Dementias Platform UK
Medical Research Council

ETHICAL, LEGAL AND SOCIAL ISSUES IN DEMENTIA RESEARCH

Work Package 12

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DPUK REPORT

Contents

Executive Summary

Dementias Platform UK marks a new phase in the development of data science and experimental medicine for dementias research in the UK. Drawing on relationships with pre-existing studies and participant populations, DPUK has the potential to impact on researcher practices and participant experiences of dementias science. This report examines the ethical, social and practical issues related to the development of a cross-cohort data platform and the potential recontact of participants from existing cohort populations. Based on empirical research with researchers and participants, this document provides recommendations on key ethical, social and practical areas. The recommendations provided are not exhaustive and do not supersede existing rigorous local study ethical review. As DPUK develops it will be necessary to return to the issues raised in this document to examine how, in practice, data requests and experimental medicine proposals affect researcher and participant experiences of dementia research.

The report identifies and provides recommendations on the following areas:

- **Ethical practices in the development of a cross-cohort data-sharing platform;**
- **Re-contacting cohort participants for experimental medicine studies;**
- **Participants' social and ethical concerns around data-sharing and linkage;**
- **Social and ethical issues around re-contacting cohort participants for experimental medicine studies.**

These themes are summarised in the following section. The full document draws on empirical data to demonstrate the evidence and rationale for the recommendations suggested.

Summary of recommendations

1.1 Ethical practices in the development of a cross-cohort data-sharing platform

- Open and early negotiation with parent cohorts will facilitate greater trust and willingness to share data. DPUK can provide recommendations to researchers to support effective collaboration including early engagement with parent cohorts, recognising local cohort governance and study variation, and working with existing management and participant structures with realistic timelines.
- Where data requests raise local ethical concerns, the study must clearly evidence scientific need, consideration of ethical risks, and approach cohorts with an appropriate timeline.
- DPUK can enhance trust and transparency in data practices by making DPUK's current informatics structure publicly visible using web content and cohort engagement. It would be advisable to review this content with willing cohort participant panels to ensure accessibility.
- To address concerns around data security in public-private data sharing, DPUK can use web content and cohort engagement to make the data controls which apply to researchers across both sectors publicly visible.
- To address cohort anxieties around industry involvement in health care analytics and contemporary bioinformatics, DPUK can work with their private partners to develop cohort and public engagement, examining motivations, practices and governance in the private sector and public-private partnerships.

1.2 Recontacting cohort participants for experimental medicine (EM) studies

- EM studies should evidence that the scientific benefits of recruitment from the cohort outweigh issues of study burden and potential negative impact on the cohort and their data set.
- EM studies should consider existing cohort governance structures. Researchers should familiarise themselves with the structure, timelines and meeting dates of existing cohort governance groups.
- DPUK can provide recommendations to support effective EM proposals wanting to recontact participants from a parent cohort. These recommendations should include early engagement of the cohort in the development of the study design, and expectations for research practice, particularly around issues such as disclosure, incidental findings, participant engagement and feedback.

2.1 Responding to social and ethical issues around data sharing and linkage

- DPUK can support confidence in data sharing by increasing the visibility of information on data protection standards and secure data analysis procedures, particularly around data confidentiality and anonymity.
- DPUK can support participant feedback and engagement, working with cohorts and researchers to ensure publications using cohort data are recognised and enhance dissemination of this information to participants.
- DPUK can increase the visibility of secure data practices across public and private domains and support open and transparent discussion of the role of commercial research in secondary data analysis for health science.
- There is interest in and a need for public engagement on the role, utility and security of data science for dementias research. DPUK can support such activities through the DPUK website, disseminating public-level information on data practices, and encouraging public engagement on the role of data in dementias research.

2.2 Responding to social and ethical issues around recontacting cohort participants for experimental medicine studies

- EM studies need to recognise the implications of recruiting from an experienced research population where there may be pre-existing expectations of research engagement. Where practices for an EM study differ substantially from the parent cohort, participants should have an opportunity during recruitment to discuss any issues this raises.
- Recontact approaches and study designs for EM work should recognise and respect the pre-existing cohort-participant relationship and meet common standards of research, including scientifically good, ethically sound and non-harmful research design, aimed at achieving broad public benefit.
- By working with cohorts and willing cohort participant panels, DPUK can help establish and review guidance on broad expectations for 'good' research practices and experiences in EM study design, recontact and recruitment processes.
- EM studies should share a common commitment to maintain a good research experience for participants. Negative participant experience can have a permanent effective on public and participant confidence, trust and willingness to take part in research.
- It is important to respect participants' freedom to make choices about research informed by a complex range of personal and social factors and circumstances, and to recognise that these choices will change over time.
- Recontact and recruitment procedures should allow participants to make free and informed decisions about participation, ensuring they retain the confidence to refuse participation and to withdraw from a study at any time.
- DPUK can support effective EM research by encouraging researchers to examine issues such as study burden, how research designs may impact on a participant's life, and the burden of the recontact process as a whole.

- EM researchers must evidence that appropriate cohorts are being contacted, that the use of a cohort is more effective for the study design than recruitment through other means. In turn DPUK must ensure that specific cohorts or specific groups within cohorts are not overburdened with recontact requests.
- Specific populations of the 'highly willing' should not overburdened by recruitment pressures.
- Organisations such as DPUK, which enhance access to dementia research in healthy populations, need to consider how such activities impact on local support services. This can be supported through public and participant engagement and research on the impact of dementia research on health-seeking strategies and behaviours.
- There is a need for increased responsible and effective public and cohort engagement around dementia research. DPUK can address the availability and accessibility of current research findings and opportunities for research participation, particularly around the modifiability of biological and life-style risk factors associated with dementias.
- DPUK can undertake engagement between participants, researchers and media and communications groups to examine issues around effective and responsible communication about health and health research findings around dementias.

Overview of research design

Innovation and responsibility in data science and experimental medicine

The main objective of work package 12 was to interrogate and advise on the ethical and social issues arising from the development and potential implementation of the platform, in which existing cohorts are the core. We examined the views of cohort researchers and participants on the practical, ethical and social considerations raised during the process of establishing a cross-cohort platform hosted by DPUK.

This report engages with the four fundamental ethical principles outlined by Childress and Beauchamp (2004): beneficence, non-maleficence, autonomy and justice. These principles aim to ensure that research design and practice respect and safeguard human participants from harm, protect privacy and maintain confidentiality. These principles ensure that research participation is a positive experience realising broad individual and public benefits. Codified in national governance and regulatory legal frameworks, and operationalised through professional roles and responsibilities, normative bioethics provide a baseline of ethical principles and a starting point for the maintenance of best practice in the development of biomedical research (World Medical Assocation, 2001).

The rapidly-evolving fields of data science and experimental medicine create novel modes of research engagement, which challenge the classic boundaries and regulation of ethical roles and responsibilities. As a result, the work of WP12 has taken an empirical approach to ethics, informed by the process of Responsible Research and Innovation (RRI) (Owen, Macnaghten, & Stilgoe, 2012). We examine current and potential future challenges of changing research practices, emphasising the need for innovation to proceed as a transparent and collaborative process. Where research pushes the boundaries of existing practices, there is a responsibility to consider how such changes are viewed by and may impact upon different research stakeholders, including existing researchers, research organisations and those who participate in studies involved with DPUK.

The RRI model has been adopted within science policy frameworks at UK, EU and international levels as a means of exploring and assessing ethical considerations associated with research practice, and viewing these in relation to broader questions of societal need and relevance. As defined within the EU's Horizon 2020 work programme:

"Responsible research and innovation is an approach that anticipates and assesses potential implications and societal expectations regarding research and innovation, with the aim to foster the design of inclusive and sustainable research and innovation."[1]

The approach involves aligning the research and innovation process and its outcomes with the values, needs and expectations of society through engaging with the diverse stakeholders and publics involved in and affected by it. We examine how different research actors define the ethical nature of research practices by exploring their views on trust and responsibility to understand the 'acceptability, sustainability and social desirability' of research innovations (Stahl, Eden, & Jirotka, 2013; von Schomberg, 2011). This approach allows us to examine wider frameworks of research 'anticipatorily and reflexively', examining mutual and competing responsibilities in ways that draw inclusively on different perspectives. This enables research innovation to proceed in a responsive manner (Stilgoe, Owen, & Macnaghten, 2013), informed not only by existing formal ethical guidelines but grounded in emerging social norms and ethical perspectives.

[1] https://ec.europa.eu/programmes/horizon2020/en/h2020-section/responsible-research-innovation

Overview of methods and research process

The MRC Dementias Platform UK, a platform for data sharing and experimental medicine in a pre-clinical disease setting, raises a range of ethical, legal and social questions. Given the broad scope and evolving nature of the platform WP12 approached these questions qualitatively, in a strategic three phase model that was informed by grounded theory, to establish the domains and definitions of ethical issues as they emerged in situ (Glaser, 1992; Strauss & Corbin, 1997).

Phase 1

Phase 1 of the study used an ethnographic approach, working with research leaders, policy makers, cohort and industry representatives involved in the development of DPUK to establish the key actors and domains of ethical focus. This work established that research actors in DPUK were primarily interested in working with data from pre-existing longitudinal cohorts, with the potential to identify non-symptomatic participants who could be recruited to future studies including presymptomatic risk stratification and biomarker research. We therefore focus on two central questions at the heart of DPUK:

1) Factors involved in data sharing and cross-cohort collaborations;
2) Factors involved in recontacting participants in existing cohorts for further research.

Phase 2

Examining these domains necessitated intensive work with cohort representatives involved with DPUK, to understand how they viewed the issues involved in data sharing and recontact. Representatives were recruited from 24 of the 32 cohorts, representing 75% of the participating cohorts at the time of this study. The study included cohorts in England, Scotland and Wales. Reflecting the structure of DPUK, most of the studies were based in England, but a proportionate number of Scottish and Welsh groups were represented. Studies nominated the most appropriate contacts to take part. In some cases, this was the leading principal investigator, in others this was the study co-ordinator, study manager and data manager. Based on the structure initially used to define cohorts in DPUK, this included 11 studies initially defined as 'case rich', seven studies defined as 'familial', and six studies defined as prodromal. These definitions have since evolved.

Cohort type	Number of studies
Case rich	11
Familial	7
Prodromal	6
Total no. of studies	24

Region	Number of studies
England	19
Scotland	4
Wales	1
Total no. of studies	24

Cohort representatives	Number of individuals interviewed
Principal investigator	18
Study manager/coordinator	10
Data manager	3
Total no. of individuals interviewed	31

Interviews involved a combination of up to three members of the cohort team. The interviews were semi-structured, addressing four key themes:

1) Cohort engagement with DPUK
2) Practical, Ethical & Social Issues
3) Experimental Medicine
4) Ongoing engagement with DPUK

Phase 3

In Phase 3 we identified and worked closely with three participating cohorts in England and Scotland to develop a combined focus group and interview study (NHS REC approval 16/NW/0270). 90 participants were selected by the study coordinators: 30 participants from each cohort with a spread of 45 men and 45 women across the entire study. 18 individuals participated in 6 sessions in total. Of those who participated, six participants were under 60 years of age, two participants were over the age of 70 years.

