, which is suitable as it can show video recordings and allows the research participant to interact by choosing options directly (screenshots in figure 4 below). Participants will complete this on a study computer during face-to-face data collection, or a link can be sent by email to participants in case of pandemic-related

restrictions on face-to-face meetings in which case completion of tasks can be guided by video or phone call. Data is stored securely and Gorilla is compliant with GDPR.

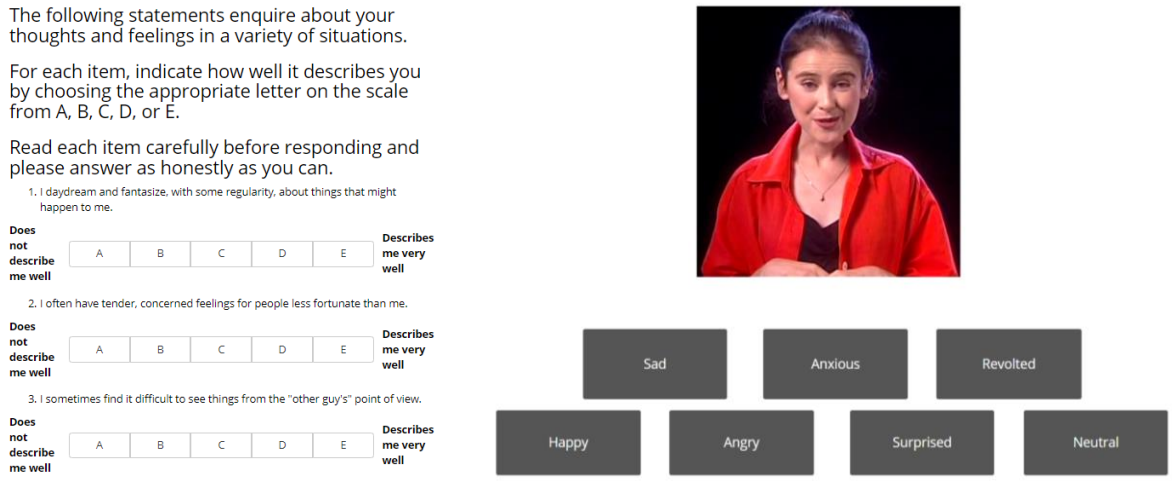

Figure 4. Gorilla data collection platform examples: From Interpersonal Reactivity Index (left) and The Awareness of Social Inference Test – Short (right).

Each participant dyad will receive a gift certificate in the form of either a physical gift card or e-gift card (depending on personal preference) after the interview or focus group to the value of £20.

4 and 8 month follow-up

The family/friend informant will be contacted by phone or email and we will check the participants' ongoing agreement to participate. They will then be asked to complete the SF-DEM scale – carer-rated. This data will be collected via a further Gorilla data collection form which can be completed by the researcher during a phone call with the family or by the friend/family informant directly via an emailed link to the Gorilla website. The task will take around 5 minutes.

1 year follow-up

At this meeting, to be held in person at a university or NHS office, the participant's home, or virtually via Microsoft Teams, depending on participant preference and any COVID-19 related restrictions (face-to-face rather than virtual prioritised), we will first check ongoing agreement to participate. We will then collect social cognition and functioning data and data about other dementia symptoms. This will in total take around 55-70 minutes for the person with Alzheimer's dementia and 25-35 minutes for the friend/family informant. Participants can have a break during this or can continue testing on a separate occasion if required.

The following information will be collected:

Person with dementia: (55-70 minutes, in-person or virtually if required)

1. Social Functioning in Dementia (SF-DEM) Scale (5 minutes)
2. Interpersonal Reactivity Index (IRI) (9 minutes)
3. The Awareness of Social Inference Test short form (TASIT-Short) (30 minutes)
4. Addenbrookes Cognitive Examination-III (ACE-III) (15 minutes)
5. Quality of Life in Alzheimer's Disease scale (QOL-AD) (10 minutes)

Friend/family informant: (30-40 minutes, in-person or virtually if required)

8. SF-DEM scale – carer-rated) (5 minutes)
9. Neuropsychiatric Inventory (NPI) (10 minutes)

10. Cornell Scale for Depression in Dementia (CSDD) (10 minutes)
11. Bristol Scale for ADLs (BADL) (5 minutes)
12. Revised Self-monitoring Scale (RSMS) (5 minutes)
13. Charlson Comorbidity Index (CCI) (5 minutes)

These data will be computerised using Gorilla Experiment Builder. Participants will complete this on a study computer during face-to-face data collection, or a link can be sent by email to participants in case of pandemic-related restrictions on face-to-face meetings in which case completion of tasks can be guided by video or phone call.

End of study

Completion of these tasks at 1 year follow-up will be end of the study for participants.

Agreement to participate will be ascertained at follow-up points but we will not re-consent participants for follow-up assessments. If participants wish to withdraw from the study then they will be able to do so immediately, and have been advised via the PIS that information that was collected before they left the study will still be used in order to help answer the research question but that no new information will be collected without their permission and the remaining research procedures will not be carried out. They are assured that decision to withdraw at any time, or a decision not to take part, will not affect them in any way.

