



A Study of Participant Experience of Alzheimer's disease Research (SPEAR)

Final Report

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Introduction

The SPEAR (Study of Participant Experience of Alzheimer’s disease Research) study was carried out as part of EPAD’s Work Package on the Ethical, Legal and Social Implications of the project (ELSI). In the early stages of EPAD, the ELSI team pointed to the extent and intensity of tests and measurements deemed necessary to provide a sufficiently detailed picture of disease progression in contemporary Alzheimer’s disease research. The EPAD Longitudinal Cohort Study (LCS) aims to generate a detailed picture of biological and cognitive change over time, which potentially represents a significant burden on participants, with further implications for recruitment and dropout. We recommended that work be undertaken to assess participants’ experience of taking part in EPAD research, including dimensions of psychological, physical, and/or economic hardships associated with research. In the fifth year of the LCS, we carried out this research with EPAD participants from across four UK sites.

The SPEAR substudy aimed to better understand participation in Alzheimer’s disease research, in order to improve study experience, informing future approaches to recruitment and retention and provide evidence for the assessment of ethical questions related to study participation. SPEAR was a mixed-method study. Both quantitative and qualitative arms of the study consider:

- Motivations for taking part in EPAD and prior experience of research
- Experience and ‘burden’ of EPAD research tests and assessments
- Willingness or ‘readiness’ to take part in future clinical trials

In addition, the qualitative arm of the work further explored the role of care in the research context, and how questions of the burden and the value of research are influenced by the nature and degree of caring relations in the study.

Methods and analysis

The SPEAR study involved a questionnaire survey, qualitative interview and observational data from EPAD centres in the UK. Recruitment focused on the UK for both methodological and pragmatic reasons, particularly the advantage of working within a comparatively uniform clinical research setting (albeit with some differences in the organization of both healthcare and research governance between England and Scotland), and in a single language. The design and implementation of the study was discussed with the EPAD participant panel in Scotland and feedback incorporated. The study received NHS Research Ethics approval (REC Reference 19/NW/0315).

Questionnaire Survey

The survey was structured in three stages which address the different study questions:

- Part A examines motivations to participate and continue to participate
- Part B examines participants’ experience of the study as a whole and of specific procedures
- Part C examines factors associated with the willingness to take part in future clinical trials

Study partners, who provide informant responses to neuropsychological testing in the studies, completed a short survey about their experience of participation.

Survey participants were contacted through the EPAD LCS after completion of at least one study visit. Links were generated and sent to each participant by the local study team. Surveys were emailed or posted to all participants at EPAD centres in Edinburgh, Oxford, West London and Bristol, a total of 191 participants (October 2019). 101 completed participant questionnaires were returned (52.9%; 92 online, 9 by post), with 7 study partner questionnaires. Data was collected using Qualtrics survey software, and analysed using SPSS 25. Given the low number of study partner responses, we here concentrated on responses from EPAD participants only.

Of questionnaire respondents, 61% were female, 46.5% were over 70 and 71% educated to degree level or above. 84% of respondents had had EPAD visit within the last 6 months.

Qualitative Study

Recruitment for interview and ethnographic observations took place over a period of 6 months at the same 4 sites (Edinburgh, Oxford, West London and Bristol). Observational data was collected through the shadowing of study visits where participants and staff were happy to have an observer. This work has informed the findings in this report but will be reported in full in future publications.

Semi-structured interviews were conducted with 25 participants, sampled purposively to include current EPAD participants who had attended at least one study visit as a main participant (i.e. not study partner). We spoke to 9 men and 16 women, and this included both those with and without mild cognitive impairment (MCI). Reflecting the wider EPAD population, the majority of participants were cognitively healthy and did not have MCI. There was very little ethnic and cultural diversity in the sample, and the majority were of high socioeconomic status. However, recruitment was carried out in conversation with the EPAD study teams who indicated that the sample were generally typical of the cohort at large (at least in the UK). This informed us that it was appropriate to stop recruiting when data saturation was reached, despite the lack of socio-cultural and ethnic diversity.