	50-60 years	60-70 years	70-80 years	Total no. of participants
Male	3	4	1	8
Female	3	6	1	10
Total no. of participants	6	10	2	18

Structure of focus group information:

How data can be used for dementias research
Examples: a cross-cohort data study, a study using electronic health record linkage.

Coordination between existing cohort and external research studies
Examples: a wearables device study, brain donation.

Recruitment from an existing study for further research
Examples: Observing Alzheimer's disease biomarkers (DFP), a pharmaceutical clinical trial.

The focus groups examined themes of data practices and recontact for research. Prior to the focus groups, participants received a booklet with six research examples.

The examples chosen were based on DPUK proposals being considered by current researchers and were designed to reflect the use of different technologies and different degrees of research intensity. The examples were developed in consultation with work-package researchers to be accurate, simple and accessible. They aimed to provoke discussion and questions about the practices and techniques involved, and to help explore participants' motivations and willingness to taking part in a variety of forms of research. After the group sessions, one-to-one interviews were arranged with group participants. All focus-group and interview data was transcribed and coded for thematic analysis using a situated analysis approach (Clarke, 2005).

Limitations of the report

DPUK involves over 14 work packages, cross-cutting networks and nested studies. Consequently, this report is a representative but not exhaustive review of key ethical and social issues arising from the wider DPUK project. Remaining responsive to the lifecycle of DPUK within which we worked, this report focuses on the two specific fields outlined above: data sharing and recontact of participants in existing cohorts for further research

The report specifically addresses these issues within participating cohort populations. DPUK concentrates on working with parent cohorts to utilize existing data and facilitate recruitment, primarily in the field of early and pre-symptomatic dementias research. Ethical issues in the development of research registries (Grill, 2017; Grill & Galvin, 2014) and clinic-based recruitment of people with a diagnosis of MCI or a dementia (High, Whitehouse, & Post, 1994) have been addressed broadly. We do not therefore cover that ground again in this report. However, the issues associated with recruiting participants from pre-existing longitudinal, non-disease-specific research populations has been little studied (Milne et al., 2017). Recruitment from existing cohort studies raises specific questions for both cohorts and their participants. This report focuses specifically on issues such as the willingness and motivation of current participants for repeat research participation, and examines issues related to study burden, research saturation of specific populations, and the potential impact on long-term cohort participant populations. Because of the stage of development of DPUK we have addressed these issues broadly, again identifying how current researchers and participants within a selection of participating cohorts understand and view ethical concerns in this area.

There remain some practical limitations to this study. At the point of this study, cohorts were not ready to consider further recruitment from their participant populations, or had specific concerns about this process. In addition, cohorts had not undertaken the processes of disclosing involvement in DPUK to their study participants. It was therefore only possible to recruit participants from three of the 32 cohorts involved. The remaining cohorts, whilst interested in seeing the outcomes of the work-package research, did not feel able to participate in the participant phase of the study at this time. Despite this limitation, what is reported here remains a unique cross-cohort study producing a wealth of qualitative data and representing valuable insights into both cohort researcher and participant views.

The three cohorts involved in Phase 3 of this study represent some of the most 'research ready' populations within the wider population of cohort studies associated with DPUK. Due to the nature of the study design it is also important to acknowledge that whilst broad recruitment from the three participant cohorts was undertaken, the 18 final participants are essentially a self-selecting population. These participants are therefore likely to represent a highly-willing subset of their wider cohort, a population which itself tends to be skewed toward the highly willing. As a result, the evidence of this report needs to be considered in the context of a biased sample which is likely to be more willing to consider research participation and more highly motivated to take part than the wider individual cohort population and the general population. We have therefore drawn specific attention to the variation within this sample. The study remains the first UK-wide, cross-cohort comparison of participant views on willingness to be recontacted for further research. As such it provides highly-valuable insight to the issues raised by DPUK and in data and recruitment innovations in health research more broadly.

Finally, because of the ongoing development of DPUK, at the point of this study it has been necessary to examine researcher and participant views in a prospective way. As a result, we are looking at people's views through broad discussion and hypothetical scenarios. As DPUK develops into a more operational phase it will be necessary to return to the issues raised here to see how they apply to actual research developments and experiences.

Part I. Researchers' views on data sharing, recontact and cohort collaborations

1.1 Ethical practices in the development of a cross-cohort data-sharing platform

One of DPUK's primary goals is to develop the infrastructure for a data platform that will facilitate and maximise access to research data across existing longitudinal cohort studies. National and international initiatives in dementias research such as DPUK (Deetjen & Meyer, 2015; Hodes & Buckholtz, 2016; OECD, 2014; Vaudano et al., 2015) reflect growing mobilisation among researchers and policy makers around the value of changing data practices in biomedical science (Drazen, Morrissey, Malina, Hamel, & Campion, 2016; Piwowar, Becich, Bilofsky, & Crowley, 2008; Warren, 2016). The work involved in data sharing presents distinctive challenges: from those associated with the ethics and governance frameworks required for data sharing, to more social, political and economic considerations.

Recent policy documents have examined the normative ethical considerations around data sharing in biomedical and health research (OECD, 2014). To date however, there has been a lack of empirical data on ethical practices (Parker, 2015). This report draws on empirical interview data representing 24 UK cohorts. We examined how ethical issues around data sharing are experienced by cohort researchers, study managers and principal investigators. Rather than emphasising normative ethical standards, the data reveals a more complex discussion about the values and attitudes around data sharing and the ways in which practices are defined as ethical or ethically problematic.

Cohort teams, broadly, view increased data sharing as a highly positive and valuable step in the development of dementia research. Where views diverge it is around the specific limits, boundaries and operationalisation of data-sharing practices. At the heart of these concerns is the attempt to anticipate and mitigate local negative consequences of implementing change. For researchers there is a clear overlap between the issues that are identified as ethical considerations for the cohort, and the practical, technical and regulatory issues associated with data management and sharing.

Responsible ethical innovation in a federated data platform

The federated and facilitative model of the DPUK Portal means that DPUK has minimal involvement in the scrutiny of data requests and project proposals. DPUK does not have any direct engagement with participants or participant data. Participants and participant data remain under the existing governance and ethical management of parent cohorts. Secondary use of data can never be presumed or attempted without the agreement of the parent cohort once a proposed study has gone through the formal approval process.

It remains both socially important and practically useful for DPUK to demonstrate a clear understanding and an informed and transparent position on ethical practice in data science involving personal data. The platform, working with participating cohorts, can promote best practice in secondary data usage and re-contact for further research involvement. This will support researchers proposing data and experimental medicine studies to engage with and meet existing ethical regulations and expectations. Engaging with ethical data practice in this way will increase cohort and external researchers' understanding, awareness, and ultimately trust in the process and data accessed through the platform and ensure that DPUK and associated partners develop and maintain a social license to act as a publicly and professionally-trusted facilitator of cross-cohort data research.

We focus in this section on understanding how existing governance, data regulation and consent (1.1.1), and views on issues of data, privacy and confidentiality (1.1.2) shape cohort views on the development of the platform.

1.1.1 Existing governance, data regulation and consent

Working with existing governance

Each of the 32 cohorts involved in DPUK has a different position on the regulation and associated ethical conduct of data sharing. Such variations are not superficial, but associated with the scientific and social development of a cohort. Governance structures for example have been established prior to the availability of certain data analysis techniques and evolve in the context of specific university-based data regulation approaches. There is therefore wide variation across cohorts in governance structures for data sharing. Some cohorts have explicit limits to data sharing embedded in their governance which informed their consent procedures. Some of the more contemporary cohorts have been set up with explicit governance and informed consent which facilitate relatively broad sharing and linkage. Cohorts established prior to the expansion of data sharing have renewed governance frameworks to allow for current data-sharing legislation, however this may be confined by the original informed consent and the limits it places on whom data can be shared with. There are exceptions to these generalised descriptions. For example, some historic cohorts have adopted broad data-sharing agreements and some contemporary cohorts have explicit restrictions on sharing data with certain organisations, such as commercial partners.

Understanding this diversity enables us to consider why a broadly centralised approach to data sharing across cohorts remains, in practice, difficult and not necessarily scientifically or socially desirable to local studies (see section 1.3).

Conclusion: For researchers developing multi-cohort data requests, it would be advantageous to be aware of potential variation across cohorts, and demonstrate willingness to engage in early and open discussion about how data requests fit with local cohort governance. This can be facilitated by the federated platform model to enable local cohorts to ascertain whether data requests work within their existing structure.

Governance and regulation: complex, uncertain and changing

As the Wellcome report on data sharing (2003) observes, the 'incremental growth' of regulatory frameworks in data science, associated with rapid technological change and reactive regulation has resulted in a layered system which is "complex, contradictory and confusing" (p. 26). In the field of data science for health, this complexity is heightened by the distributed nature of data-management processes and data repositories that increasingly require linkage of data from multiple, independently-regulated services.

While international and national guidelines on the regulation of personal data put ethical standards into practice (World Medical Association, 2015), these guidelines are interpreted and operationalised at the local level. This operationalisation is situated within certain hosting relationships, for example, a Higher Education Institute and regional NHS Research Ethics Committees. Cohorts frequently described how local decisions around data sharing and linkage involved regulatory uncertainties, conflicts and negotiations between different governing institutions. Cohort researchers expressed uncertainty that existing consent provided coverage for greater data sharing and they were concerned about the impact of becoming involved in lengthy regulatory renegotiations.

Cohort researchers described cases where they had encountered uncertainty about the limits of the data sharing permissible under existing cohort data sharing agreements. This occurred particularly in relation to rapid changes in data practices, the potential for data sharing, and the issue of unanticipated future use. The ambiguity and 'unknownness' of 'future use' is not just a philosophical challenge. It reflects the reality that developing technologies or procedures may make new, unforeseen use of data or biological samples possible. PIs raised the issue of infrastructural, ethical, legal and governance changes which in effect created new categories, legislation and organisations. The creation of new categories of governance created a range of strategic challenges for historic cohort studies. In some cases, historic consent was deemed insufficient or not appropriate because it didn't specify uses of data or sharing of data across legal or infrastructural organisations which did not exist and could not have been anticipated at the time original consent was defined.

There was general understanding that where the potential use of data had clearly changed from the agreement for its original collection, it would be reasonable and proportionate to gain reconsent from participants. However, given the variation already identified, there was no consensus on what such a change would constitute. Many cohort researchers felt that where the use of data was for wider health research within the public and academic sector, the principle of the original consent remained unchanged. This even included scenarios where the technology and scale might have evolved. Indeed, given participants' investment and commitment of time and effort into the long-term donation of health data, researchers felt that broad data use was ethically, socially and scientifically responsible.