For any individual losing capacity to consent to any study follow-up assessment, any data already collected with consent would be retained and used in the study. We will ask people at initial consent whether, if they lose mental capacity, they would like to 1) complete the study (e.g. complete 1 year follow-up assessment) as long as they do not object, 2) or that they would like to withdraw from the study, 3) or that they would like us to speak to a friend or family as consultee to decide on their behalf if they complete the study. If at any time, a participant is unwilling to participate, then they will be withdrawn from the study and no additional data will be collected.

5.2 Behavioural observation sub-study (SOCIAL-BO)

Up to 50 participants who are recruited from Camden and Islington NHS Foundation Trust or University College London, whose data is collected directly by the research team (for practical reasons related to video-recording interviews), will be asked to participate in the behavioural observation sub-study. In this study, research procedures will be identical to the main SOCIAL study with the addition of a further assessment at baseline and 1 year. This assessment is an observation and rating of social behaviour in a naturalistic conversation, modifying an approach used study of people with frontotemporal dementia (FTD) [22]. This approach was supported in my preparatory patient and public involvement work for this proposal as a discussion group of dementia family carers told me that the quality of social relationships was adversely affected.

At the time of identification, these participants will be provided with a separate PIS specific to the sub-study. At the time of obtaining consent, they will be asked to sign an additional consent form. A dyad of person with Alzheimer's disease and friend/family informant will be required to consent to this so PIS and consent forms are provided for both.

Baseline and 1 year follow-up

Following the main SOCIAL study assessments, for consenting dyads, we will set up two small GoPro video cameras in the meeting room – which will be a university building, clinic or participant's home,

in a configuration shown in figure 5. We will then ask the person with AD and the friend or family member who is involved in the study to have a 5 – 10 minute informal conversation about the person with dementia's current or favourite hobbies. We want this to be naturalistic so will minimise the information that we provide but will ask both people to contribute to the conversation. We will audio- and video-record this conversation using the GoPro cameras.

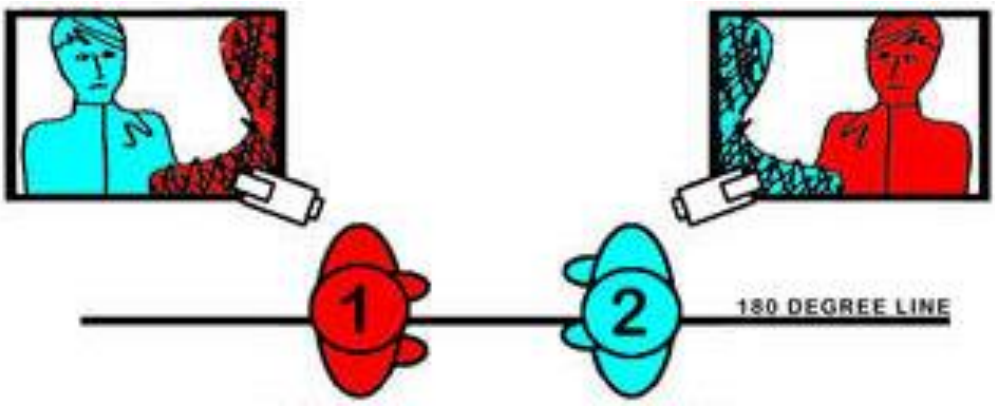

Figure 5: Go-Pro camera configuration

We will then ask the friend or family member to leave the room momentarily and ask the person with AD, without their friend or family member, to have a further 5 – 10 minute informal conversation with the researcher about their previous employment or, if this is not appropriate, with their family.

These video recordings will be transferred as soon as practicable to the UCL Data Safe Haven where they will remain until the research team have been able to analyse these. The data will then be analysed for verbal and non-verbal communication using approaches including the Social Behaviour Observation Inventory [22] and these data will be used as a secondary outcome in the SOCIAL study.

5.3 Remote monitoring sub-study (SOCIAL-RM)

Up to 50 participants who are recruited from Camden and Islington NHS Foundation Trust or University College London (for practical reasons related to downloading the mobile phone app) will be asked to participate in the remote monitoring sub-study. These participants may be the same or may be different from those recruited for the SOCIAL-BO sub-study).

In this study, research procedures will be identical to the main SOCIAL study with the additional use of a mobile phone application (RADAR-Base) to collect information relevant to their social functioning – including phone call frequency, diversity and duration, text frequency, geolocation, and Bluetooth proximity. This assessment has been used in people with other neuropsychiatric problems and in those with dementia [35] and this approach was agreed with my patient and public involvement participants to be a valuable addition as potentially accurate objective measure of social functioning. The data will be tested for feasibility, acceptability and validity and used as a secondary outcome measure.

At the time of identification, potentially eligible participants (those in the SOCIAL study who possess an Android smartphone) will be provided with a separate PIS specific to the sub-study. They will

have an opportunity to ask questions and consider their willingness to participate. Only the person with AD will be required to participate but we will inform the friend/family informant who will be present and discuss this sub-study with them as needed. At the time of obtaining consent, the person with AD will be asked to sign an additional consent form.