Interviews were either face-to-face (at clinical research facilities or home visit) or over the telephone (where participants were already familiar with the researcher from study visit observations). All lasted approximately 45 minutes. Interviews were audio-recorded, transcribed and thematically analysed. All participants were assigned a pseudonym (or false name) immediately after data collection, which we use in the reporting below.

Findings

For the majority of participants, EPAD was either the first or second medical research study that they had taken part in (figure 1). However, some participants had a long history of being involved with medical research, and become involved with EPAD via other studies – reflecting the study’s recruitment from existing cohorts such as Generation Scotland. Indeed, 36.3% of the sample had taken part in more than three studies in the past, while 7 participants were *currently* taking part in between 3 and 5 research projects.

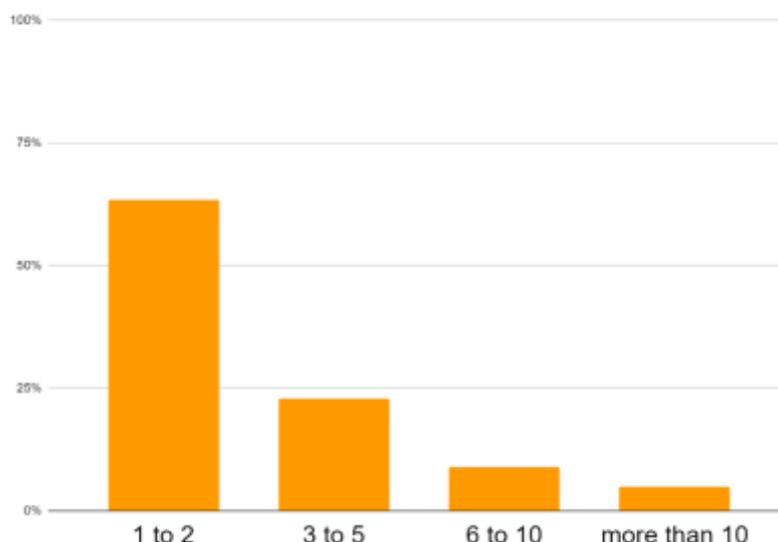


Figure 1: How many medical research studies have you ever joined (i.e. studies that involve more than an online survey, including EPAD)?

Motivations for initial and continued participation

The primary reason identified in the survey as very or somewhat important by respondents for *joining* the EPAD study was to help others (99%), echoing previous research that emphasizes the importance of altruism in study participation. However, respondents identified a range of other motivations as important, including the topic of research, and the opportunity for them to learn about Alzheimer’s research (figure 2). While comparatively few respondents in this sample described taking part in order to find out about their condition (32.3%), this is still a considerable number given that the LCS is a cohort whose participants do not have symptomatic dementia, and, at the time of recruitment in mid-October 2019, 69% of the EPAD cohort (1068/1529) had a Clinical Dementia Rating (CDR) of 0.