Importantly, cohort researchers stressed that in cases where a data request is outside the norm, it can be unclear whether a practice is permissible. In such cases, cohorts rely on guidance from the cohort management structure, local REC bodies and associated HEI to provide oversight for data practice. Where a negative conclusion had been reached by a local REC, the cohort had either been unable to proceed with a proposed study amendment, or had endured a lengthy appeal process. As a result, cohorts rely on, and to some degree are bound by, local level interpretation and enforcement of practices by regulatory bodies.

Cohort PIs suggested that breaches in data security are an important issue for their participants and a matter of wider public concern. There is a strong belief that actual or potential breaches in data security arising from changes in data practices would have a real, long-term, detrimental impact on the local cohort. This impact would be in terms of both scientific and public reputation, and participant retention. As a result, cohorts describe the need for confidence in the security, management and sanctions associated with any system that facilitates access to data outside of existing cohort data-management systems. Concerns specifically occur around any potential intentional and unintentional data breaches, leading to personal data crossing into the public domain.

Conclusion: DPUK's current informatics structure includes researchers agreeing to a data security and confidentiality statement, and sanctions for data misuse. In addition, the Farr Institute has developed a data protocol to maximise security. To support trust and transparency, it would be advantageous to make such information publicly available through the DPUK website in a clear and appropriate manner. It would be advisable that the content of an overview be presented to a selection of willing cohort participant panels to ensure accessibility. In the future, as data practices evolve, it would be advantageous to revisit this agreement in open consultation with stakeholders.

Informed consent

Cohort researchers view informed consent as a fundamental basis for the ethical conduct of clinical research. Such consent relies on the principle that autonomous individuals are under no compulsion, obligation or enticement to agree to take part in research; that they have a full understanding of what they are being asked to take part in; that they have time to consider their decision and the opportunity to ask questions about their involvement. For some cohort researchers, advances in bioinformatics and experimental medicines research may have implications for their existing consent, such as unanticipated use of data or unforeseen implications of research participation. As such, there is concern amongst researchers to address the implication of involving participant data in new research relationships.

As already highlighted, some cohorts have broad consent, whereas others are more restrictive, ie some cohorts explicitly exclude sharing data with commercial partners and yet others explicitly include it. The content of the cohort consent is seen to reflect the underlying ethos of the cohort, upon which basis participants have agreed to take part. Involvement in any practices which go counter to existing consent, therefore, are identified by cohort researchers as ethically unacceptable and socially undesirable, with the potential to directly harm the reputation of the cohort and participant retention.

It is thus not the principle of data sharing itself which raises ethical and practical concerns for cohort researchers. Rather, it is the impact that changing practice may have for cohort researchers and participants and the identity of the cohort. Researchers describe their responsibility to anticipate and address these uncertain implications before implementing any change of existing practices.

It is also important to note that many cohorts rely not solely on informed consent, but on the involvement of a participant panel and/or a data-management committee to support decisions on novel requests for data. Some novel requests may require consideration and it may take time for a cohort to agree on a specific proposal as it follows internal decision-making processes. External researchers applying to use data will need to take these processes into consideration when they are structuring and managing a data request and interacting with a cohort. The already-mentioned complications around 'future-use' are pertinent here also. Consequently it would be advisable for DPUK to stay engaged with cohort concerns and recognise the potential impact of changing data practices on informed consent. This could be achieved by monitoring the range of data requests

processed by the platform, identifying requests which cohorts identify as problematic, and revisiting such issues through cohort workshops.

Recontact for reconsent or further research

Where a cohort's existing consent clearly does not cover a change in data practices, there is the potential imperative to recontact participants for reconsent and conduct recontact for further rounds of data collection (ie at two to five-year intervals). Cohort researchers identify the process of repeated approaches of participants asking them to renew their consent for further rounds of data collection as time and resource intensive, both in terms of organisational and administrative burden.

Beyond time, staff and organisational costs, reconsent is understood to have the potential to directly damage the existing cohort and data set. Cohort researchers highlighted the threat repeated reconsent made to attrition, to the withdrawal and destruction of data, and to the administrative and management cost to the study. Attrition following recontact/reconsent was considered to occur for a range of reasons, including loss of contact with participants due to change of address, ill-health or death, and frustration or lack of understanding of the need for reconsent. For long-running studies where participants were particularly elderly, frail or deceased, cohorts' researchers indicated that they needed to weigh the scientific value of the data against the burden of attempting recontact or re-onsent for the overall cohort and individual participant.

Conclusion: Cohorts do renew consent as a proportionate response to clear research needs or ethical risks, and undertake recontact where the social and scientific benefits can be clearly evidenced. To undertake this for a proposing study would, therefore, require clear justification and an appropriate timeline. As some cohort teams undertake recontact with some regularity, to minimise the burden for researcher, cohort and participants it would be advisable for proposing studies to work with the cohort to consider if they can merge with the cohort timeline for recontact.

1.1.2 Data, privacy, confidentiality and identifiability

Cohort researchers identified maintaining the security and confidentiality of participant data as a principal area of ethical interest in the development or extension of data-sharing practices. Interviews reflected a range of views on the kinds of data, sharing practices and research partners involved in ensuring participant data remains secure. Cohort researchers' views frequently referenced what they believe to be most acceptable to their participants.

Commercial research partners: data security, motivations and reciprocity

Where the motivations and goals of public-private data collaborations aimed to explicitly inform public health and population-based medicine, most researchers believed that data sharing was a positive practice - beneficial to science and society. However, there was a lack of consensus among researchers regarding the ethical limits associated with sharing data with industry and commercial research partners. While some cohorts shared data with commercial and industry groups as part of their normal and acceptable research practices, for others it was a cause of concern, either not addressed by, or explicitly excluded in the cohort's existing consent. In such cases, data sharing with private research partners was considered less acceptable to participants recruited for publicly-funded research.

Principally there was concern that data sharing should be well safeguarded from potential misuse. Some cohort researchers had less confidence in commercial organisations' understanding of,and motivation for the transparent protection of participant data, especially regarding future use.

There is broad recognition among cohort researchers that large-scale bio-informatics and bio-technological research takes place in relationship with commercial and industry partners. Some researchers express concern that industry involvement could lead to decisions which run counter to the motivations of publicly-funded health research. Cohort researchers also expressed concern that the economic and funding benefits of research based on cohort data should create reciprocal investment to sustain cohort-based research. Where private partners had the potential to develop proprietary products or techniques using cohort data, some researchers emphasised the need to ensure a return on investment to the cohort system. Without such reciprocal investment, researchers expressed concern that industry benefitted from low-cost access to data, extracting value from publicly-funded cohort data. Researchers felt this would be viewed as unacceptable to participants and the wider public.

Cohort researchers suggest that to share data with confidence, they required a clear commitment from research partners that identifiable data will only be used for the agreed research purpose, and clear sanctions for any misuse. Concerns were raised about the future use of data from research for targeted marketing of medicinal, health care or insurance products, or further contact for recruitment outside of the cohort. Whilst cohort researchers reflect that such uses are currently speculative, they considered them a specific and current concern for participants. This position is supported by the data presented in section 2.1 and in recent research publications (Carter, Laurie, & Dixon-Woods, 2015; Kaplan, 2014; The Wellcome Trust, 2016). There was a clear concern that engaging in wider sharing with commercial and industry partners could have a real-terms impact on participant retention and engagement. Consequently, there continues to be uncertainty about data security in relation to commercial research practice, and the risk to cohorts of potential breaches of personal data into the public or commercial domain is real and problematic.

Conclusion: In response to concerns about the involvement of research partners, more research and public engagement could be undertaken to communicate the role of industry partners in contemporary bioinformatics, and the security controls in place for all data use from whether public or industry researchers. Undertaking such work in a clear and transparent way at the public level has the potential to increase understanding of cohort and participant anxieties around industry involvement in health care analytics, and to enhance trust.

Levels of data and the acceptability of data sharing: identifiable, aggregate and tabulated data

Researchers across the cohorts described the kinds of data they considered sensitive or problematic for sharing. Specific reference was made to the de-identification of imaging data, data from disease-specific cohorts where common identifiers were integrated into the data set, or data which included genomic, biomarker and risk stratification information. In such cases, the potential for reidentification and the consequences of intentional or accidental disclosure were considered much greater for participant safety and wellbeing. Disease specific cohorts described specific protocols in place for ensuring deidentification of data for sharing. However, they identified this as a specific resource burden for the cohort. Other cohort researchers expressed more general concern that they had a responsibility to ensure the ethical reliability of research partners and address deidentification of such data before they could consider sharing.

There was a degree to which specific cohort researchers felt that the only secure way of sharing data would be at aggregate, deidentified level. These researchers expressed concern that it had become increasingly feasible to re-identify aggregate data. Whilst this was contested between cohorts, some felt the only secure way to share data was at the level of a tabulated data count. A lack of consensus on this issue however meant that some cohort researchers indicated that data with some identifiers could be shared on a case-by-case basis. In these circumstances, it was argued that the external researcher requesting the data should be required to demonstrate that the study was well designed, that the data requested were clearly justified, that they had a clear understanding of data security and the data would be used for no purpose beyond the agreed design.

Conclusion:

Proposing researchers should be aware that there may be variations across cohorts in the way in which they are prepared to share data and that some data will be considered more sensitive than others. In such cases, negotiations with the cohort may facilitate trust and willingness to share.

Unintentional, deliberate or malicious reidentification

Researchers expressed concern about the potential breaches of confidentiality of identifiable participants data at three levels:

1) Accidental release of identifiable data leading to misuse
2) Deliberate re-identification for commercial purposes

3) Malicious attempts to access identifiable data.

A fourth level of reidentification applies to the identification of existing research participants with specific characteristics for recruitment to further observational or interventional studies. We address this issue further in section 1.2..

Conclusion: To address concerns around data security in public-private data sharing, DPUK could work with the informatics team to provide public and transparent guidance on the controls which apply to researchers in both the public and private sectors. DPUK could also work with their private partners to increase the transparency and communication of the interest, motivations, practices and governance which apply in the private sector and public-private partnerships.

1.2 Recontacting cohort participants for experimental medicine studies

Due to the federated structure of DPUK, the platform itself does not engage with participants or recruitment. DPUK also does not take a role of scientific oversight of proposed studies. Each cohort study retains control over whether their participants can be recontacted for further research. Thus, the principal issue for experimental medicine (EM) research is whether, and under what circumstances and safeguards, cohorts would be willing to recontact participants to make them aware of further research.

Recontact through cohorts makes explicit use of a cohort's population, identity and structures, including trust and reputation. Consequently, the experience of follow-on external participation, facilitated through a cohort, is viewed by cohort leads to have direct reputational consequences for the parent cohort. Recontact also requires cohort teams to locally approve a study, to identify eligible participants, and to manage initial re-contact. Thus, recontact for EM studies also involves local staff and administrative resources. These factors need to be considered when examining cohort views on involvement in future EM studies.