Baseline

Following the main SOCIAL study assessments, for consenting participants, we will install the RADAR-Base app on participants' phones and log them into the SOCIAL-RM study using a unique anonymised ID. The participant will then not have to do anything different to normal throughout the study follow-up. The app will run passively in the background of the phone to collect data, restarting automatically when the phone is switched on, although it is possible for the app to be stopped. It will collect information about:

- Telephone call time, duration, target (anonymised) and whether the call is incoming, outgoing, missed. Content is not recorded in any way: each telephone number will be anonymised using a code, rather than using the telephone number, which will allow the research team to count how many different telephone numbers contact or are contacted by the study participant.
- Phone message time, target (anonymised), length and whether the message is incoming, or outgoing. Content is not recorded in any way.
- Number of phone contacts added or removed.
- Number of paired Bluetooth devices and number of nearby devices (reflecting number of people in immediate area)
- Relative location, through GPS or network using latitude and longitude coordinates (offset to a reference point meaning these do not reflect actual location but instead reflect degree of geographical movement).
- Use of other apps (e.g. Whatsapp, email, Facebook) – time open in foreground of phone
- Other data relevant to the functioning of the app – battery life, RADAR-Base application status and interaction with phone.

The app requires some battery usage and also sends information to our computer servers either using wifi networks or mobile phone contract's data, but we have minimised battery use and data use by limiting the data we collect, and this is further limited if the phone is running low on battery – e.g. changing location log from every 10 minutes to every 50 minutes. Our extensive pilot-testing of the app indicates that around 5-7% of battery life is used per day by the app which reflects a small proportion of the phone's general battery use.

We will prioritise that data is sent to our servers by a wifi network, which will be free of charge, but if the phone does not connect to any wifi network, then the mobile phone's contract data would be used – this is also expected to be free of charge as most mobile phone contracts include data packages covering much higher data use than the app. The cost of the app's data in the event that it is not uploaded via wifi or covered by an existing data plan would be up to £15 over the course of a year, so we will give participants an additional £30 shopping voucher to compensate them and to thank them for their contribution to the research.

Full information about data processing is provided in section 12.1.

Participants can choose to withdraw from the SOCIAL-RM study at any time – and can remain or also withdraw from the main SOCIAL study. If they request to do so, then we will deactivate the app's data collection via the RADAR-Base server, meaning no more data will be collected from the app. If the participant chooses to, then the app can also be deleted from their phone manually by them or a friend/family member (and the research team will give instruction on how to do this) or, if they are unable to do so, then the research team can visit the participant to remove the app from their phone for them.

6 ELIGIBILITY CRITERIA

The target for recruitment for the SOCIAL study is 414 people - 207 dyads (people with Alzheimer's dementia and a family or friend informant). The SOCIAL-RM and SOCIAL-BO study aims to recruit a subgroup of these participants with target sample size for each study 50 dyads.

6.1 Inclusion Criteria

6.1.1 People with Alzheimer's dementia

1) Clinical diagnosis of probable Alzheimer's disease dementia made by dementia specialist clinic.
2) Mini-Mental State Examination score ≥20 or Addenbrooke's Cognitive Examination III score ≥52 (consistent with mild dementia) [36]
3) English speaking ability sufficient to be able to complete standardised social cognition tests (TASIT-S) which is only available in English language

Additional criteria for SOCIAL-RM study

4) Possess Android smartphone

6.1.2 Family / friend informant

1) Family/friend informant must see person with Alzheimer's disease at least monthly to be able to report on social functioning and other symptoms.
2) English speaking to be able to complete English language questionnaires

6.2 Exclusion Criteria

6.2.1 People with Alzheimer's dementia

1) Lack of mental capacity to consent to participate
2) Previous diagnosis of schizophrenia, severe traumatic brain injury, or autistic spectrum disorder
3) Aged under 50 years
4) People who do not speak or understand English

6.2.2 Family / friend informant

1) Lack of mental capacity to consent to participate
2) Diagnosis of dementia or other serious mental illness
3) Aged under 18 years
4) People who do not speak or understand English

7 RECRUITMENT

Participants will be recruited from the following sources, with their permission:

1. Memory clinics in Camden and Islington NHS Foundation Trust in which Dr Andrew Sommerlad works as Consultant Psychiatrist. All patients are asked to consent for involvement in research.
2. Memory clinics in Oxford Health NHS Foundation Trust, University College London Hospitals NHS Foundation Trust, Brighton and Sussex University Hospitals NHS Trust, and Devon Partnership NHS Trust.
3. People who have previously taken part in research at UCL Division of Psychiatry who have consented to contact about future research studies.

Potential participants will be notified of the research opportunity through a *Participant Recruitment Ad* allowing interested potential participants to contact the study team directly where they will be provided with additional study information. Clinical and professional staff (separate from the research team) will also approach potentially eligible participants directly and provide a study information sheet. Where systems are available within electronic health records to identify eligible participants who have consented to contact about research, such as the 'Count Me In'/CRIS in Oxford Health NHS Foundation Trust, we will use these to contact potential participants directly and provide a study information sheet. At least 24 hours after the potential participant received the information sheet, the research team will contact the individual to answer any questions they have and arrange to meet them (in person or virtually) to answer their questions and obtain consent if they wish to participate in the study.