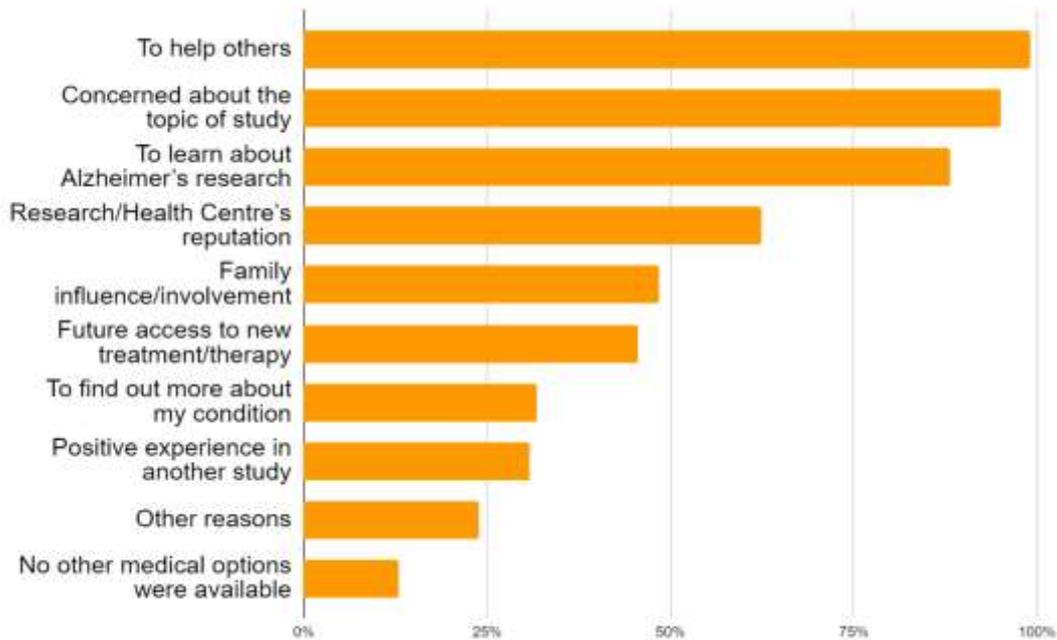


Figure 1: When you considered joining the EPAD study, how important were these reasons for you (somewhat/very important)?

Helping others was also the primary motivation selected by participants for *continuing* to participate in EPAD (figure 3), with 99% again selecting it as somewhat or very important. Indeed, the three most significant motivations were unchanged from those associated with joining the study in the first place. 79% of participants highlighted the importance of feeling valued as research participants, although a smaller percentage (47%) highlighted the importance of the relationship with the research team.

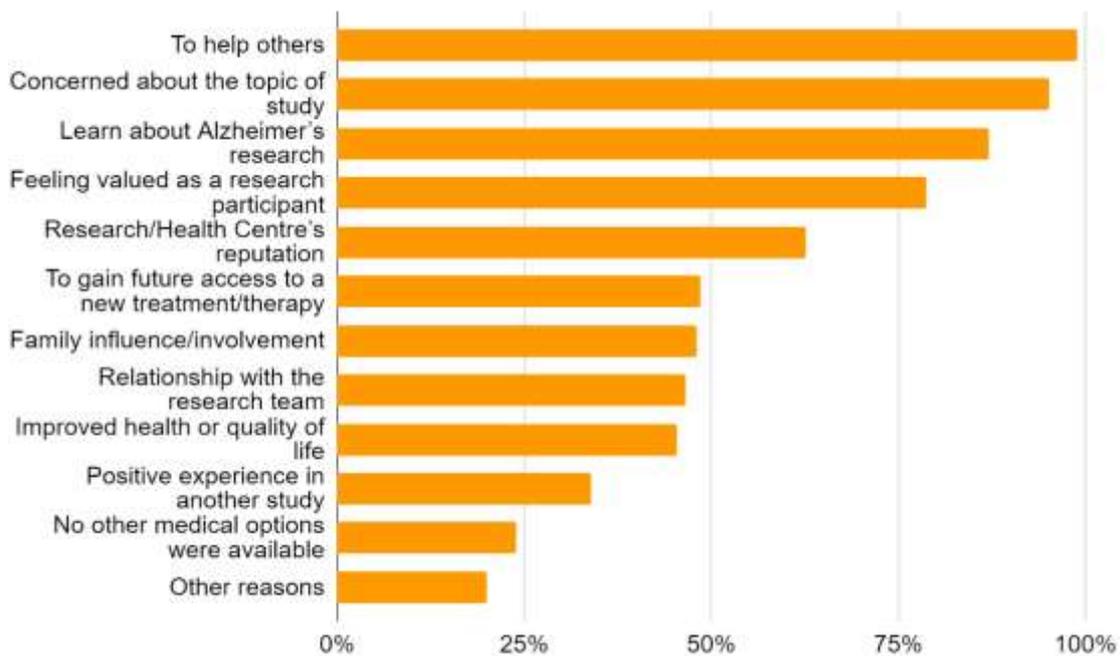


Figure 3: How important were these reasons for you in staying in the research study (somewhat/very important)?