1.2.1 Cohort willingness and concerns around recontact for experimental medicine

Cohorts' views on recontact for EM research can be categorised in the following ways:

1) Cohorts currently involved in the EM stream for specific studies who may consider further re-contact from external studies
2) Cohorts currently involved in the EM stream for specific studies who would not currently consider further re-contact from external studies
3) Cohorts who are uncertain whether EM recontact is covered by their existing consent
4) Cohorts who would be willing to discuss future studies, but are concerned about issues such as study intensity and burden
5) Cohorts who would be willing to discuss studies, but are concerned about how participants will view re-contact, and how recontact may affect participants and the cohort.
6) Cohorts who would not consider recontact for future research
7) Cohort no longer active: explicitly will not recontact participants.

Among those researchers interviewed, no cohorts were ready, at this point, to recontact their participants for externally-proposed EM studies. Among studies which already have a built-in experimental theme (5/24), four were not currently considering allowing recruitment outside of the pre-agreed experimental theme. This was in part due to the intensive nature of the work already being undertaken, and the potential for additional work to negatively impact upon participants and the cohort.

A small number of cohorts were interested in hearing more about potential EM studies. These cohorts had identified a desire from participants to be involved in further research. These cohort leads see intervention research as reasonable extension of their cohort's existing purpose, and one which fits both with their participants' views and expectation of the evolving nature of the cohort. These cohorts would be willing to consider external EM studies on a case-by-case basis.

For some cohort leads, recontacting people within cohorts for experimental and secondary prevention research was understood to exceed the original purpose and intention of the cohort, and consequently existing consent.

EM studies and existing cohort structures

Those cohorts willing to consider EM proposals can best be described as highly cautious. As in the case of reconsent for data sharing, the principal risk was seen to be attrition from the study due to negative participant experience or reaction.

A key issue raised was the potential for follow-on recruitment to confuse participants' understanding of the different studies they were involved in, and the roles and responsibilities of those different studies. This confusion was characterised in three ways: a negative study experience with an external EM project could have a negative impact on parent cohort reputation and retention; parent cohorts might find themselves called on to manage issues with external studies; participants may lose their identification with the parent cohort, leading to lower ongoing cohort engagement. Further, while the use of existing cohorts to identify and recruit participants may be one means of enhancing and streamlining the EM research process, identifying and recruiting based on specific characteristics raises concerns about the return of research results and inappropriate disclosure of risk information. It was essential the EM studies demonstrate they had fully recognised the implications of this process, including the issues of accidental or deliberate disclosure of a specific health or risk status.

Whilst many cohorts described their participants as highly willing and motivated to take part in research, building on the pre-existing cohort relationship requires considered thought. Participants' prior research experience provides an understanding of the structure of research that may be of advantage when recruiting people for new experimental studies. However, this prior experience also creates different baseline expectations regarding the structure, aims and objectives of research in a manner that potentially impacts on expectations around the mode of contact, feedback, disclosure and return of results, post-research support and ongoing involvement.

One cohort described being approached for EM recruitment in a manner they found unacceptable, where their involvement with DPUK was assumed to mean they would agree to contacting participants for external research. It is important for external researchers to have a strong rationale for identifying cohorts for participant recontact, a clear understanding of the process involved, and that involvement in DPUK is not confused with open and immediate access to a participant population.

Conclusion: Researchers proposing EM themes need to recognise that cohort research practices and expectations for participant engagement may differ from those contained in their proposed study. It is important that studies make explicit the exact terms of their engagement with participants. Where there is an intention to re-contact from specific cohorts, those cohorts should be involved in discussion as early as possible. The new research will need to evidence that the scientific benefits of recruitment from the cohort outweigh issues of study burden and potential negative impact on the cohort and their data set. Such discussions would need to involve existing cohort governance bodies. Due to scheduling restrictions, these groups often meet to a prearranged schedule. Researchers interested in proposing a study with a specific cohort would therefore be advised to engage the cohort early in discussion, and to familiarise themselves with the dates of such meetings.

1.2.2 Risk stratification and disclosure

Re-identification of cohort participants for further research

Approaches to experimental medicine and clinical trial studies may involve the recruitment of participants identified through stratified assessments of dementia risk based on cohort data. This raises the possibility that participants may unintentionally or incidentally learn the results of prior assessments or that they are at higher risk because of recontact for further research through DPUK.

Conclusion: Any study which aims to identify people or groups of people based on existing data must have a clear procedure for preventing, limiting or managing risk disclosure. This procedure should be discussed with, and transparent to, both cohort researchers and research participants. This is true both where there is the intention to disclose and where there is not.

1.3 Structures shaping cohort views on data practices and recontact

As we have identified in section 1.1 and 1.2, understanding the cross-cohort variation is essential for the successful development of a cross-cohort data platform and EM study recruitment process. Often the challenge of developing increasingly-centralised resources for research has resulted in calls for a culture change at local cohort level. Section 1.3 considers the complexity of cohort structures. The relations that each individual cohort already manages will be pivotal to the effective ongoing development and use of the platform. For the purposes of this report we focus on the impact that three levels of research relations have on views of data sharing and re-contact practices:

1) Local cohort relations
2) Organisation and institutional relations
3) External research relations.

These local, organisational and external levels of relations interact with one another, locating cohorts in a complex hierarchy of structures which directly and indirectly impact upon their views and responses to changing research practices.

1.3.1 The impact of local cohort relations on views on data sharing and EM involvement

Local study teams

Cohort researchers consistently highlighted the network of relations between local data, local researchers and the local study team. The structure of local study teams demonstrates important internal aims, needs, and responsibilities. Thus, cohorts define themselves chiefly as active research communities, producing and publishing original research findings to address specific research aims, thereby fulfilling current funding obligations and winning new funding awards. This process is essential to build and sustain high-quality, knowledgeable cohort study teams and data-collection practices.

Changing data-sharing and recontact practices are viewed as having the potential to directly impact upon a cohort's ability to sustain funding for its structure and function. Consequently, any change in practice is met with cautious consideration. Efforts are made to demonstrate that the benefits of changing practices outweigh the potential costs or risks involved. Cohort researchers emphasised the time, recourse and career investment involved in the development of longitudinal cohorts, and expressed concern that treating cohorts solely as data and recruitment resources had the potential to undermine the work they were undertaking and the participant relationship upon which this work is based.

Participants and governance

Cohort researchers draw heavily on their understanding of the reciprocal relationship between their responsibilities to participants and participant expectations for the cohort. Here complexity is strongly apparent, emphasising a responsibility to use data and participant re-contact as effectively as possible, whilst also anticipating and safeguarding against misuse. Thus researchers balance a commitment to cohort data and recruitment, ensuring that the terms of current consent and governance are not breached, and protecting against data or recruitment practices which may negatively impact participant experience.

Such considerations are not only at the ethical level of safeguarding participants' interests, but also safeguarding the continuation of the cohort where both data and participant retention rely on the ongoing willingness of participants to engage with and take part in the cohort.

Cohort identities, history and ethos and the issue of 'culture change'

Cohort researchers demonstrated that the variation in how practices are considered to affect a cohort and its participants are not superficial. Located in the historical structure of its social and scientific settings, the specific objectives of an individual cohort will also have evolved over time. As already shown, this is exemplified in significant variations in the way practices of research, data, recruitment, ethics and governance are understood and operationalised.

Cohorts to date have largely been self-organising research groups working to develop and analyse data not readily available in pre-existing short-term studies. Cohorts therefore provide unique data, but also require high levels of time, finance and skills resources for their long-term maintenance.

Thus practices and views are oriented through a local cohort 'identity', and realised in a web of relationships which make data collection possible. Cohort studies are not simply collectors of data, but complex research entities, where research values are embedded in the sites, structures and relations through which data is collected, stored and maintained.

Engaging with existing cohort systems

Cohorts have highly-developed governance structures to protect the relationship of trust and retention of participants in the study. Whilst the long-term goal may be to enable cohorts to have a single trusted system to minimise cohort burden, until the wider DPUK research process has been tested and is trusted, cohorts are unlikely to adopt a new process over existing structures. Such governance structures provide a strong basis for a cohort's understanding of what makes their work ethically and scientifically robust and play a strong explanatory role in communicating the protection the study offers participants. The federated DPUK data access and experimental research proposal system has been designed to address this issue. By working with a system that allows cohorts to continue to use their trusted systems in tandem with the DPUK access process, cohorts can retain their individual controls.

1.3.2 Organisational and institutional relationships

Descriptions of local practices demonstrate that cohort views and decisions take place within wider networks of relations. These mediating relationships directly impact upon the kinds of practices cohorts engage with.

Institutional relations

Host institutions, such as Higher Education Institutes (HEIs), act as key intermediaries between local cohort studies and national regulatory frameworks. Such organisational relations structure access to human, technical, financial, legal and regulatory resources that enable cohorts to conduct research. As such, institutional relations enforce and direct legal, regulatory and economic cohort practices. Maintaining this relationship requires the cohorts to sustain ongoing funding, based on achieving externally-recognised, novel scientific contributions. This framework requires maximum control to preserve research credit and thus the economic value of research. The commodification and competition of research culture creates barriers to collaborative research activities that risk the loss of credit or novel research value.

Ethics and governance bodies

National regulation and ethical structures are realised though regional Research Ethics Committees (RECs), located within local HEIs. As we described in section 1.1.1 the complex nature of regional bodies can lead to uncertainty and inconsistent interpretation or guidance on the application of national policy. It is within this system that cohorts currently must respond to regulatory practices and pre-empt evolving structure and technical research systems. Their relationship with regional bodies is therefore a vital but challenging environment in which cohort practices are shaped.

Funding and recognition

There is broad cohort consensus that collaborative working is a pre-existing, mutually beneficial scientific process, with the potential to maximise recognition for the contributing cohort. Access to participants and data is part of an internal network driven by scientific aims, underwritten in funding agreements that require recognition and credit for research activities to be retained. A cohort's collaborative research practices are thus mediated by their relations with institutional and funding

bodies. This results in conflicting pressures, whereby cohorts must demonstrate that they collaborate as widely and openly as possible, while doing so in a manner which ensures that they control, trace and evidence outputs and credit back to the host institution and funder.

Research policy and incentives to change research practices

Cohort researchers express concern that external research policies do not recognise the aims and objectives of their work. Whilst concerns about the potential risks and challenges of changing cohort practices were quite widely covered in the interviews, there is much less clarity about the real-term benefits of engaging with new data-sharing and recruitment processes for cohorts, cohort teams and the participants who make up this national resource.

1.3.3 External research relations

Cohort researchers emphasise that in a research environment characterised by competition, effective collaborations rely on trust and confidence in scientific quality and the motivations of external groups. There was an emphasis on the importance of working with the parent cohort to establish mutually-beneficial collaborations, whether this can be realised in terms of authorship recognition, reciprocal funding or feedback of data to enhance the cohort resource.