8 CONSENT

Potential participants who show interest in the study will be provided with the study information sheet and will be given at least 24 hours to review it before the researcher contacts them to discuss the study and give an opportunity to ask questions. If, after all their questions have been answered, they are interested in participating in the study, we will arrange to meet in-person, or virtually if necessary, and they will be provided with the consent form which will be discussed. If they are willing to participate then they will be asked to sign the consent form and will be provided with a copy for their records. The research team will be trained by the Principal Investigator to evaluate the capacity to consent to participate in research. We will adhere to the principles of the Mental Capacity Act, in which Dr Andrew Sommerlad is trained as a Consultant Psychiatrist.

For consent obtained virtually through video calls, if COVID-restrictions require this or a participant prefers, we will provide copies of the documentation by email and ask participants to provide a simple electronic signature and return the form to us, in line with HRA/MHRA econsent guidelines.

Participants must have capacity to consent to initial participation in the study. We will inform clinicians and care staff who will be identifying potential participants that lack of capacity to consent is an exclusion criteria to this study. If the researcher is concerned at recruitment that an individual lacks capacity, they will assess this formally and participants will be withdrawn from the study.

For any individual losing capacity during the course of the study to consent to any study follow-up assessment, any data already collected with consent would be retained and used in the study. We will ask people at initial consent whether, if they lose mental capacity, they would like to 1) complete the study (e.g. complete 1 year follow-up assessment) as long as they do not object, 2) or that they would like to withdraw from the study, 3) or that they would like us to speak to a friend or family as consultee to decide on their behalf if they complete the study. If at any time, a participant

is unwilling to participate, then they will be withdrawn from the study and no additional data will be collected.

If a consultee is to be consulted for a participant who has lost mental capacity, then we will provide a consultee PIS and ask the consultee to sign a consultee consent form.

9 DATA ANALYSIS

9.1 SOCIAL Main study

Participant characteristics will be summarized. We will test the cross-sectional association of theory of mind performance on TASIT-S with social functioning by comparing SF-DEM domain score between those with and without impairment of different levels of theory of mind using linear regression adjusted for relevant confounders – cognitive impairment, functional impairment, neuropsychiatric symptoms including depressive symptoms. We will analyse the longitudinal association of theory of mind performance with trajectories of social functioning during 1 year follow-up using mixed linear models with random intercept. This approach will make use of all available follow-up data, including participants with missing follow-up data and accounting for baseline functioning.

A sample of 207 participants will give 90% power at 5% significance level to detect a moderate effect size (d=0.45) – 1 point difference on the 'spending time with others' domain of SF- DEM assuming standard deviation 2.2 [4] – between those with and without theory of mind impairment, assuming that as in earlier studies one third of the sample have impaired theory of mind [12]. We will have 80% power to find a smaller effect size (d=0.35). We will therefore be able to detect a clinically-important difference in social functioning.

9.2 SOCIAL BO study

Acceptability will be assessed by looking at participation rates. The data will be analysed independently by two researchers for verbal and non-verbal communication using approaches including the Social Behaviour Observation Inventory [22] and these data will be used as a secondary outcome in the SOCIAL study. A sample size of 50 people will give 80% power at a significance level of 5% with two-tailed t-test to find a difference on the social behaviour observation inventory of 13 points between those with and without impaired theory of mind, which is a large effect size consistent with previous research on people with AD and healthy controls [22].

9.3 SOCIAL RM study

Acceptability will be assessed by looking at participation rates and missing data. Criterion validity of each measure (telephone call frequency, diversity; text message frequency, diversity; geolocation; connected Bluetooth devices at baseline (first one week of data collection) will be calculated against the SF-DEM, ACE-III, QOL-AD, B-ADL and NPI. It is hypothesized that more social functioning derived from the RADAR-Base app will be positively correlated with social functioning, cognition, quality of life, and activities of daily living and inversely correlated with neuropsychiatric symptoms. Depending on the validity of the data from this baseline period of assessment, valid metrics will be used as secondary outcome measures in the SOCIAL study. 50 datasets will give 90% power at a significance level of 5% to find correlation of 0.40 between remote monitoring data and the hypothesised associated measures.

10 PATIENT AND PUBLIC INVOLVEMENT (PPI)

We held patient and public involvement (PPI) discussion groups with family carers for people with dementia to refine and improve this proposal with their suggestions. The PPI group agreed on the importance of the overarching aim of this research. They additionally asserted the importance of assessing the behaviour of the person with dementia interacting with someone not known to them, and we therefore amended our secondary outcomes in light of this suggestion, by adding two social behavioural observation paradigms in the SOCIAL-BO study.

In addition, Mrs Sue Boex and Mr Frank Arrojo have agreed to join the study steering committee, to guide the conduct of my study, ensure that study materials are suitable, and support the interpretation of our findings. We will have additional PPI input at crucial study time-points, such as interpretation of findings through PPI discussion groups and meetings. We have costed the involvement of all PPI members including travel, time compensation, and respite care for their relative with dementia. Our PPI members will be invited to help with the dissemination of my results and gaining experience and perspectives of the public in any future public engagement work.

11 FUNDING AND SUPPLY OF EQUIPMENT

The study funding has been reviewed by the UCLH/UCL Joint Research Office, and deemed sufficient to cover the requirements of the study. NHS costs will be supported via Camden and Islington NHS Foundation Trust and/or the Local Clinical Research Network.