Reflecting the quantitative findings, participants in the in-depth interviews spoke about altruism or helping others (in society now or in future generations) as core motivation for participating in EPAD. However, motivations to participate and to continue participating were not static. We found that motivations for participation and expectations of future research emerge and change throughout the *research process* (i.e. before and during the LCS, and looking to future trial participation) and relate to participants' *lives and experiences of ageing*. This reflects the fact that EPAD is a longitudinal study but it also participants' broader life experiences. Below, we outline a number of themes around motivations that relate to various past and present experiences. Then we outline themes relating to participants' expectations for *future* trial participation. In the final section, we discuss more general experiences of participating in EPAD.

The qualitative data indicated that some participants recognised themselves specifically as “the sort of person who volunteers” in biomedical research:

“I think the answer is once you're involved in one research project people then, somebody says, oh there's this other research project I think you'd be interested in and we already know you're the sort of person that volunteers.” (Denise¹)

Previous demonstrations of willingness to participate was a major reason for being approached via registries and other channels they had consented to be contacted through. Several participants also mentioned other forms of medical donation, such as blood or bone marrow.

Participation as active ageing (keeping busy, staying useful)

Discussion of participants' motivations situated participation in the context of individuals' lives.

“In terms of the Alzheimer's study, I guess, yes, we all have a responsibility to try to ensure that, if not we, that others don't spend 10 or 20 years of their lives as cabbages. I mean, one of the things that makes life worth living is feeling useful, and if you can't give anything, if you can't be a part of society and react to it, then it would be pretty miserable”

These are the words of Marion, a sixty-eight-year-old woman who still worked full-time alongside participating in EPAD. For her, the imagined future of living passively “as a cabbage” is compared to her present possibility to be responsible and active in preventing this future, for herself and others. She goes on:

“I hope that my participation in the study is going to be useful...But as you get older, you are conscious that what you can give is decreasing” (Marion)

Losing the capacity to “give” in the future (due to cognitive decline or just ageing in general) creates an imperative to ‘act now’ in the present.

Several participants, like Malcolm below, located their research participation in a very particular moment in their working lives: the period of entering retirement.

“...to do something positive because there is this sense of ‘what's the point of retirement? Because it's very difficult when you stop full time work” (Malcolm)

¹ As described above, all names are pseudonyms, not actual SPEAR participant names

There were also several examples of people whose participation was a continuation, or slight adaptation of careers in research or medicine; a way of contributing, but now in a volunteer capacity.

The M.O.T – an ‘incidental benefit’

All participants had a clear understanding that they should not expect to be given feedback or test results on a routine basis, so knowing specific details about biomarkers or cognitive change was rarely cited as a motivation to participate. However, knowing that there had been *no change* to speak of (that they had not dipped below the threshold of cognitive decline) and the possibility of having *incidental findings* flagged up, did emerge as an attractive reason to continue participating. Because this benefit often became apparent during the research process, we refer to the health check as an ‘incidental benefit’ – comparable to the notion of ‘incidental findings’ in the study context

“That is a benefit that I wasn’t really expecting, so yes, it is useful” (Elizabeth)

This benefit was often described jokily as “the M.O.T”, referring to the regular check that cars undergo in the UK for roadworthiness. The metaphor of the M.O.T. was used by participants to refer to a functional check-up where you would be alerted to any (actionable) problems or given the ‘all-clear’ without needing to know the inner mechanics of what was going on.

The M.O.T was something that emerged during the research process and came to be seen as almost immediately useful. This is in contrast to biomarker/risk information, which was seen as a more uncertain benefit that may or may not become useful, depending on how successful treatment trials for early Alzheimer’s disease are in the future. As a result, there was a great deal of diversity in preferences for how much biomarker information participants wanted to be told.