There is wide variation in cohort collaborative practices, from relatively open policies to closely restricted ones. However, many cohorts are highly cautious about the boundaries of research collaborations where external researchers can be direct competitors for analytical and funding opportunities. The more distant the researcher is from the parent cohort, the less implicit trust there will be, and the greater the reliance on formal permissions and restrictions to ensure research quality, compliance and reciprocity.

No cohorts allowed undifferentiated access to the full data set or to their participants. Full open access was considered neither practical, ethical nor scientifically desirable. Cohorts managed collaborations to minimise unintentional duplication or concurrent analysis, and ensure the analytical quality of work undertaken. This approach emerges in response to concern that external researchers can lack the understanding of variables to conduct effective analysis, resulting in critical errors or misinterpretations. Distributing metadata was understood to go some way towards facilitating good centralised data sharing. However, there was concern that availability and access to metadata is not necessarily equivalent to knowledge or understanding. This was particularly pertinent for data sets collected over a long period where early practices were described as idiosyncratic.

There was also concern that peer reviewers are unlikely to be familiar with the specifics of variable complexity. As a result there was the potential for erroneous analysis to reach scientific publication. The implications of this ranged from a concern for long-term reputational damage to the cohort data set, through to other researchers not having confidence in the data, and, significantly, a perceived impact on participation if errors in analysis came into the public domain and were associated with the cohort.

Conclusion: It is important to consider how platforms such as DPUK work with the research community. The research conducted for this report demonstrates that the complex hierarchy of relations in which parent cohorts are located structures their views on changing data and recontact practices. Understanding and working with this complexity can shed light on the challenge of developing a national dementia research resource. The findings and guidance presented here can support continuing efforts to actively engage, and work with, cohorts to make best use of the resources available

Part II: Participants' views on data sharing and recontact for research

2.1 Social and ethical concerns around data sharing and linkage

To describe their views on data sharing and linkage, participants draw on a range of experience, including their knowledge of data practices within their cohort, and wider encounters with data use in both research and non-research contexts. When health research was considered broadly there was consensus that responsible data sharing enhances health research, and is a broadly positive and acceptable activity. When exploring specific data-sharing and linkage scenarios, participants raised four key issues: the importance of trust, the need to safeguard privacy and confidentiality, concerns about potential negative consequences of data re-use, and the motivations of the organisations involved in data sharing.

2.1.1 The acceptability of expanding data sharing

Benefits of data sharing and collaborative working

Participants viewed the sharing of existing cohort data for further health research as an accepted part of their ongoing relationship with their cohort and a good research practice. Participants described collaboration between researchers as supporting effective use of their data and advancing health research. Participants viewed the collective use of data across cohorts as a means of conducting more effective research into health and increasing the potential benefits of research for society.

Participants describe their data as the product of long-term investment of time and energy in research. The broadest use of their data is therefore understood to increase the potential for meaningful and positive outcomes. Thus, participants value their data. As a result, it is essential to recognise that participants care about data use and application and, as we explore further in section 2.1.3, have expectations about effective and responsible data sharing.

Understanding data use for dementia research

Participants believe that broader data sharing for research can improve understanding of illness and inform the development of health care and treatment. For dementia research specifically, participants are less clear on the benefits of working with participants who did not have a specific condition or family history associated with dementia. This was reflected in the surprise expressed about the importance of data on healthy research participants for dementias research.

Participants have a clearer understanding of the role of data in research into lifestyle risks such as diet and exercise. However, their awareness of the use of existing data to understand early or presymptomatic biological markers to develop future therapeutic targets was limited. Largely participants' discussions tended to conflate this kind of research with family history and potential genetic markers.

These discussions around data use suggest a need for further public and research engagement on the role of healthy participants in data studies, and the role, implications and current limitations of presymptomatic biomarker studies for dementias research.

Feedback on data use in research

Participants expressed interest in receiving feedback about how aggregate cohort data was used in research. The cohort newsletter or website was cited as a means of finding out what research had been published using their data. However, within each cohort, knowledge about access to this information was highly varied. Participants were also interested in knowing more about current developments in dementia research, and how their data had been or could be used in this field. Participants felt that there was limited public information about how data are used for dementia research. Participants also discussed the role of the media in the dissemination of information on

research and drug development related to dementias. Media reports of research 'breakthroughs' were associated with both hope and confusion or uncertainty about research currently taking place, and raised questions about how to access balanced or reliable information on research developments.

In one focus group participants expressed interest in individual feedback on their personal data, with the goal of understanding their personal health data relative to the wider cohort. In two cohorts, participants were uncertain whether their research data was shared directly with their general practitioner. Participants also questioned whether involvement in one research study made them more likely to be approached for further studies. These discussions suggest that participants can be uncertain about the limits of data interpretation, and restrictions on data sharing and contact for research.

The risks of expanding data sharing

Participants, although broadly supportive of data sharing, described concerns about changing how their data was shared. These concerns focused on the increased potential for accidental or intentional disclosure of personal data in the public domain. There was concern that research organisations outside of the cohort should not use data for purposes outside of public health research, such as targeted marketing or commercial use.

Participants were interested in the structure of data access and security facilitated by DPUK, including the use of a data safe-haven, restricted access to participant level data and tracking and auditing of data analysis. Participants described being both surprised and reassured by the level of consideration given to data security. This suggests there is an important role for public engagement and dissemination around how secure data research is managed. This could be supported by a public-facing element of the DPUK website and disseminated through cohort engagement systems (ie newsletters, websites and participant groups). Transparent and accessible public information on data security can enhance cohort and participant trust and confidence in the platform. Such activities begin to establish the level of social contract required to engender broader trust in the platform's data activities.

Conclusion: There is a clear interest in and a need for public engagement on the role, utility and security of data science for dementias research facilitated through DPUK.

Understanding the role and aims of research may clarify both recruitment and the role of data in the development of translational research. Exploring how data science operates can also clarify why it may neither be feasible nor scientifically and ethically appropriate to provide individual-level feedback. Communicating the broad range of research taking place and the work undertaken to explore early pre-symptomatic biological changes is particularly needed. It is important to recognise that any such engagement work considers the complexity and uncertainty around this research information.

It is also of value for researchers using cohort data to recognise the importance that participants place on knowing how their data is used and the kinds of research it is informing. DPUK, working with cohorts, can help to facilitate this by ensuring that publications using cohort data are reported as widely as possible, and to explore effective ways of disseminating this information.

2.1.2 Existing governance, data regulation and consent

Participants' views on the appropriate use of data are linked to their understanding and experience of their cohort's data-management practices. This includes participants' understanding of how their data are valued and used and their role within their parent cohort. The cohort relationship is shaped by long-term and repeat involvement and engagement. Consequently, it is essential to recognise that existing cohort governance, regulation and consent structures play a key role in participants' confidence in their cohort to safeguard their data and manage data sharing.

Existing consent

Participants describe the secure and responsible secondary use of data for health research as consistent with their original consent for data use. However, one participant felt strongly that the secondary use of data for interventional research was not consistent with their understanding of the cohort study. For this participant, the observational nature of the cohort was significant, and this person felt that de-identified use of their data in the development of experimental work went beyond their current consent. Whilst this is one participant's view, given the sample size of this study relative to the cohort population, it is important to acknowledge that there may be a range of perspectives on the acceptability of secondary data use. It remains important therefore to work with cohorts and existing cohort participant structures to robustly demonstrate that participant views on the permissibility of emerging practices are addressed in a fair and proportionate manner.

Trust and confidence in existing cohort data management practices

Participants trusted their parent cohort to manage data requests in the best interests of participants and in a manner consistent with the aims and objectives covered in their current informed consent. Such management included ensuring that data was shared with research groups who could be trusted, for research in the public interest which had the potential to achieve broad social benefits. Because of participants' long-term, trusted relationship with their cohort, the cohort structure represents an important gatekeeper for participants in the effective and acceptable conduct of secondary data analysis.

Organisation and researcher trust

Participants have less trust and confidence in unfamiliar public or private research organisations. When discussing the role of a third party to achieve secure data access and data linkage, participants wanted to understand who was involved, their motivations, how they were funded and their commitment to data security. This suggests that there is a lack of accessible public information on the organisations and procedures involved in DPUK's support for secure data sharing and linkage. Increasing public awareness of the role, structure and motivations of third parties involved in data linkage and sharing for health research can enhance public confidence and trust in the process.

Motivations for use of public research data

Participants' main concern around secondary data use addressed the involvement of commercial and industry researchers. Participants demonstrated a relatively high degree of awareness of the role of industry in UK health research, identifying the technological and economic necessity and value of working across public-private boundaries. However, participants also felt less confident about the motivations and ethical conduct of such organisations. Academic or publicly-funded research was believed to be motivated by broad public and social benefit. In contrast, commercial research was primarily understood to be motivated by profit, even where the benefits might eventually be made available to the public. Participants emphasised that private organisations should not profit disproportionately from data contributed to publicly-funded research. Rather, they described an expectation of reciprocal benefits from the involvement of commercial organisations which access data made available by and funded through public research. Participants considered how to ensure economic benefits came back to publicly-funded research, and how the wider knowledge and health care developments should contribute to the delivery of the National Health Service.

Participants were more sceptical of the security of their data when used in commercial research. This was particularly true in the case of identifiable data which they felt should not be shared in the commercial domain. There was concern that identifiable data could be employed for unacceptable or unconsented future uses, such as targeted marketing or appraisal of insurance coverage. Participants also expressed concern that commercial organisations would be less motivated to manage their data in a secure and responsible way.

Conclusion: Open transparent discussion of the role of commercial research in secondary data analysis for health science may be of benefit for the development of DPUK. Increasing engagement between public-private partners, research participants and the public can help stakeholders to understand and address the mistrust and uncertainty that exists in the involvement of commercial partners in data research. Demonstrating how the platform's secure data analysis procedures function across both the public and private domain, and the gatekeeping role of the cohorts in specifying the level of data accessible, would begin to address some concerns.

2.1.3 Data privacy, confidentiality and identifiability

The importance of anonymity, confidentiality and data security

In discussions around data sharing and data linkage, participants expressed strong interest in the theme of data security and particularly anonymity and confidentiality. Participants felt that their data should be deidentified, such as removing personal details like names, addresses and contact details. They also felt that the sharing of such data was largely beyond their existing consent and required explicit consent. This was especially true where the sharing of data crossed the public-private research boundary. Participants were generally unconvinced that it was acceptable or scientifically beneficial for commercial research partners to receive participant-level identifiable data such as personal details including names and addresses.

The issue of reidentification and accidental disclosure of participant information was of concern when discussing data linkage broadly and linkage to health care records specifically. Participants felt that it was, in principle, acceptable and potentially scientifically beneficial for their health-record data to be linked to their research data. However, they raised specific concerns around information which they identified as highly sensitive. This included sexual and mental health information and treatment for conditions which carry significant social stigma. Participants considered the potential harms of accidental or deliberate disclosure of such information to be high and lasting.

