

Ethics Review

When Patient Engagement and Research Ethics Collide: Lessons from a Dementia Forum

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Abstract. The importance of patient engagement in research has been gaining recognition since the turn of the 21st century. However, little is known about the perspectives of people with dementia on the process of discovery. To fill this gap and to inform priorities in patient engagement in the context of dementia research, the Clinic for Alzheimer Disease and Related Disorders at the University of British Columbia hosted an interactive session for members of the patient community and of the general public to share their views on various ethical aspects of the research process. Results from the session indicate that several current research ethics policies and norms in dementia research are not in line with participants' preferences. Here we discuss the importance of bridging the gap between researchers and patients and call for reforms in current standards of dementia research.

Keywords: Alzheimer's disease, dementia, ethics, informed consent, public policy, research ethics

INTRODUCTION

The role of the research participant has been greatly elevated since its dark days in Tuskegee [1]. At the turn of the 21st century, the concept of patient engagement emerged, opening a new chapter in the relationship between researchers and participants [2]. The current emphasis on patient engagement denotes a cultural shift in which patients participate in health research as partners rather than just test subjects and are involved at every step of the process, from study design to knowledge translation [3].

Patient engagement is especially critical in the context of research with vulnerable populations whose perspectives have traditionally been neglected, such as in the case of people with dementia [4]. As there still does not exist a cure for Alzheimer's disease (AD) [5] and other dementias [6], and as the number of people living with dementia worldwide is expected to exceed 130 million by 2050 [7], more clinical trials are needed to discover and develop disease-modifying interventions. These clinical trials, whether for pharmaceutical or technology-based interventions, are not possible without the participation of the dementia patient community [8]. Patients, their families, and caregivers can contribute a wealth of knowledge and experience that may otherwise be missed [9], and ensure meaningful and relevant research is conducted. Integrating patient

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perspectives into the design and execution of research helps promote a democratic process for all stakeholders [9, 10]. Patient engagement initiatives can also result in higher quality research, for example through a decrease in attrition. Finally, patient engagement can guide the communication of findings to the public, which in turn helps to build trust in the research establishment and facilitates future research participation [10, 11].

Despite these potential benefits, there are several challenges and complexities in patient engagement unique to dementia research. Cognitive decline may impede communication between the patient and the researcher, calling for the development of unique methods to overcome this barrier [10, 12]. Caregiver perspectives must also be considered alongside those of the patient, as caregivers are often heavily involved in the decision-making of the dementia patient, especially in the more advanced stages of the disease [13]. Currently, there is little research on patient engagement specifically in the context of dementia research.

While it can be difficult to engage members of the patient community in certain aspects of research such as drug target selection, there are key areas along the research process in which the patient perspective can be integrated. For example, the patient community can contribute critical insights into preferred methods for recruitment, risk tolerance for new therapeutics, and effective means of obtaining consent, all of which are typically governed at least in part by institutional research ethics boards. Here we explore this overlap between opportunities for patient engagement and requirements from research ethics boards through a discussion of findings from an interactive event involving members of the dementia patient community. The aim of the session was to demonstrate the feasibility of gathering patient perspectives on dementia research in a context where this has traditionally been perceived as a challenging endeavor. In addition, we gathered perspectives on specific aspects of the research process to lay the foundation for further empirical investigation into issues at the intersection of patient engagement and research ethics.

METHODS

We conducted an interactive patient engagement session during the 2016 Dementia Forum hosted by the Clinic for Alzheimer Disease and Related Disorders at the University of British Columbia. The

purpose of this annual event is to provide the patient community in British Columbia with an update on research in the field of dementia. Advertising for the event is specifically targeted to people with dementia and their families and caregivers. In 2016, the Forum welcomed over 370 members of the patient community and the general public and as such represented an opportunity to gain insight into patient and caregiver perspectives on key ethical issues using a convenience sample. As this was an interactive priority-setting session aimed at gathering pilot data to inform future empirical work and not a formal study, no personal information was collected from the participants.