The research costs for the study have been supported by the Wellcome Trust (£594,603, 222932/Z/21/Z, 20/07/2021).

The Chief Investigator has no direct personal involvement in the organisations sponsoring or funding the research which would give rise to a conflict of interest.

12 DATA HANDLING AND MANAGEMENT

The Chief Investigator will ensure there are adequate quality and number of monitoring activities conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality. The Chief Investigator will inform the sponsor should he have concerns which have arisen from monitoring activities, and/or if there are problems with oversight or monitoring procedures.

The study is compliant with the requirements of General Data Protection Regulation (2016/679) and the UK Data Protection Act (2018). All investigators and study site staff will comply with the requirements of the General Data Protection Regulation (2016/679) with regards to the collection, storage, processing and disclosure of personal information, and will uphold the Act's core principles. UCL is the data controller; the UCL Data Protection Officer is Alexandra Potts (data-protection@ucl.ac.uk). The data controller is UCL and data processors are UCL and The Hyve, who manage the RADAR-Base platform.

The names and contact details (email addresses, phone and/or postal addresses) of participants will be collected for the researchers to send study information. The contact details will also be stored separately from participants' responses and will be not be present in any files that are used for analysis. NHS sites who identify eligible potential participants will send their names and contact

details via secure email or Onedrive. Once received by the research team at UCL, these personal data will be stored securely in UCL Data Safe Haven and will be deleted after data collection is completed.

Participants' age, gender, ethnicity, marital status, occupation, education, and dementia symptoms and functioning will be collected using an online data collection platform such as Gorilla and used to facilitate the analysis and write up of the study. These information will be associated to each response. To make the individuals less identifiable, we will assign pseudonyms to each participant. We will also not use any data that might lead to identification. Since the above data will be collected, there is potential for indirect identification of participants from the information in combination with other personally identifiable information, namely their email addresses. The online data collection platform will comply with General Data Protection Regulation (GDPR) regarding personal data, meaning that this will have minimal risk to the privacy of participants' data. Data on Gorilla is hosted on Microsoft Azure within the EU (Republic of Ireland) which is compliant with ISO/IEC 27001:2005. Gorilla is compliant with GDPR.

We need to collect data from participants over several days and therefore want Gorilla to email participants to remind them to take part. Consequently participant email addresses will be uploaded to Gorilla.

- To ensure complete confidentiality and data security, participants are first given a Public ID (ABC123456) which they can use to log in with.

- Performance data is stored against a Private ID (X1Y2Z345).

- The relationship between the email address and Public ID is stored separately from performance data.

- The relationship between the Public ID and Private ID is stored separately from performance data

We decided to collect these data to allow us to examine our primary research questions about whether social cognition affects trajectory of social functioning in people with dementia and because we wanted to consider the potential influence of other sociodemographic and disease-related factors on the association. We will collect as little personal information as needed. We will also keep these personal information separate from participants' email addresses. Additionally, these personal information will become fully anonymised once the participants' names and contact details are deleted at the end of data collection. By then, the risk of indirect identification of participants is very low, since it will not be possible to re-connect the data to named individuals. Once the data has been fully-anonymised, it will be made available to other researchers via a data sharing platform such as Dementias Platform UK.

12.1 SOCIAL-RM study

For the remote monitoring sub-study, we will also collect data using a mobile phone application (RADAR-Base) on application status, application usage, telephone log, text message log, geolocation, number of connected bluetooth devices, and number of phone contacts. This data will be collected as it will allow us to examine a secondary study research question of whether remote monitoring data can be collected acceptably and whether it is a valid marker of social functioning in people with

dementia. All this mobile phone data will be securely transferred by HTTPS and stored on secure servers through Microsoft Azure, UCL Research Data Storage Service, and UCL Data Safe Haven. Data from participants' phones will be sent to an instance of the RADAR-Base platform hosted on a Microsoft Azure server where it will be automatically validated and organised. UCL's Research Data Storage Service will be set up to automatically sync with the cloud servers' S3 storage on an hourly basis, and upload daily updates to the Data Safe Haven where analysis of the data will take place. The Microsoft Azure service we will use is based in in the EU provided through a contract with UCL ISD. Microsoft Azure complies with GDPR and the data will be pseudonymised with a participant ID and will not contain personal data.

12.1.1 Pseudonymisation process

The identifiers (phone numbers) are pseudonymised by hashing them with an unknown key. Identifiers are hashed using the cryptographically secure HMAC algorithm, ensuring that hashes are not traceable to the actual identifier. Assigning a unique key per participant ensures that identifiers cannot be compared between participants, while they can be compared within one participant (a particular phone number always gets the same hash for that participant). The keys are not shared. Location data is pseudonymised by converting it to locations relative to an unknown reference location. Location data is stored in degrees latitude/longitude with WGS84 projection. At the start of the analysis, each participant gets a unique reference location. A relative location for a participant is computed by subtracting the reference location from the actual location. The reference latitude is a uniform random number between -4 to 4 degrees. This way, the relative latitude is close to the actual latitude and distances between locations can be accurately estimated from the relative locations. The reference longitude is taken as the first longitude that is encountered for a participant, which will set the first relative longitude to 0. Altitude is pseudonymised in the same way as the longitude. The reference locations are not shared.