Experience

In the survey data exploring the experience of the study, the lumbar puncture was more likely to be reported to be somewhat or extremely physically (figure 4) and mentally (figure 5) uncomfortable. Further, 16.7% of participants reported feeling a moderate or lot of unexpected pain as a result of the lumbar puncture. However, only 7 participants would either probably or definitely not undergo one in the future.

Experience of cognitive tests: “where the anxiety comes in”

Overall, the tiring and challenging nature of cognitive tests were stressed more than physical tests (except specific when specific challenges were faced). Despite the lack of feedback about cognitive test scores, participants felt they had an acute sense of how ‘well’ or ‘badly’ they were doing on each test, which could be encouraging or anxiety-provoking:

with some of those tests, it’s really obvious that you can’t remember something. It’s like trying to remember the basic, who liked the food and their animal. I got to mine and I just said, I have no idea, I can’t remember and then the whole thing was lost and I felt...I felt a degree of failure and concern.” (Charlotte)

Many of the participants singled out the Four Mountains and Supermarket Trolley tasks as particularly hard-going:

“To be honest, it’s like you go really brainy fog dead. With the mountains one they are so alike... Like the first couple is probably okay, but by the fourth one you kind of start to lose the will to live ... And I think that’s where the anxiety comes in...” (Alison)

An exception was when participants had professions or hobbies that required orientation skills, (for example hill-walkers), which made the 4 Mountains test in particular easier or more enjoyable.

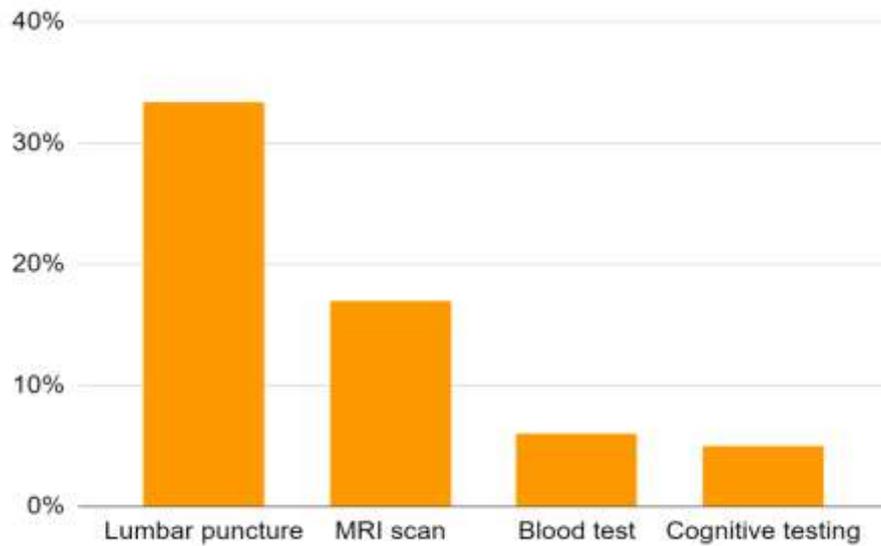


Figure 4: How physically uncomfortable was the assessment (percentage of somewhat/extremely)