During the 15-minute session, questions about various aspects of the research process were posed in a two-pronged approach. First, the story of Pat, a fictional patient recently diagnosed with AD, was introduced through a slideshow presentation and described through a story told by the presenter. The two slides that were used to introduce the story of Pat as well as two slides featuring examples of questions are shown in Fig. 1. The story was maintained to be as generic as possible to allow the audience to identify with Pat. During the introductory slide (“This is Pat”, Fig. 1), participants were asked to imagine themselves in Pat’s situation. During the remainder of the presentation, some terms were defined by the presenter (e.g., “clinical trial”), and each question and all its potential answers were read out loud. Minimal additional context was provided in the narrative. For example, no information was provided about the severity of Pat’s symptoms or their level of disability. The presentation incorporated multiple choice questions related to different aspects of Pat’s participation in a clinical trial, such as barriers to participation, consent, risk tolerance for new interventions, and data sharing (Table 1). After each question was presented, attendees were provided time to answer the question using i>Clickers, a remote-control system that allows participants to anonymously answer multiple choice questions. Results were shown on the screen immediately following each question and were recorded manually for analysis. Individual responses to i>Clickers questions were not tracked. Next, placemat surveys were completed, which provided a visual depiction of questions probing participant perspectives on data sharing. The placemat surveys were collected at the end of the session (Fig. 2). Answer choices for each question were totaled and descriptive statistics were used to characterize the results.


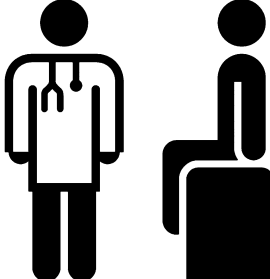


<p>A This is Pat.</p>  <p>Pat was just diagnosed with Alzheimer disease at the UBC Hospital Clinic for Alzheimer Disease and Related Disorders.</p>	<p>B Pat is invited to participate in research.</p>  <p>Pat's doctor mentions an ongoing clinical trial for a new drug to treat Alzheimer disease.</p>
<p>C What do you think is the best reason to participate in research?</p>  <ul style="list-style-type: none"> A. Pat will help scientists to better understand Alzheimer B. Pat might benefit from the experimental treatment C. Pat will help future generations with Alzheimer D. Pat will be followed more closely by a doctor E. I don't think Pat should participate in research 	<p>D What do you think is the biggest obstacle to participating in research?</p>  <ul style="list-style-type: none"> A. Learning about opportunities to participate B. The fear of undergoing all the tests C. The possibility of experiencing side effects D. The cost and inconvenience of traveling to the clinic

Fig. 1. Sample slides from the interactive presentation.

RESULTS

An average of 190 participants answered each i>Clicker question and a total of 160 placemat surveys were completed. The most popular answers for each question are described below. The full distribution of results for each question can be found in Table 1.

Research participation

When queried about the best reason to participate in research, over one-third (35%) of session participants indicated that Pat might benefit from experimental treatment. Another 30% of participants indicated that the best reason to participate was to help scientists better understand AD, while 26% mentioned helping future generations with AD.

Obstacles to participating in research

When asked about the biggest obstacle to participating in research, 38% of participants cited

the possibility of experiencing side effects. An almost equally popular response was the difficulty in learning about opportunities to participate (34%).

Informed consent

The majority of participants (60%) expressed that they would prefer to learn about the risks and benefits of the study by discussing it with the research coordinator, while only 24% indicated they would prefer to discuss it with their physician. The least popular answer was “Reading a form” (4%).

Risk tolerance

When queried about how much risk participants would accept in a clinical trial, 63% indicated a chance of moderate side effects, such as headaches, was the highest risk they would be willing to tolerate.