12.2 SOCIAL-BO Study

For the behavioural observation sub-study, we will additionally collect video-recordings of study participants on GoPro cameras. This data will allow us to address a secondary study aim of examining the validity of video-recording as a measure of social functioning and relationships of people with dementia. The main risk of collecting this data is breach of sensitive information. To mitigate this risk, we will ensure that the cameras are protected by password, that recordings are transferred to the UCL secure network as soon as practical, and that recordings are deleted once their content has been analysed.

See data flow diagram (figure 6) below for more information.

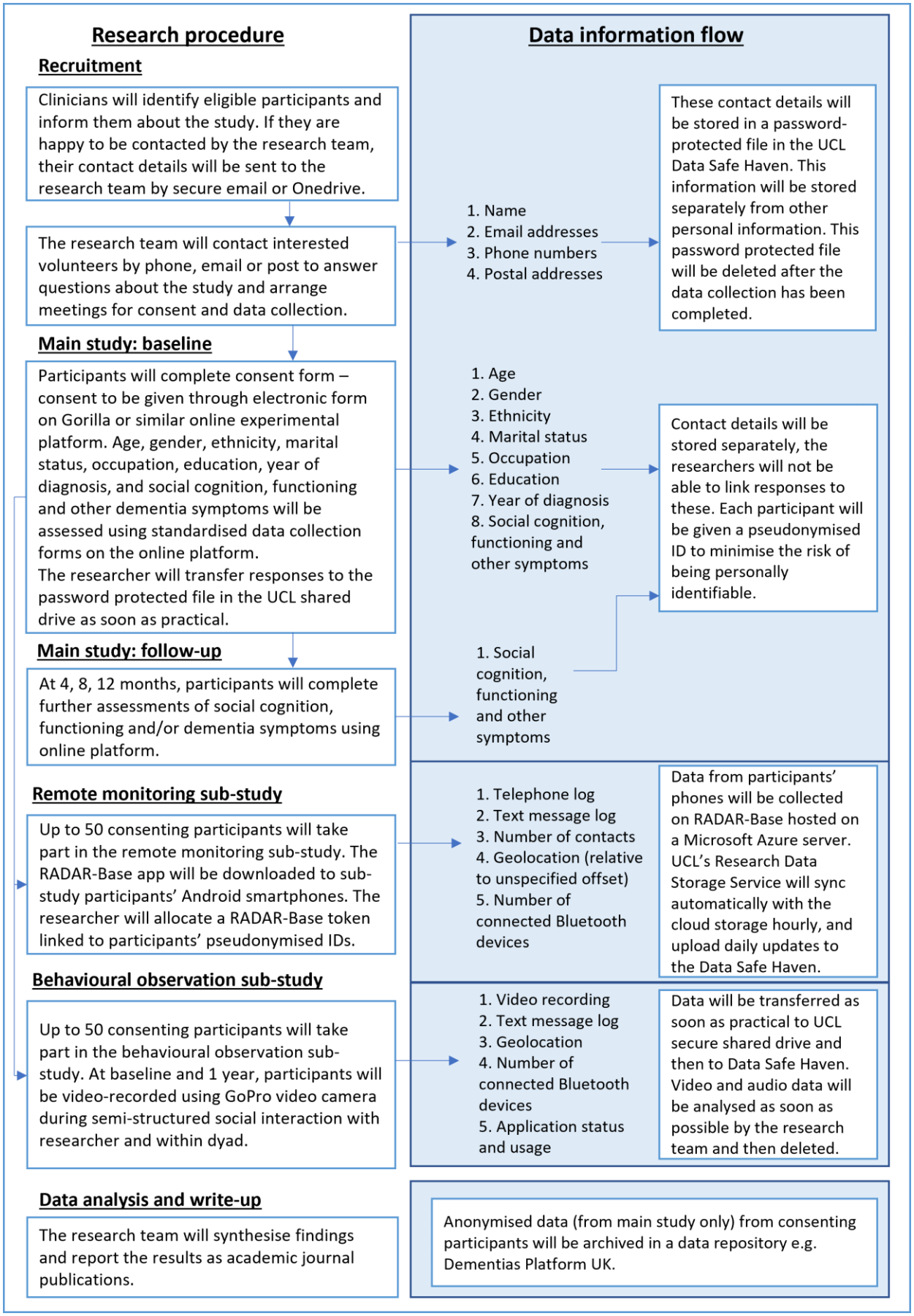

Figure 5. SOCIAL study dataflow

13 PEER AND REGULATORY REVIEW

14 PEER AND REGULATORY REVIEW

The study has been peer reviewed in accordance with the requirements outlined by UCL. The Sponsor considers the procedure for obtaining funding from the Alzheimer's Association to be of sufficient rigour and independence to be considered an adequate peer review.

The study was deemed to require regulatory approval from NHS REC Favourable Opinion and HRA Approval. **Before any site can enrol patients into the study,** the Chief Investigator/Principal Investigator or designee will ensure that the appropriate regulatory approvals have been issued, and NHS Confirmations of Capacity and Capability and Sponsor green lights are in place.