Participants wanted to understand how data linkage was achievable in ways that protected participants' identities, and the rationale for any research requesting identifiable data. Again this would suggest the availability and accessibility of information and engagement on data research and processes such as data linkage for health research can be improved.

Making sense of data security across social and digital domains

To make sense of the security of data in health research, participants drew on three types of information: personal experience of data in everyday life, experiences of data security in the cohort and in research more broadly, and media reports on data issues. This study demonstrates that in this sample of participants between 54 and 83 years of age, there was a relatively high level of engagement with digital technologies and resources in everyday life. This included the use of digital platforms for activities such as banking, shopping and utility management; and the use of digitally-integrated 'smart' devices such as smart phones, televisions and automotive satellite navigation. Experience of technologies was both primary and secondary, through family, friends and colleagues at work. Participants also described the impact of media reports on issues such as digital fraud, identity theft, accidental government data breaches, intentional theft of commercial data and unconsented sale or exchange of personal data by commercial groups.

When making sense of the security of their research data, participants used a range of experience. Participants felt that their data security was well managed by their cohort and in their experience of health research broadly. However, they described data in general to be highly insecure. Some participants expressed the view that in the long-term, data breaches were an inevitable if not acceptable facet of modern life. It was therefore important to know how any organisation planned to manage data breaches. However, participants felt that public-health research data was of less interest for malicious misuse than other forms of personal data such as banking and personal identity. Participants also expressed the expectation that health research which they viewed as publicly funded would react more transparently and responsibly to a data breach than a commercial group. Again, there was implicit trust and confidence in academic and government-supported health research. This confidence does not translate to commercial and industry health research which tended to be conflated with perceived data management issues in the wider commercial domain.

Conclusion: Assurances of confidentiality and anonymity remain central to participant's willingness to share their data. This confidence is highest in public and government-funded health research and lowest in research involving commercial partners. Transparent guidance on the data protection practices and standards expected of all data studies accessing data through DPUK-facilitated cohorts should be made available through the DPUK website, and disseminated to cohorts to make available to participants. DPUK can also benefit from exploring such issues through public engagement and further research.

2.2 Social and ethical issues around re-contacting cohort participants for experimental medicine studies

At the time of this study, it was anticipated that existing cohorts may facilitate follow-on recruitment for secondary research. The hypothetical process involved parent cohorts facilitating recontact by selecting and contacting participants on behalf of a secondary study. The processes of recruitment, consent and participation itself would be agreed between the parent cohort and secondary study, and managed solely by the secondary study. Consequently, in exploring experimental medicine this project focused on participants' views on recontact for a range of observational and interventional dementia studies. As a secondary theme, we examined participant's expectations of participation in these studies and their willingness and motivation for taking part. This study does not, therefore, focus on consent to secondary studies.

Participants from across all six groups were broadly positive about the potential of being recontacted about experimental studies through their parent cohort. They felt this was a logical extension of the cohort's aims and objectives. There was a high degree of interest among participants to hear more about further research opportunities. However, this finding should be treated with caution for three reasons: there is some variation in willingness to be recontacted; there is a clear divergence between participants' willingness to be contacted and their willingness to take part in EM studies; and, given the structure of the study, there is a likely to be significant bias among the participants consulted for the purposes of this project.

Willingness to be recontacted for interventional research was not universal. However, One participant felt that follow-on recruitment for interventional research such as clinical trials went beyond the parent cohort's original remit. 15 participants were willing to be contacted but would carefully judge any participation decision. Only two participants expressed willingness to be contacted and to take part in any ongoing studies. It is necessary therefore to consider that there will be a range of views across cohort populations on the acceptability of recontact and participation. This variation is particularly apparent for interventional research, and research which involves test processes to be invasive or highly burdensome.

It is essential to recognise that participants' willingness to be recontacted did not mean they would necessarily be prepared to take part in any one specific study. Willingness to participate was subject to much greater variation depending on the design of the study and participant views on the kinds of research activities involved. This study also demonstrated that the factors which do motivate participation are complex and, in some cases, raise important ethical questions (2.2.2). Furthermore, there are specific factors which participants take into consideration when making decisions about participation which can help inform future research recruitment design (2.2.3).

We summarise participants' willingness to be recontacted and motivations for involvement in research into three overlapping categories: participant confidence and commitment to their parent cohort and health research; the benefits and advantages of research involvement for society; and the perceived positive benefits of research participation for the individual and their extended family.

2.2.1 Confidence and commitment to the parent cohort and health research

In focus-group and interview discussions it is evident that participants associate further research facilitated by a parent cohort with the practices of that cohort. Existing cohort practices, therefore, play a significant role in participant understanding and expectations of external research and their willingness and motivation to take part.

Trust and confidence in cohort practices: study structures, research expectations, regional identity and research socialisation

Participants identified having significant trust and confidence in their parent cohort to manage future research contact. This confidence was associated with four characteristics of longitudinal cohort research participation: long-term, repeat research engagement; strong cohort identification; confidence in existing governance and regulation; and positive past experiences of research involvement. Therefore, participants felt that a study facilitated by their cohort would meet four core expectations of research: scientifically -good, ethically-sound, non-harmful design and aimed at public benefit.

In addition, the three cohorts involved in this study had strong regional and community identities. Combined with the longitudinal structure of the studies, this engendered a further sense of commitment and engagement from participants. Participants described a desire, responsibility and drive to continue to take part in their parent cohort, and to give due consideration to any request for participation facilitated by them. As we emphasise in section 2.2.4, whilst this does not mean that participants will participate in a study without carefully consideration, it does suggest that participants may make assumptions or hold expectations about follow-on research based on their cohort experience. Consequently, such factors should be considered in the design of follow-on research.

Due to the process of repeat participation within cohorts, people in the ELSI study were highly familiar with the structure, design and procedures involved in research recruitment. This familiarity can be understood as a form of research socialisation, in which participants become accustomed to the roles and uses of recruitment materials such as participant information sheets and informed consent forms. Participants described how this familiarity shaped their view of research involvement and participation over time. Participants self-identified as both highly willing and highly compliant, suggesting an increased threshold for willingness to consider research participation.

However, participants identified the right and freedom to refuse to take part in research as central to the acceptability of being recontacted. 15 of the 18 participants described being willing to give any request consideration, but having the confidence not to take part. Two participants said that although they recognised they had the right to say no, they felt they would say yes to any research opportunity. Therefore, whilst the freedom to say 'no' to research is central, this finding needs to be considered in light of the social and personal factors described in section 2.2.2 and 2.2.3, which clearly influence participants' decision to say 'yes' to research. Research needs to consider the motivations which underlie a proportion of participants' extreme willingness to participate.

Trust and confidence in academic and public health research

Participant trust was limited not only to the parent cohort. Approximately 20% of participants in this study had taken part in other health research. Across the ELSI study participants described having broad confidence in health research. This confidence was associated with the organisations involved. Participants described confidence in research supported by a well-known university or facilitated through the National Health Service. Such organisations were considered to share similar commitments to those of their parent cohort, that is scientifically-good, ethically-sound and non-harmful research design, aimed at public benefit. However, participants did not describe universally-good research experiences. Participants described specific cases where poor interpersonal experiences or a lack of feedback and engagement had resulted in less-good research experiences. However, this had not overall affected their willingness to consider research participation in the future.

Conclusion: Studies recontacting participants for recruitment from existing cohorts have the potential to benefit from the established sense of trust, strong commitment and research socialisation of existing participants. It is therefore essential that in their study design and recontact approach studies are both aware of, respect and preserve that relationship. This would be facilitated by ensuring that studies requesting recontact work effectively with the parent cohort, and attempt to meet and demonstrate the same common standards of research: scientifically good, ethically sound, non-harmful research design, aimed at achieving broad public benefit. This can be supported by addressing cohort involvement in the DPUK's guidance to study proposals exploring the possibility of follow on recruitment.

2.2.2 Social factors motivating participation

Participants emphasised the social importance of taking part in research, stressing that involvement did not primarily benefit them as individuals, but provided long term benefits for society. Supporting wider social benefit was framed as significant motivating factor for participation.

Societal benefits: Supporting the UK health service and health care improvements for the wider UK populations

By being involved in dementia research, participants felt they would contribute to better understanding of the diseases that lead to dementia, thereby supporting the development of care, diagnosis and effective therapeutic treatments. Participants framed their desire to participate in terms of their understanding of the personal, familial, health and social care and economic impact of this range of neurodegenerative disease. Participant understanding of these factors was motivated by both personal experience and wider social perception around dementias.

Members of the cohorts felt that future health care and treatment development relied on current research participation. Consequently they viewed participation as a social responsibility and necessity. Across all three cohorts participants framed research involvement as an altruistic act which may not lead to direct benefit for themselves, but may lead to health care improvements which benefit current and future society. However, as we demonstrate in section 2.2.3, participants also reference direct and indirect personal benefits as motivating their decision to get involved in research.

Participants from all three cohorts described being motivated by having benefitted from personal or family health care within the NHS. Participants who identified as having experienced treatment for severe health problems felt they had a responsibility to support the development and delivery of treatment and care through the NHS. However, participants who reported having experienced very good health also described feeling a responsibility to support health care development for those who had been less fortunate.

Cultural, community and religious influences

Participants across the three cohorts identified other significant cultural factors which influence their sense of social responsibility. Two focus groups discussed how their religious beliefs had a significant influence on their sense of a responsibility to contribute to society. This included three people who identified as having a specific faith and one participant who identified as an atheist. One group of participants described feeling that they had been privileged to have led successful, healthy lives and therefore felt an obligation to contribute back to society. Across the cohorts, participants described being motivated by a sense of community and regional responsibility. This motivated them to contribute to their parent cohort which they identified with the area in which they and generations of their family had lived.

Conclusion: Cohort participants draw on a range of social and cultural beliefs and values when considering whether to take part in further research. These factors are often understood and experienced as a sense of responsibility, duty or obligation to contribute to society. Such factors are associated with both positive and negative life experiences. It is important to value and respect these motivations, but also to be aware of how they may structure participation. It is essential therefore to continue to ensure that participants remain confident that there is no obligation to participate, and aware of their freedom to refuse participation and to withdraw from a study at any time. There has been a recent trend in research recruitment to engage with participants' sense of social responsibility to encourage participation in research. Whilst there may be mutual value in drawing on such associations, it is important to ensure that research engagement does not overemphasise social responsibility and obligation, and that specific populations of the 'highly willing' are not overburdened by recruitment pressures.

2.2.3 Personal factors motivating participation

In addition to the broad social benefits of research involvement, participants across the three cohorts raised themes which demonstrate how personal experience and circumstances influence motivations for research participation. In addition, they discussed how perceived direct and indirect personal benefits from research participation motivated their decisions.