Table 1
i>Clicker questions

Question	Answers	Results (%)
What do you think is the best reason to participate in research? (n = 205)	A. Pat will help scientists to better understand Alzheimer B. Pat might benefit from the experimental treatment C. Pat will help future generations with Alzheimer D. Pat will be followed more closely by a doctor E. I don't think Pat should participate in research	A. 30 B. 35 C. 26 D. 9 E. 0
What do you think is the biggest obstacle to participating in research? (n = 200)	A. Learning about opportunities to participate B. The fear of undergoing all the tests C. The possibility of experiencing side effects D. The cost and inconvenience of traveling to the clinic	A. 34 B. 13 C. 38 D. 16
Would you prefer to learn about the risks and the benefits of the study by: (n = 206)	A. Discussing with your doctor B. Discussing with the research coordinator C. Reading a form D. Watching a video	A. 24 B. 60 C. 4 D. 12
How much risk do you think would be acceptable? (n = 202)	A. A chance of a minor side effects such as a stomachache B. A chance of moderate side effects such as headache C. A chance of severe side effects such as stroke D. If there are any risks, Pat should not participate in the study	A. 27 B. 63 C. 4 D. 5
If you were Pat, would you want to know the results from the tests for research purposes? (n = 202)	A. Yes, I want results from all the tests B. I only want the results if they provide information I can act on C. No, I don't want the results from the tests	A. 74 B. 26 C. 0
How do you think the data should be shared? (n = 122)	A. Anyone should be able to access the data B. Any researcher should be able to access the data C. Researchers who want to use the data should apply to a committee D. Researchers who want to use the data should obtain consent directly from Pat E. No one outside of the original study should be able to use the data	A. 19 B. 59 C. 6 D. 14 E. 2
Which of the issues Pat faced do you think is most important? (n = 194)	A. Finding ways to maximize research participation B. Improving the consent process C. Determining how much risk is acceptable D. Creating policies for how to return test results E. Improving how we share data	A. 47 B. 3 C. 25 D. 4 E. 21

Return of results

When asked if they would like to know the results from tests conducted for research purposes, most participants (74%) indicated that they would want the results from all tests.

Data sharing

Forum participants were generally in favor of sharing all forms of clinical data (Fig. 3A). Over half (59%) of participants believed that any researcher should be able to access research data. When asked specifically about whom they would be willing to share their data with, participants showed high support for other researchers studying AD (88%), especially within Canada (94%), and less support for researchers in other fields (62%), with approval further decreasing if they were based in a different country (49%; Fig. 3B). One third of participants were in favor of sharing their data with non-profit organizations (33%) or pharmaceutical companies (31%), and few participants would be willing to have

their data shared with industry other than pharmaceutical companies (12%).

Priority setting


Almost half (47%) of participants believed that finding ways to maximize research participation was the most important issue discussed during the session, while one-quarter of participants believed it was determining how much risk is acceptable when developing new therapeutics for AD.


DISCUSSION


Our data demonstrate that a brief 15-minute session with the patient community and the public about their views on issues in dementia research can provide a wealth of information to researchers and to the research ethics boards that govern the interactions between researchers and research participants. Although the issues explored during the session are not exclusive to dementia research, the


Share your opinion about research! Please answer the two questions below.


Question 1: I would be comfortable sharing this type of information with researchers, provided my name is not associated with it (check **all** that apply):



 My blood


 My DNA


 Images of my brain


 Images of my body


 My medical history


 My family history

Question 2: When you participate in research, who do you think researchers should share your data with? (check **all** that apply)

- Other Canadian researchers working on Alzheimer disease
- Researchers from outside of Canada working on Alzheimer disease
- Other Canadian researchers working on other topics
- Researchers from outside of Canada working on other topics
- Companies in the pharmaceutical industry
- Companies in other industries
- Not-for-profit organizations

Thank you! Please leave the survey at your desk – we will pick them up.



Fig. 2. Placemat survey.