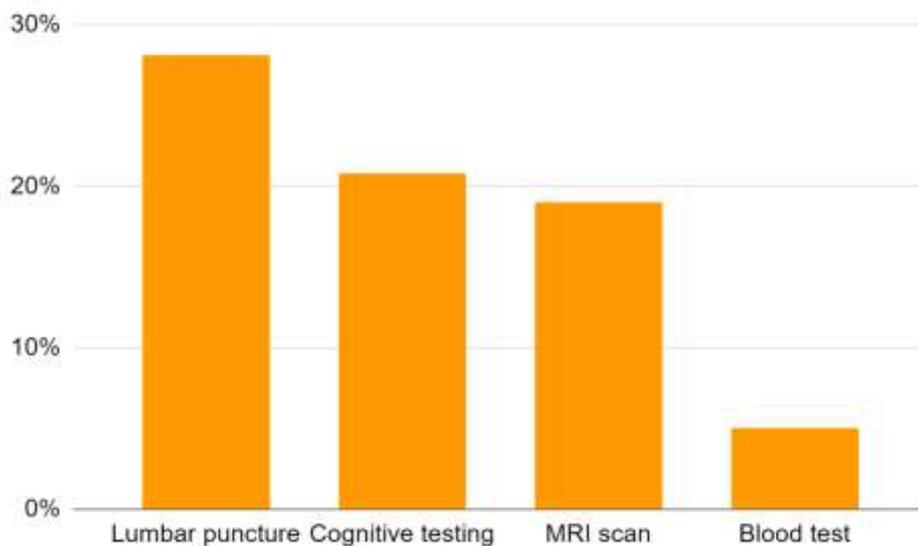


Figure 5: How mentally uncomfortable was the assessment (percentage of somewhat/extremely)

Experience of Lumbar Puncture (LP)

Overall, people were surprised at how smoothly this went, with people with experience or contact with professionals who use LPs in clinical practice being particularly apprehensive:

“you should have seen my GP’s face when I told them I’d had a lumbar puncture for research... he’s, you know, super sensitive to the risks... Yes, I was a little bit [apprehensive], but the

doctor who I think was a consultant was absolutely superb, and I barely felt anything at all and there certainly was no effect afterwards, I was okay.” (Audrey)

However, five participants we spoke to had adverse reactions to the LP: two of them less severe (mild headaches and feeling faint), and three severe headaches for about a week.

Experience of MRI

Participants had a wide range of experiences with the MRI, with most finding it went smoothly, or even finding it enjoyable (with two reports of participants hearing music in the noises!). Others who found it more challenging had various coping strategies, for example:

“The MRI scan actually I was surprised at myself - I hadn’t thought that I had any problem with confined spaces... I thought of my cat and my heartbeat went down and I started to get a grip on my breathing, and I calmed right down.” (Gordon)

Also, reflecting the importance of caring relations with researchers:

“Going back to the MRI scan the radiologist was brilliant. He sat me up, he talked to me because he could see how anxious I was and I was anxious at the MRI scan even afterwards... he talked to me and he probably gave me ten minutes he didn’t have and he was really helpful.” (Collin)

‘Burden’ is mediated by caring relations between researchers and participants

While participants rarely described participation as burdensome overall, individual study visits (mainly the baseline) were intense and tiring:

“Some of the sessions are very long. Once you’ve been staring at a screen for so long, I mean, I can’t stare at screens for very long, your eyes start going and your brain starts.... I mean, ideally fresh air... does bring you back but maybe a bit more - sort of break it up a little bit” (Janet)

Discomfort and burden were almost always described in the context of interactions with researchers and study doctors and nurses. Generally, the researchers and research context went a long way in creating a sense of being cared for, which mediated these burdens:

“I think it’s just the general ambiance and the feeling that this team are very close to each other and very motivated by this potentially quite exciting research they’re on. So that’s reflected in the way that they take care of us when we’re there” (Audrey)

Crucially, difficult and uncomfortable experiences (with tests and technology) often ran in parallel to positive experiences with people delivering them.

Trial participation

A final set of questions on motivations explored potential *future* participation in an EPAD clinical trial. 13 participants had previously taken part in a clinical trial. 61% of respondents stated that they would participate in a clinical trial at this time, with a further 37% stating that they would consider doing so in the future. One participant stated that they would never join a clinical trial.

Motivations for participating in a clinical trial

Motivations for participating in a clinical trial were again focused on the potential to help others and the importance of the object of study. However, a high proportion of participants emphasized the

potential for improved health or quality of life (82.2%), or access to new treatments or therapies (74.2%). This re-emphasizes the importance of providing participants with clear information about future clinical trials, the randomization process and the uncertainties associated with trial outcomes.