Family history, the health of future generations: contributing to and benefiting from research

Personal experiences of dementia shaped participants motivations in a range of ways. Participants with close family and friends who had lived with dementia described this as a strong motivating

experience in their decision to participate in research. This was particularly true for, but not limited to, cases where the participant had been a primary carer and where the relation was direct biological kin. Participants described how the pain of watching a person live and die with dementia made them particularly committed to research to ameliorate their and others' future suffering. Participants felt their involvement could contribute to understanding the risks, causes and potential future treatments for dementia, improve clinical and social care and support for carers. These participants were interested in finding out about research taking place, and opportunities for participation in their region.

Participants who had one or more biological relations who had experienced dementia were particularly motivated to understand their own risk of developing dementia in the future. They described wanting to understand what action or research they could utilise to understand or modify their risk. Individuals believed this knowledge would help them to manage their own health and to prepare should they find they are at increased risk of, or experience, dementia in the future. Participants framed this concern both for themselves and for family members who might become their carers should their health deteriorate. Participants identified improving future research into dementia treatment and care for their families as a highly-powerful motivator for involvement. Participants with children and grandchildren discussed how they viewed research participation as a responsibility for these and future generations.

There was a strong perception that genetic risk was a highly-significant factor in the development of a disease leading to dementia. However specific knowledge about the nature of genetic risk was relatively undefined. There was extremely high interest, but also uncertainty, across the groups about the significance of other risk factors and their degree of modifiability. This was true of lifestyle risks such as diet, brain training, exercise and broader lifestyle factors. Participants identified media coverage of research as a factor influencing both their understanding and uncertainty about the kinds of activities which might reduce their risk of developing dementia.

Although personal experience was highly significant for those who described it, a significant proportion of participants (30%) described no personal or familial experience of dementia. These participants also described themselves as extremely interested in opportunities for dementia research. This group described motivations which overlapped with those with direct experience of dementia. These included addressing anxieties about their future cognitive health, understanding and ameliorating their own risk, and improving care for their own futures and the future of others.

Personal health benefits: addressing personal health and existing health care provision

In addition to this sense of broad benefit to health, participants discussed the potential for specific, direct and immediate benefits from research involvement.

Participants described being part of their cohort and health research as a means of monitoring their health, in addition to their general health care provision. This included the regular attention and surveillance of scientists and medical practitioners who conducted thorough physical evaluations, with the potential to identify actual, underlying or potential health issues. Participants also described research engagement as a means of staying aware of and assessing changes in their own sense of wellbeing. Thus, there is a perception that the action of regular monitoring may be a helpful and even beneficial act in and of itself.

This led to extensive discussions around the study feedback and reporting of incidental findings. Participants recognised that broad health feedback and clinical care was not formally part of the research context. However, they felt that if specific and actionable health concerns were apparent, they would be told by the research team or referred to their GP.

Across the six focus groups, participants discussed their role in research in relation to their experience of primary health care and their local general practice. There was variation in experience across the groups. Two groups were broadly satisfied with their primary care. However, four focus groups said that they were generally dissatisfied with the health care through their general practice. Common concerns included an unwelcoming and impersonal service, inability to get a timely appointment, inability to see a regular doctor or nurse, high staff turnover, poor continuity of care, poor experiences generally and during consultations specifically. Across these four groups discussion examined feeling of not being taking seriously by their local health practitioners, particularly around cognitive issues, and concern that their age affected their treatment. Participants also expressed the view that taking part in health research meant their GP was more likely to take their concerns seriously, especially if the cohort referred them back to their GP with an incidental finding. Across all three cohorts participants felt the physical and cognitive tests they received as part of a research study were more intensive and thorough than those they received from their GP. Consequently, they believed that research participation was more likely to reveal an underlying cognitive health problem than routine attendance at their GP.

In one focus group, two participants discussed how they felt participation in their cohort had directly benefitted their health. Both had been referred to their general practitioner following incidental findings through a cohort study visit. One participant described how taking part in the study had detected a health problem of which they were unaware. Consequently, this participant had been referred by their GP to the local hospital for further assessment. The participant received treatment, was reassured they required no further treatment, and was monitored on an ongoing basis by their GP. The second participant was referred to their GP following incidental findings for a condition they had been made aware of during routine screening. Their GP had advised her they did not currently require treatment. Following a research study visit the participant was referred to their GP for this condition. Following this the GP referred the participant to the local hospital where they received treatment and the condition was now resolved. The participant felt that the information from the cohort study had directly influenced their GP's decision to send them for referral at this point in time, speeding up their access to treatment.

Two respondents from different cohorts and focus groups described being extremely concerned about their cognitive health and well-being. This was described as a primary factor in their desire to be involved in dementia research. In focus group and interview sessions these participants had described, in detail, concerns about their memory. Both had sought guidance from their GP but felt their concerns had not been addressed. For these participants, taking part in research served a twofold purpose. Firstly, research participation was a means of identifying specific symptomatic problems which would lead to referral back to their GP. This would prompt closer scrutiny of their reported concerns by their GP and lead to possible referral for support. Secondly, research was a means of accessing experimental interventions which might improve or prevent deterioration of their current cognitive health, or reduce their risk of developing further problems. Both these participants reported regular participation in research and described themselves as highly interested and willing to take part in future studies for experimental and interventional research related to cognition and dementia.

Participants tended to relate their research experience and feedback within their parent cohort to their expectations of health research more broadly. This was reflected in dissatisfaction, where some research experiences did not match their expectations. These expectations included feeling valued and respected at research visits, and receiving general feedback on the outcomes of the research.

These examples raise several important issues. They illustrate broad concern around the provision of local GP care, particularly related to the treatment for older adults and more specifically for cognitive concerns. There is also a perceived lack of access to support for such concerns. As research increases awareness about the risks, symptoms and impact of dementia, there may be increased anxiety and awareness around cognitive issues. This may result in demand for services and support which local areas may not be equipped to deliver. Furthermore, participants across all three cohorts and regions clearly access research in relation to their experiences of local health care. Participants experience and perceive research participation to have the potential to directly affect their experience of and access to effective health care and treatment. DPUK as part of the wider research network raising awareness of dementia risks and symptoms and facilitating wider access to research could collaborate with other researchers to ensure that the impact of such issues is examined and addressed.

Personal interests

One factor in participants' motivation to take part was their level of interest in a type of study or technology. Participants who expressed a 'fascination' with science and technology described being strongly motivated to take part in research using techniques such as neuroimaging, bioinformatics and wearable devices.

Research as a response to social isolation, personal value and legacy

Participants also referred to other perceived personal benefits of taking part in research. A common theme was that participation was a means of responding to feelings of social isolation and a loss of social value in later life. Participants across the three cohorts described feeling that they had, over time, experienced the fragmentation of their local communities. They described feeling a loss of community and particularly the loss of contact with neighbours and friends, following people's movement for work or to be near family, or following their death. Participants who had felt socially isolated also described a loss of feeling socially valued or valuable. Consequently they described research and cohort participation as one means of socialising and reconnecting with a sense of community and contributing to society.

This finding should not overemphasise the role of research and cohorts in participants' lives. Whilst taking part in research, including their cohort, was an important facet of their response to social inclusion, it functions as part of a wider network of relations participants use to achieve this. This network includes participation and volunteering in a range of community-based activities. Whilst research involvement was valued and important to participants, they stressed that this was one route of interaction, and that it did not overlap with other parts of their life. For instance, none of the participants within the group knew one another. Although participants did report knowing other people who were part of the parent cohort, this was often discovered accidentally. Broadly speaking, outside of specific events and research study, engagement participants did not use their cohort participation for active everyday socialisation.

However, participants did describe receiving a lot of personal satisfaction from their participation in their cohort and in research more broadly. This satisfaction was derived from making a personal and valued contribution to research which would lead to positive benefits for their family, community and society, both now and in the future.

Conclusion: A broad range of personal factors shape participants' views on research and their motivation to take part. Again, it is helpful to acknowledge, respect and consider the impact of such factors on the design and implementation of recontact, recruitment and involvement in research.

There is a need and desire amongst participants for increased responsible and effective public and cohort engagement around dementia research. Engagement needs to address issues such as the availability and accessibility of current research findings and opportunities for research participation, particularly as they relate to biological and lifestyle risk factors associated with diseases that can lead to dementia. Open and transparent engagement is required to address current knowledge and its limitations around risk factors and their modifiability. It may be beneficial to engage participant, researcher, media and communications groups to consider the aims, objectives, current impact and future development of effective research and health communication in this field.

Personal experience, like social factors shape expectations and motivations for involvement in dementias research. These factors and their potential impact need to be considered to inform best research design and practice. This is particularly true where there is the potential for participants to want direct benefits from research which may not be possible. Although participants are aware of the limited direct benefit of their involvement, it is beneficial to take time to discuss their expectations and address any potential questions they may have about these limitations. It would also be useful to address these themes in public engagement about involvement in clinical research.

It is important to acknowledge that long-term participation in a cohort may create specific expectations about the research experience. To ensure that research participation is a good experience, external research can benefit from working with the parent cohort to ensure that requirements and expectations for research practice are addressed and met. It is also beneficial to discuss, early and transparently, approaches to issues such as disclosure, incidental findings and participant feedback. Where these differ substantially from the parent cohort, it is important to discuss this with participants who are approached for recruitment, ensuring that there is a match between practice and expectation. Where expectations cannot be met, it would be helpful for researchers to be prepared to discuss this with participants, for instance where experimental findings cannot be fed back to participants because of lack of current clinical significance.

Social motivations indicate that there is a core expectation among cohort participants that if recontacted for secondary research, the benefits of this research should be accessible across society. This research suggests there may be an important relationship between health care experience, provision and expectation and the role of increasing research awareness and engagement around dementia in the general population. This field requires further urgent research.

2.2.4 Considerations and limits for participation

Participants included in this study are clearly a highly-motivated and willing group, predisposed to future participation. This does not mean that participants' choices are naive or indiscriminate, or that their willingness to participate is limitless. In debate across the range of research examples provided, participants demonstrated considered decision-making processes. Participants weighed their personal and social understanding of the value of research against the potential risks of participation. Participants identified four significant factors involved in this process: the perceived benefits of the study; the perceived burdens of the study; the potential impact of participation on family members; and how their circumstances may impact their decision.

Social, scientific and medical benefits

When assessing willingness to participate, participants considered whether they thought the study sounded scientifically robust, whether it would lead to direct or eventual medical benefits, and whether those developments would have a positive impact for them, their families and society.

Study burden, risk, and physical or emotional discomfort

The most debated examples discussed were brain donation, lumbar puncture and clinical trials. Two participants described being willing to take part in all research cases regardless of potential risk and discomfort, whilst one participant described being unwilling to take part in any research outside of the cohort study. The remaining 15 participants expressed their willingness on a case-by-case basis. Participants gave attention to the potential physical or emotional impact of the study involved. This was particularly apparent in any interventional study, particularly those involving invasive testing or experimental treatments. Participants drew on a range of experience and evidence to decide how tolerable they would find a particular study type or test and whether they felt that these burdens outweighed, for them, the potential scientific, medical and social benefits.