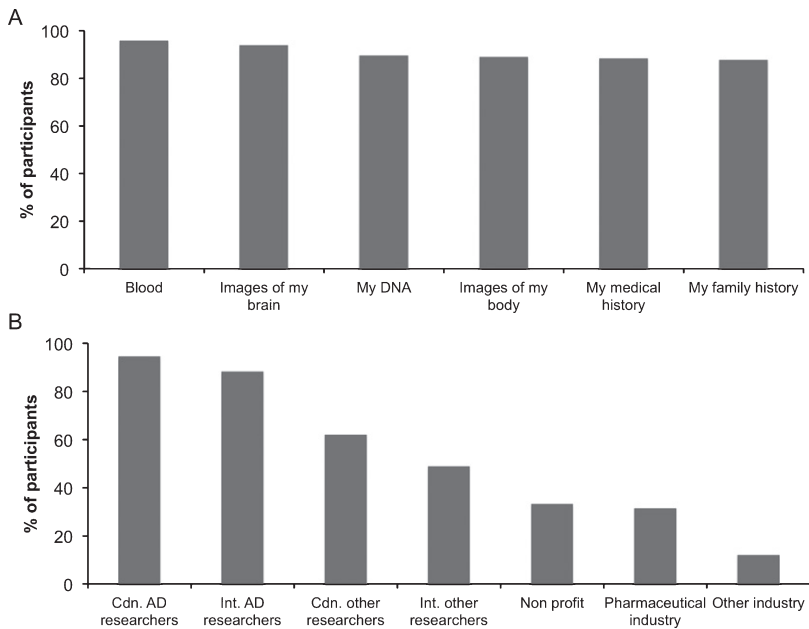


Fig. 3. A) Percentages of participants who would share different types of data with researchers. B) Percentages of participants who would share their data with different stakeholders.

context of the event and the story in which the questions were framed provide insights unique to this disease.

Regarding research participation, a significant proportion of session attendees indicated that a major reason to participate in clinical trials is that participants may stand to gain benefit from the experimental treatment. This is a clear example of therapeutic misconception, as the majority of dementia research is non-therapeutic, despite there being a therapeutic intention [14]. Albert and colleagues [15] found that there exists no difference in long-term outcomes between AD patients who participate in clinical trials and those who do not. Other studies, including those exploring the perspectives of AD patients and their caregivers, have also found therapeutic misconceptions to be prevalent [16, 17]. These findings highlight the need for continued education initiatives about the role of research for both patient communities and the general public. Participants of the interactive session also indicated that helping scientists and future generations with AD were good reasons to participate in research. This finding is consistent with studies showing that altruism is a key motivation for enrolment in clinical trials [17, 18].

Risks of side effects arose as a major obstacle to participating in research. The current literature on barriers to enrolling in AD trials is mixed. Some studies confirm that participants are concerned about the side effects of experimental drugs [18], while other studies suggest that is not the case [17], and that the time and transportation required to participate in research were instead the critical obstacles [19]. We also found that difficulty in learning about research opportunities was a barrier to research participation, and many attendees felt that finding ways to maximize research participation should be a key priority among all the issues discussed during the session. This finding is at odds with research ethics requirements that limit the ways in which potential participants can be contacted for research [20]. Barriers to research participation may be addressed by strategies such as clinic referrals, social media, and community-based participatory research [18, 21]. As we move forward with patient engagement initiatives, it will be crucial to carefully balance the desire from the patient community to be aware of ongoing research with the ethical requirement to not overly burden potential participants.

Given results from studies indicating that most patients prefer that their physician be the one to

obtain their consent for research [22, 23], our finding that most participants preferred a research coordinator for this task was unexpected. We postulate that this may be explained by the time constraints faced by physicians, while research coordinators may be more likely to have sufficient time to thoroughly discuss the benefits and harms of research participation [24]. On the other hand, this preference may also be attributed to the unique role of the research coordinator as an unbiased figure and independent of the patient's medical care. Indeed, there are ethical guidelines regarding physicians obtaining consent if the patient is under their care, due to the dependent relationship of the patient on their physician [25]. In addition, a crucial aspect of the research coordinator role is human subjects protection and patient advocacy [26], which may contribute to the perception of research coordinators as being more concerned with patient well-being rather than research outcomes, and therefore more trustworthy. Reading a form was the least preferred method of obtaining consent. Traditional consent forms are often lengthy and employ complex language [27], and while consent forms are currently standard practice required by research ethics, results presented here and in the work of others also call for revisiting the process of obtaining consent. In particular, the dementia research community must consider innovative and interactive solutions that are more closely aligned with patient preferences and that address the challenges specific to dementia, such as cognitive and memory impairments. For example, several groups are now investigating the integration of new technologies to facilitate the consenting process such as slideshows and videos [28, 29].

The acceptance of headaches as the highest risk that participants would tolerate should be considered in the context of the common side effects of currently recommended treatments for AD, such as donepezil and memantine, which include fatigue, nausea, and vomiting [30, 31], and the risks of experimental treatments, which may include nausea, upper respiratory tract infections, and urinary tract infections [32, 33]. The findings on risk tolerance in the AD literature are mixed, often varying depending on the probability and magnitude of benefit. For example, Oremus and colleagues [34] found that most caregivers were unwilling to accept moderate side effects such as headache or nausea, while other studies showed that many older adults would accept a chance of severe side effects such as death or brain inflammation

[35, 36]. As there are many aspects of risk tolerance that should be addressed, including the nature of the side effects and the risk-benefit ratio, further investigation into this issue in the context of dementia clinical trials is warranted. This is especially important as a significant proportion of participants felt that determining how much risk is acceptable is a priority among the issues discussed during the session. Should our finding be confirmed in a larger, representative sample, it has clear implications for priorities in the development of drug therapies for AD.