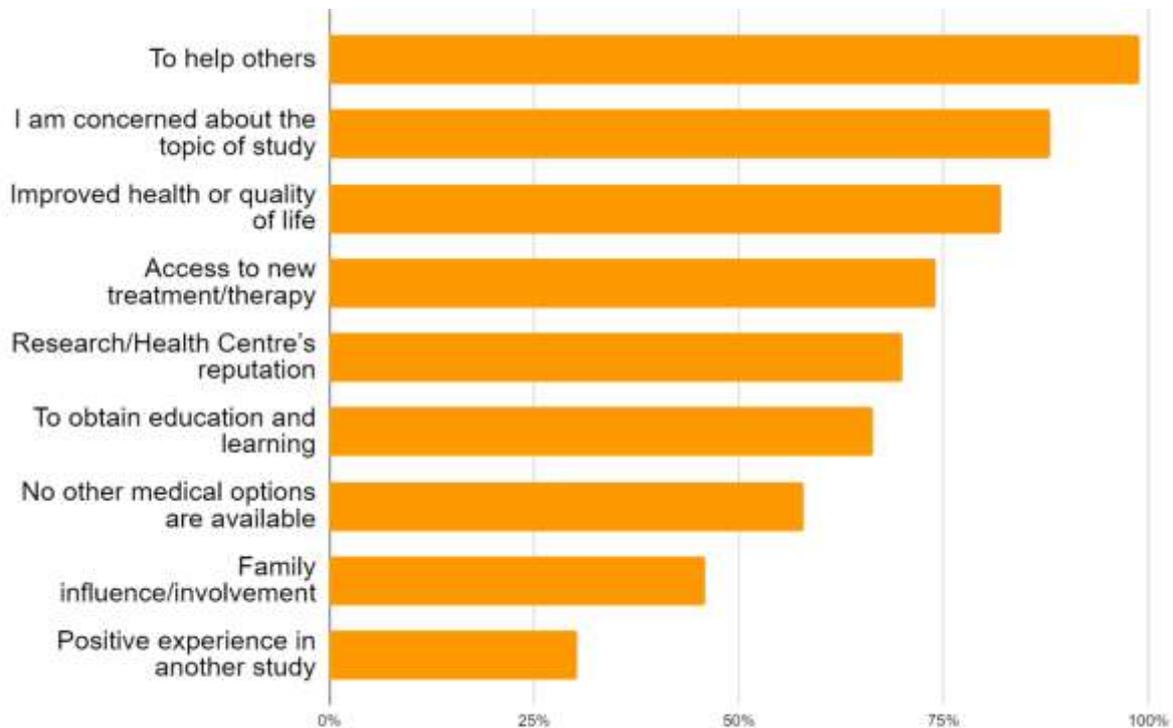


Figure 6: How important would these reasons be for you in joining a clinical trial of a new medicine (somewhat/very)?

A minority of qualitative interview participants had high hopes and expectations for the trial and cited this as one reason they were motivated to continue with the study:

NB: Did you think about [a drug trial] as something that you'd be open to?

Sarah: Yes, oh, I thought that was a positive. I mean, if it happened, I thought it was definitely a positive.

NB: And why is it positive?

Sarah: Because there might be...they might have got a treatment and... what's to lose, in effect, really. If you're in that situation, what's to lose?

For Sarah, being "in that situation" refers to having early symptoms of dementia, emphasising the importance of a particular future in shaping motivations. Another participant, Christine, was keen to prepare for a future where she might develop dementia by doing everything she could to gain access to care and potential future treatments. Whilst she was no less aware than other participants that treatment benefits were unlikely, she was more motivated to access possible benefits of the trial:

"It's almost a little...selfish is probably the wrong word. You know, I'm thinking about me going forward. Of course, you know, I'm more than happy to help anyone else, you know ... but, of

course, I'm thinking about my future, and, you know, how I...how best I can be looked after or look after myself and be looked after perhaps at a stage when I would need, sort of, third party help... if I'm part of this exercise, this study, then going forward ... I'm hoping it just paves the way for perhaps future studies and help." (Christine)

A key message from Christine and others with a family history of dementia and/or limited options for future care is that people's experiences and expectations of ageing shape their motivations to participate in different ways.