For any amendments to the study, the Chief Investigator or designee, in agreement with the Sponsor, will submit information to the appropriate body in order for them to issue approval for the amendment. The Chief Investigator or designee will work with sites (R&D departments as well as the study delivery team) to confirm ongoing Capacity and Capability for the study.

All correspondence with the Sponsor, REC and HRA will be retained. The Chief Investigator will notify the Sponsor and REC of the end of the study.

It is the Chief Investigator's responsibility to produce the annual progress reports when required; an annual progress report (APR) will be submitted to the Sponsor and REC within 30 days of the anniversary date on which the favourable opinion was issued, and annually until the study is declared ended.

If the study is ended prematurely, the Chief Investigator will notify the Sponsor and REC, including the reasons for the premature termination.

Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the Sponsor and to the REC and HRA.

15 ASSESSMENT AND MANAGEMENT OF RISK

It is possible that participants may at times feel emotional when talking about their experience of their or their relative's dementia. These topics may be distressing for individuals to discuss. We will take the following steps to minimise these burdens for participants:

1. We will be explicit when introducing the research to potential participants, in the information sheet and on the consent form about the topics to be covered and the limits of confidentiality.
2. The chief investigator has extensive experience of conducting interviews with people with dementia and their relatives in a number of areas, as a Consultant Psychiatrist. He will train the research team in recognising and addressing distress.
3. In the unlikely event that participants do become upset whilst taking part in the study, the researcher will ask them if they want to have a break from the interview, continue or to stop. It is possible that individuals may tire quickly during the interview and the researcher

will be particularly alert for this. Participants will be reminded that they may choose not to answer any question that makes them uncomfortable.

4. We will signpost any distressed participants to the Alzheimer's Society or their local clinical service and invite them to contact the research team if they wish to discuss the issues raised further.
5. A PPI group with lived experience will be consulted throughout the study. They will be given an opportunity to provide input regarding the interview guides and questionnaires that will be used in the study.

If information disclosed by a participant or carer leads us to believe that a participant is at significant risk of harm, the researcher will discuss this with the principal investigator to determine next steps which may include disclosure to the referring clinician, hospital trust, or safeguarding team (with or without consent).

16 RECORDING AND REPORTING OF EVENTS AND INCIDENTS

Potential research-related events and incidents include a member of staff being injured whilst conducting the study, participants not being consented properly, collected data being misplaced or stolen, data losses or breaches in confidentiality, protocol violations or non-compliances with regulatory requirements or Sponsor conditions of approval.

All events and incidents (and near misses) that occur to participants and/ or staff that are **unexpected** and directly **related** to the research study will be reported to the Sponsor via UCL: research-incidents@ucl.ac.uk or UCL REDCAP incident reporting form) and host sites via their Trust reporting systems, and documented in the Trial Master File/Investigator Site File via study-specific incident logs (and related correspondence). This will be completed by the CI or PI. The Sponsor will be responsible for investigating, reviewing, or escalating to a serious breach if required.

16.1 Personal Data Breaches

Personal data breaches will be immediately reported to the UCL Information Security Group (ISG) and the UCL Data Protection Officer Alexandra Potts (data-protection@ucl.ac.uk), (as per form and guidance: https://www.ucl.ac.uk/legal-services/guidance/reporting-loss-personal-data), and to the Sponsor via the UCL REDCAP incident reporting form (https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo). The following information will be provided: full details as to the nature of the breach, an indication as to the volume of material involved, and the sensitivity of the breach (and any timeframes that apply). Sites will additionally follow their Trust incident reporting mechanisms and will document this within their TMF/ISFs.

16.2 Incidental Findings in Research

If information disclosed by a participant, family carer, or clinician (paid carer) leads us to believe that a resident or carer is at significant risk, the researcher will discuss this with the local investigator. If appropriate they will approach the participant and seek their consent for disclosure. The consent documents will specify that “we respect confidentiality but cannot keep it a secret if anyone is being seriously harmed or is at high risk of serious harm”. If there is reason to believe that harm is occurring or there is a high risk it is likely to occur, the study team will report this to the LTC home

without consent if this is refused. All research staff must follow participating sites' incidental findings policies.

16.3 Protocol deviations and notification of protocol violations

Protocol deviations are usually an unintended departure from the expected conduct of the study protocol/SOPs, which does not need to be reported to the Sponsor. The CI will monitor protocol deviations, and if found to frequently recur, will discuss in the first instance with the Sponsor to determine re-classification and reporting requirements.

A protocol violation is a breach which is likely to effect to a significant degree: –

(a) the safety or physical or mental integrity of the participants of the study; or
(b) the scientific value of the study

The CI and Sponsor will be notified immediately of any case where the above definition applies via research-incidents@ucl.ac.uk or UCL REDCAP incident reporting form.

16.4 NHS Serious Incidents and near misses (delete if no NHS sites are involved)

A serious incident or near miss is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:

(a) It is an accident or other incident which results in injury or ill health.
(b) It is contrary to specified or expected standard of patient care or service.
(c) It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.
(d) It puts the Trust in an adverse position with potential loss of reputation.
(e) It puts Trust property or assets in an adverse position or at risk.

Serious Incidents and near misses will be reported to the Sponsor and Trust Quality & Safety department as soon as the study team becomes aware of them.