Most participants supported the return of results of all tests conducted during clinical trials. Currently, there exist very heterogeneous research ethics guidelines on the return of results to research participants, which vary between countries and even between institutions [37, 38]. To some extent, the issue of return of results is addressed by ethical guidelines that recommend reporting incidental findings that are clinically relevant [39]. However, we found that participants were in favor of receiving their test results regardless of their medical significance. Some ethicists opposed to the return of results invoke the separation between research and clinical care. They argue that researchers are not morally obligated to disclose results to participants, to do so would require large amounts of already limited resources [40, 41] and may lead to potential harms [42]. However, studies have indicated that disclosing APOE genotype to individuals potentially at increased risk for AD did not increase their anxiety [43]. Results from a study by Christensen et al. [44] suggest that even after the disclosure of APOE results, participants still believed there were more benefits than harms to learning about their genotype. Furthermore, Chao and colleagues [45] found that research participants who learned about their higher genetic susceptibility were more likely to take proactive steps to reduce their risk of AD. It remains unclear whether data from APOE studies also apply for different test modalities such as amyloid imaging. Further work in this area promises to provide evidence-based and participant-driven research ethics guidelines for the return of results in dementia research. Moving forward we must carefully consider how to develop measures that respect the wishes of the patient community but reduce the potential negative impacts of the disclosure, such as by including options regarding the return of results during consent and offering services such as genetic counselling following the disclosure of genetic test results [46].

The majority of patients were in favor of data sharing among researchers, especially within the field of AD research, although support for the sharing of personal information decreased with a higher risk of re-identifying the data [47–54]. Trinidad and colleagues [55] also found that both current and prospective research participants are generally supportive of the sharing of non-identifiable data among researchers. In addition, results from other studies also indicate low support for sharing data with industry outside of pharmaceutical companies [55, 56].

There currently exist many research ethics restrictions on data sharing due to concerns over participant privacy [57, 58]. However, we did not include scenarios that include risks such as potential breaches of privacy. The concept of privacy breach as a risk of research participation warrants further investigation as these risks may influence support for data sharing and research participation. As we move toward international longitudinal and intervention cohort studies, addressing the challenges of balancing data sharing, individual preferences and priorities of the dementia patient community will require concerted global efforts. These findings, in conjunction with other work in this area, indicate that the current movement toward open access is consistent with the views of prospective participants [59].

We acknowledge the limitations of the methodology and findings presented here. As this was not a formal study and no demographic data was collected from session participants, the sample may not be representative of the broader patient community. The lack of demographic data limits our ability to determine the proportion of patient to caregivers and whether the participants have had previous experience participating in research, amongst other variables. Future work will take this exploratory session into the realm of empirical research by gathering demographic data in addition to perspectives on dementia research from a representative sample. Despite these limitations, the results highlight the imperative for the careful consideration of patient views on ethical issues in dementia research. While the event did not address any single issue in-depth, our findings suggest a tension between the needs and desires of the patient community and research ethics requirement. Addressing this tension is of critical importance for the benefit of both the patient community and the growing cohort of researchers that are frustrated with the detachment between patient wishes and traditional ethics procedures.

Thus, our findings call for an expanded discussion of priorities in research ethics.

Conclusions

As patient engagement becomes an integral component of dementia research, we must shift from research ethics grounded in theory to ethics that incorporate the needs and wishes of the dementia patient community. Events such as short, interactive presentations during public conferences can serve as useful starting points to gather perspectives and set the agenda for larger-scale patient engagement initiatives and empirical research into ethical issues. These activities will in turn allow for the co-production of high quality research aligned with the views and values of research participants and will foster a respectful and reciprocal relationship between all stakeholders in the discovery and development of new therapeutics for dementia.

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