Participants generally had a clear understanding that they were unlikely to gain treatment benefits from the study. Although for some, the initial motivation for "jumping in" was altruism, they described the potential personal gain in some circumstances. Overall however, participants did not talk about gaining access to potential treatments as a primary motivation for participating. The most common expectation and attitude towards the trial was a sense of having made a commitment.

"[I]t would depend on the details but otherwise I'd sort of feel morally obliged to continue."
(Ross)

This participant was describing the kinds of caveats he and his wife (who was also an EPAD participant) anticipated they might have to agreeing to participate in the trial, but ultimately he was expressing a sense of responsibility to take part, even if there were some "acceptable" risks. Consequently, although most participants were clear that could easily opt out of the trial, some felt that to do so would be a deviation from what they had initially signed up for:

"I think it said very clearly when I read through all the documentation before I agreed to do the study that they didn't want people who would be unwilling to go on a drugs trial so I felt committed then that I would go on a drugs trial if I was asked to." (Claire)

However, a (relatively small) number of participants did have serious misgivings about taking part in a drug trial. We found a range of tentative attitudes towards the prospect of being contacted to take part in a clinical trial. From "not wanting anything to hurt" to knowing quite simply that "I don't want a drug," some participants were far from certain that going into a clinical trial was the best thing for them.

"I'll try dietary, herbal, other things that could do it or even exercise rather than go for drugs every time because so many drugs have side-effects and the long-term knowledge of them is not always as good as it ought to be." (Janet)

Effect of trial type

In the survey data, respondents were less likely to say that they would take part in a study that involved an infusion (65.4%) than any of a pill (84.1%), lifestyle change (83%) or nutritional supplement or dietary change (91.1%). Respondents were positive about taking part in a trial that involved cognitive testing (97% likely/extremely likely), MRI (96%), blood tests (98%) or PET scans (89%). However, they were less likely to take part in trials involving lumbar punctures (78.8%) or bringing a study partner (74.2%).

Changes in the logistics and commitment associated with a clinical trial also had an effect on people's willingness to take part. For example, 88.1% of participants said that they would be likely or extremely likely to take part in a trial that involved monthly study visits, compared to 54.1% for weekly visits and only 17.4% for daily visits. Travel also had a significant effect – 93.8% of respondents said that they

would travel less than 1 hour, compared to 26.3% for travel over 2 hours. The effect of study length was less pronounced – 89.8% responded that they would be likely or extremely likely to take part in a trial that lasted 12 months, compared to 71% for a trial that lasted 4 years.

Discussion and conclusions

The SPEAR findings provide insight into motivations, expectations and experiences of research participation. They emphasise the importance of altruism as a motivation for participation, but also that motivations overlap, change over time and may differ as participants consider clinical trial participation.

In the qualitative interviews, initial motivations to participate were often linked to prior experience of research: being “the sort of person who volunteers”. However, these data also suggest that the “sort of person” who participates is also highly educated, often has a professional background in science and medicine, and feels a responsibility to “stay useful” in retirement. These findings shed some light on how ethnic and socio-economic inequalities in research participation may be perpetuated by the way recruitment processes are aligned with the lives of certain groups.

There was very little consensus about the value of the return of biomarker results, with some people keen to know as much as possible, and others happy not to know results. However, participants consistently described the return of both incidental findings and clinically actionable information about cognitive decline (i.e. results you could “do something about”) as beneficial and desirable. It is important to note, however, that this was based on people’s *expectation* of value more than *experiences* of receiving such information.

Both quantitative and qualitative data emphasise that participants’ experiences of the EPAD LCS were positive, despite the intensity and discomfort of some tests. The qualitative data in particular suggest the importance to this of the interactions and relations with researchers and staff throughout the study process.

Finally, the findings suggest that the majority of EPAD LCS participants would be willing to take part in a clinical trial, but that the timing, location and duration of such trials is critical.

Acknowledgements

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