Again participants drew on a range of knowledge when trying to establish their position on whether to participate in a study. These included direct and equivalent experiences, and personal and secondary experiences. Where participants had a direct negative experience of a procedure, this strongly shaped a clear decision not to take part in this type of study. For instance, one participant had a negative experience during an MRI scan involving vision and perception tests. She therefore automatically excluded any research that involved enclosed scanning, and was cautious about vision and perception tests. Where participants did not feel they had direct applicable experience they drew on experiences which they considered similar or equivalent. This included, for example, experience of an epidural that they related to a lumbar-puncture procedure. Participants who had a negative experience of an epidural did not want to have a lumbar puncture.

Where participants did not have access to direct or equivalent personal experiences, they drew on secondary experiences of friends and family. Again, this was evidenced in the case of the lumbar puncture procedure where participants described other people's negative experiences as a factor in their unwillingness to consider research involving the procedure. Where participants did not hold a strong view about the acceptability or the burden of a study or a procedure, they were also influenced by the accounts of others within the group. If others in the group had a strong negative or positive reaction to a study type, this impacted undecided members of the group in either direction.

Where participants felt strongly that the research would be valuable and beneficial, some participants decided they would consider taking part despite potential temporary discomfort for themselves. Generally these participants did not draw on any direct or indirect negative knowledge of the procedure, and were not persuaded by other participants' negative accounts. One participant described this in the case of the lumbar-puncture procedure. He felt this was a valuable piece of research and was therefore willing to experience a degree of temporary discomfort.

However, in the case of participation in the pharmaceutical clinical trial, the same participant had had a serious negative experience with a prescribed medication. He weighed the benefits of the research

against potential personal risk and his past negative experience and felt that he would not want to take part. Two participants felt that they would take part in a clinical trial involving a pharmaceutical intervention. Other participants' views varied. Broadly participants felt they would need to have a strong understanding of the potential risks and side effects of any drug involved, and must be strongly convinced of the benefits to them before undertaking a clinical trial.

Personal circumstance and familial relationships

Participants described how they had to consider their other existing obligations and commitments before deciding about taking part in research. Participants described having to balance taking part in studies with current work commitments, and caring commitments for partners, children and grandchildren. They described having to consider carefully how a research design would impact on them and their personal, professional and family lives. Participants took account of the logistical impact of taking part. This was particularly true for study designs which required travel and a high number of repeat visits.

Where the study involved could have an impact on family members, participants wanted to discuss this with their family to reach a decision. This was particularly apparent in the case of brain donation, where participants described needing to have full and considered discussions with all relevant family members, and the need to consider their feelings and views before making a choice.

Participants described how their willingness and capacity to take part in research also changed over time. They identified age and health as primary factors which affected their assessment of the feasibility of a research design. One participant described how her capacity and willingness to take part in research assessments involving physical exercise had changed. Whilst she had taken part in such activities in the past, she felt both energy and discomfort would make her unwilling to participate in future studies of this kind.

Conclusion: Participants' views on taking part in future dementia research are diverse and situated within wider social context, personal experience and individual circumstances. Some of these motivating factors can be extremely powerful, and can be experienced as a sense of obligation. Research design must therefore ensure that its recontact and recruitment procedures enable participants to make their decisions in a free and informed environment. Participants demonstrate a high degree of awareness and engage in complex and considered decision-making processes when making choices about the kinds of research there are willing to take part in. Consequently it is important to recognise and respect that participants' choices are influenced by a range of beliefs, considerations and social relations.

Social motivations to participate indicate that there is a core expectation amongst cohort participants that if recontacted for secondary research, this research should aim to be accessible and of benefit across society.

Whilst willingness amongst participants is high, it is not infinite or static. Willing participants can be put off by negative experiences, and just as their personal circumstances are changing and dynamic, so is their willingness to participate. Future studies require researchers to clearly address the limits of recontact and predisposed willingness, with reference to the burden of individual studies, potential personal and social impact, and the burden of the re-contact process as a whole. In managing requests for recontact therefore, researchers must evidence that appropriate cohorts are being contacted, that the use of a cohort is important to the research and that it would be more effective for the study design than recruitment through other means. In turn DPUK must ensure that specific cohorts or specific groups within cohorts are not overburdened with recontact requests.

2.3 Case Studies

Case Study 1: Wearable devices and data linkage

1. Familiarity and interest in wearable technologies and digital tools for research

14 participants had direct experience with digital technologies, wearable devices or smart phone technology. Four participants with no direct experience drew on the experience of friends, relatives and colleagues. Discussion focused on how the technology worked, the design, effectiveness and benefits of wearable technologies for research, how their data would be used and interpreted, and how data collection accounted for the variability and complexity of people's everyday lives and environments.

2. The acceptability of wearable devices: ease of use, comfort and surveillance

Participants expressed a high degree of comfort with being contacted for and using wearable devices for research. However, they raised questions about ease of use and impact on everyday activities. Participants preferred devices which would be minimally visible and obtrusive, and cause minimal physical discomfort or inconvenience.

Participants felt that data collected by wearable technology had the potential to be intrusive. However, they felt that many technologies of everyday living such as satellite navigation technologies, closed-circuit television, and smart phones were used to observe movement and activity. Whilst the use of such data was not entirely comfortable it was considered common place, and had potential value in health research.

3. Issues around data security and trust

Participants understand the desire to link data between research domains. However, they had concerns about linkage and accidental or intentional disclosure of sensitive information into the public domain (impacting family life or employment), or the commercial domain (affecting insurance agreements or exposing them to targeted marketing). Willingness to use a wearable device required trust that data would be securely managed and used in a socially-acceptable way. Participants felt it was important for digital devices research to have clear policies on data protection; however, they felt no organisation could guarantee absolute data security. Familiar academic, NHS and government-based organisations were broadly trusted to manage data storage and linkage, however participants were less trusting of unfamiliar academic organisations such as SAIL. Participants acknowledged the role of private industry in health research in the context of finite public resources and complex, high-cost technologies. However, they were concerned about use of their data by commercial organisations.

Case Study 2: Deep and Frequent Phenotyping

1. Willingness to be contacted and interest in participation

Participants were broadly willing to be contacted and receive information about this type of study. However, only five participants across the groups thought they would be willing to be involved. Eight participants said they would not consider taking part, whilst five participants were undecided. Discussions focused on the intensity of the study, the impact and discomfort of the procedures involved, how a participant's data would be used to determine their risk, and whether participants would want to know this information or be happy for it to be withheld.

2. Issues around research design burden and invasive testing

Participants raised the question of travel and the number of visits involved in this study. Participants who had caring responsibilities described considering whether participation would interfere with existing commitments. Of the measures involved, the inclusion of repeat lumbar punctures raised particular discussion. Participants had questions about the size of needle and the degree of discomfort involved. Individuals with direct or secondary negative experiences of this or similar procedures (spinal injections) were most likely to refuse involvement. Participants who were willing to be involved wanted to know if they could refuse further LP procedures if they had a bad experience during the study.

3. Issues around risk disclosure

Participants were divided over the idea of risk disclosure. There were three broad positions: participants who felt that having taken part in the study they should know if they were at increased risk so that they could take ameliorative action, participants who felt this knowledge would not change their lives, and participants who said they explicitly would not want to know and to live with this information if nothing could be done. Participants drew on examples such as genetic studies and cholesterol testing to understand how this kind of information might affect them.

Case study 3: Clinical trials for a pharmacological intervention for Alzheimer's disease

1. Willingness to be contacted for a clinical trial

Participants felt that clinical trials were an important form of research and were willing to be contacted to take part. However, they felt that a clinical trial involving a pharmaceutical intervention required the most information, discussion and consideration to weigh the benefits against the potential risks involved, particularly as currently healthy participants.

2. Views on an experimental pharmacological intervention

When considering taking part in a drug-based trial, participants emphasised the need for full, informed and honest expert engagement. Participants wanted a clear understanding of the risks and monitoring process for potential side effects. Participants drew on past and current medication experiences to describe their decision-making process. Participants were particularly concerns about the potential for an experimental drug to interact with an existing medication or condition.

3. Views on participation in a randomised controlled trial

Participants had a good grasp of the basic principles of an RCT design, and understood the need for control during the study. However, they felt it was essential that after the study all participants should be receive feedback and be informed of the outcome of the therapy being tested.

Appendix I: Research Outputs

The work package has developed the following research outputs from the research addressed in this report:

Papers

Atkinson, S., Badger, S., Milne, R, Brayne, C. & DPUK 'Recruiting from Existing Cohorts in the Dementias Platform UK: Research Participant Perspectives.' Prepared for PLoS One. Audience: Public health, bioethics of public engagement and recruitment.

Atkinson, S., Badger, S., Milne, R., Brayne, C. & DPUK. 'Data Relations: Views on data sharing in the changing landscape of UK dementias research.' Submitted to Sociology of Health & Illness. Audience: Sociology of health, social studies of science and technology and social studies of bioinformatics.

Atkinson, S., Badger, S., Milne, R, 'Local ontologies and global initiatives: Re-Imagining, governing and experiencing participation'. Accepted for Biobanks Special Issue in Technosciencza. Audience: Sociology of health, social studies of science and technology and social studies of bioinformatics.

Atkinson, S. 'Re-making connections: Imagining publics and participants for Alzheimer's disease research.' Accepted for Special Issue of New Genetics & Society. Audience: Sociology of health, bioethics of public engagement and recruitment.

External Presentations

Atkinson, S., Badger, S. Milne, R. Brayne C. & DPUK 'Relations in biomedical research participation: Building a cross-cohort platform in the context of a national health system'. Paper Presentation, 13th Conference of the European Sociological Association, Athens, Greece. Audience: Sociology of health, public health, bioethics of public engagement and recruitment.

Atkinson, S., Badger, S. Milne, R. Brayne C. & DPUK. 'Research Participants perspectives on recruitment from existing cohorts in dementia research'. Poster Presentation, Alzheimer Association International conference, London, UK. Audience: Public health, bioethics of public engagement and recruitment.

Atkinson, S., Badger, S. Milne, R. Brayne C. & DPUK. '"I'd be OK getting the letter, I still would need to discuss it first": Ethical considerations for recruitment from existing studies to dementias research. Poster Presentation, Alzheimer's Society Annual Conference, London, UK. Audience: Public health, bioethics of public engagement and recruitment.

Atkinson, S. 'Personal? to whom? Careers, custodianship and control in biomedical big-data'. Paper Presentation, BSA Medical Sociology Group Annual Conference 2016, Aston University, Birmingham, UK. Audience: Sociology of health, social studies of science and technology and social studies of bioinformatics.

Atkinson, S. 'Health or illness, person or patient: Blurring the lines in the development of pre-symptomatic biomarkers for dementia'. Invited Symposium Paper, Navigating Impasses in Bioethics: Rethinking Ill/Health 2015, Von Hügel Institute, St Edmund's College, University of Cambridge, Cambridge, UK. Audience: Public health, bioethics of public engagement and recruitment.

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