16.5 Complaints from research participants

Participants will be encouraged to contact the local PI in order to share any complaints about the study. In the first instance, research participant complaint will be reported to the local PI to investigate, as documented in the participant information sheet(s), and to the Sponsor (research-incidents@ucl.ac.uk), following the *UCL Complaints from Research Subjects about UCL Sponsored Studies and Trials* policy. For participants who are NHS patients, complaints will be reported to the NHS Complaints Manager at the Trust where the recruitment and study procedures was undertaken. Complaints from NHS patients are handled under NHS complaints policies and procedures, with involvement from Patient Advice and Liaison Service (PALS) and the Sponsor where necessary.

17 MONITORING AND AUDITING

The Chief Investigator will ensure there are adequate quality and number of monitoring activities conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality. A study advisory group will comprise several collaborators who will provide additional oversight.

The Chief Investigator will inform the Sponsor should he/she have concerns which have arisen from monitoring activities, and/or if there are problems with oversight/monitoring procedures.

18 TRAINING

The Chief Investigator will review and provide assurances of the training and experience of all staff working on this study. Appropriate training records will be maintained in the study files. Staff will be trained in Good Clinical Practice, GDPR, assessing mental capacity in line with the Mental Capacity Act, and administering study questionnaires.

19 INTELLECTUAL PROPERTY

All background intellectual property rights (including licences) and know-how used in connection with the study shall remain the property of the party introducing the same and the exercise of such rights for purposes of the study shall not infringe any third party's rights.

All intellectual property rights and know-how in the protocol, the study data and in the results arising directly from the study, but excluding all improvements thereto or clinical procedures developed or used independently of the study by each participating site, shall belong to UCL. All intellectual property rights deriving or arising from the material or any derivations of the material provided to UCL by the participating site shall belong to UCL. Each participating site agrees that by giving approval to conduct the study at its respective site, effectively assigns all such intellectual property rights ("IPR") to UCL and discloses all such know-how to UCL.

Nothing in this section shall be construed so as to prevent or hinder the participating sites from using its own know how or clinical data gained during the performance of the study, as its own risk, in the furtherance of its normal activities or providing clinical care to the extent that such use does not result in the disclosure or misuse of confidential information of the infringement of an intellectual property rights of UCL, or their funder. This section does not permit the disclosure of any of the study data, all of which remain confidential until publication of the results of the study.

20 INDEMNITY ARRANGEMENTS

University College London holds insurance against claims from participants for harm caused by their participation in this clinical study. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, as this clinical study is being carried out in a hospital, the hospital continues to have a duty of care to the participant of the clinical study. University College London does not accept liability for any breach in the hospital's duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or otherwise.

Participants may also be able to claim compensation for injury caused by participation in this clinical study without the need to prove negligence on the part of University College London or another party. Participants who sustain injury and wish to make a claim for compensation should be advised to do so in writing in the first instance to the Chief Investigator, who will pass the claim to the Sponsor's Insurers, via the Sponsor's office.

Hospitals selected to participate in this clinical study shall provide clinical negligence insurance cover for harm caused by their employees and a copy of the relevant insurance policy or summary shall be provided to University College London upon request.

Additionally, UCL does not accept liability for sites such as GP surgeries in primary care; investigators/collaborators based in these types of sites must ensure that their activity on the study is covered under their own professional indemnity.

21 ARCHIVING

UCL and each participating site recognise that there is an obligation to archive study-related documents at the end of the study (as such end is defined within this protocol). The Chief Investigator confirms that he will archive the study master file at UCL Division of Psychiatry, 6th Floor Maple House, 149 Tottenham Court Rd, London, W1T 7NF for the period stipulated in the protocol and in line with all relevant legal and statutory requirements. The Principal Investigator at each participating site agrees to archive his/her respective site's study documents in line with all relevant legal and statutory requirements. Study documents will be archived for a minimum of 5 years from the study end, and no longer than 20 years from the study end.

The Trial Master File will be archived at UCL, in accordance with the UCL Retentions Schedule and Policy. It will be archived for a minimum of 5 years from the study end, and no longer than 20 years from study end.

NB: UCL do not archive student projects and therefore, the length of storage is not subject to the standard Sponsor requirements.

22 PUBLICATION AND DISSEMINATION

Papers for publication in international peer reviewed journals will be submitted and findings presented at national and international conferences.

23 REFERENCES

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4. Budgett J, Brown A, Daley S, Page TE, Banerjee S, Livingston G, Sommerlad A: **The social functioning in dementia scale (SF-DEM): Exploratory factor analysis and psychometric properties in mild, moderate, and severe dementia**. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring* 2019, **11**:45-52.
5. Singleton D, Mukadam N, Livingston G, Sommerlad A: **How people with dementia and carers understand and react to social functioning changes in mild dementia: a UK-based qualitative study**. *BMJ open* 2017, **7**(7).
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24 APPENDICES

Participant information sheets
Consent forms
Recruitment advertisement
Participant recruitment script
Data collection form and study measures
Delegation log
Organisational Information Document
SoECAT
Research CVs: Dr Sommerlad, Professor Livingston
Insurance Registration form – UCL
Data Protection form – UCL

- Data protection impact assessment
- Study data flow diagram

Risk assessment
Funding award letter (Wellcome Trust)
Funder review (Wellcome Trust)