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Public's Approach to Surrogate Consent for Dementia Research: Cautious Pragmatism

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Abstract

Objectives—To describe how members of the older general public deliberate with one another in finding solutions to the dilemma of involving decisionally incapable persons in dementia research.

Design, Setting, and Participants—160 persons aged 50+ who participated in an all-day deliberative democracy (DD) session on the ethics of surrogate consent for dementia research. The DD day consisted of both extensive, interactive education with experts in clinical research and ethics, as well as small group deliberations.

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Measurements—Audiotaped small group deliberations were transcribed and analyzed, and the main thematic elements were coded.

Results—During deliberation, participants acknowledged the limitations of advanced research directives and discussed ways to improve their use. Although there was consensus about the necessity of surrogate consent, the participants recognized potential pitfalls and looked for ways to safeguard the process. Participants supporting surrogate consent for research emphasized societal and individual benefit, the importance of assent, and trust in surrogates and the oversight system. Other participants felt that the high risk of some research scenarios was not sufficiently offset by benefits to patients or society.

Conclusions—Members of the older general public are able to make use of in-depth education and peer deliberation to provide reasoned and informed opinions on the ethical use of surrogate consent for dementia research. The public's approach to surrogate consent is one of cautious pragmatism: an overall trust in science and future surrogates with awareness of the potential pitfalls, suggesting that their trust cannot be taken for granted.

Keywords

surrogate consent; dementia; deliberative democracy

Alzheimer's disease (AD) is incurable, devastating, and highly prevalent. The clinical research necessary to make progress against AD, however, poses the dilemma of involving patients with substantial cognitive impairment who lack the ability to provide informed consent.(1, 2) The dilemma is magnified when the research is invasive and burdensome, with unpredictable risks.(3–5) Despite several decades of debate in the U.S., no clear policy exists regarding the involvement of adults with decisional impairments in clinical research.(6) AD research centers(7, 8) research ethics review boards(9, 10), and dementia experts and advocates(11) vary considerably in their viewpoints, policies and practices in dealing with this ethical issue.

Several studies have suggested that there is considerable support for surrogate consent for dementia research.(12–15) But most of these studies have been traditional cross-sectional surveys and do not provide insights into the underlying basis for these opinions. Given the historical, ethical, and scientific complexities of the topic, understanding the underlying reasons for such opinions would provide insights into their validity.(16)

We have been investigating the views of the general public regarding surrogate consent for dementia research using democratic deliberation (DD). The practice of DD is built on normative theory that regards citizens' views as important and necessary sources of public policy. The goal is to obtain considered opinions of citizens that result from a fair, respectful, and transparent interchange of viewpoints based on thorough education and peer deliberation; such opinions can then inform democratic policy-making.(17, 18) DD is increasingly recognized as useful for soliciting public opinion on controversial policies.(19) For example, the Agency for Healthcare Research and Quality is currently conducting a large scale study of democratic deliberation to inform comparative effectiveness research(20) and the U.S. Presidential Commission for the Study of Bioethical Issues has recommended democratic deliberation to inform bioethics policy debates.(21)

In our deliberative study, members of the older general public participated in a day long session of in-depth education and peer deliberation concerning the ethics of surrogate consent for dementia research.(16) We found broad initial support for a policy of surrogate consent for research that significantly increased after deliberation.(22) We also found through detailed qualitative analysis that the quality of deliberation in our DD sessions was

quite good and that participants learned and used new information, were respectful and collaborative, and were able to "reason together" to arrive at societal policy recommendations.(23) In this article, we explore the major themes of deliberation among our participants as they discuss and debate the ethics of surrogate consent for dementia research.

METHODS

A comprehensive account of the theoretical basis and methodological procedures for this study has been published elsewhere.(16) The study was reviewed by the University of Michigan's Institutional Review Board and deemed exempt from federal regulations.

Participants

160 members of the general public (≥50 years old) who had been randomized (n=212, 75% attendance rate) into the deliberation arm of a 3-arm study (total n=503, recruited via random digit dialing within a 50-mile radius of Ann Arbor, MI) attended an all-day deliberative session. Other arms included an education-only group (receiving educational materials but not attending DD sessions, n=141) and a control group (no intervention, n=150). Since only the DD group participated in deliberations, only their data are presented in this paper (see Table 1).

Procedures

On the day of the DD session, the attendees were randomly assigned in groups of 5–7 persons per table. There were 27 tables (in two cohorts); each table was led by a trained facilitator.(16) Participants were informed that the group discussions at each table would be recorded. The procedures for the day are outlined in Figure 1.

The deliberative session involved three small group sessions. The first small group session was primarily designed to "warm up" the group to the process of group discussion, including an ice breaker exercise and general reactions to an informational video on Alzheimer's disease (AD). That small group session was not analyzed for this paper.

The second small group session immediately followed an extensive educational session by experts in AD clinical research and in research ethics (see PDF, Supplemental Digital Content 1). During this session, the participants were asked to engage in general discussion about the presentations and also about the ethical dilemma of involving decisionally impaired dementia patients in clinical research.

In the third small group session, participants were asked to evaluate four research scenarios: a study requiring a lumbar puncture, a clinical trial of a new drug, a vaccine study, and a study requiring the insertion of genetic material directly into the brain of a subject (see Figure 2).

Participants were to provide recommendations regarding whether our society should have a policy of family surrogate consent for studies such as the ones described, and to reach a group decision, by consensus or majority. The participants were also asked to provide rationales for their recommendations.

Analyses

All group discussion recordings were transcribed. Twelve group transcriptions were selected to be coded: six were randomly chosen from the groups that agreed by majority or unanimous vote – that society should allow surrogate consent for all four scenarios (n=18),

and six were randomly chosen from groups where there was at least one research scenario (by consensus or majority) for which the group would not allow surrogate consent (n=8) or where there was a tie vote (n=1).

To examine the substance of group conversations we developed a coding scheme using a systematic and iterative method common to qualitative analysis,(24) building on codes used in a previous study and identifying new codes relevant to this study.(25) Coding was conducted by two team members independently using NVivo qualitative software. Prior to analysis, coding discrepancies were discussed and resolved by three team members (AS, RdV, KR). Theme saturation was reached after coding transcripts of 9 of the 12 groups and our analysis is based on these 9 groups' transcripts. These 9 groups were fairly evenly split between groups that would allow surrogate consent for all 4 scenarios (n=5) versus those who would not allow surrogate consent in at least one scenario (n=4). After coding was completed, each group's transcript was systematically reviewed for the most commonly occurring themes and relevant quotes were identified.

RESULTS

Small Group Deliberation: General Discussion about Surrogate Consent

There was a striking pattern to the participant discussions during small group session 2, which focused on general issues related to surrogate consent. Although they learned through the expert presentations that few people complete research advance directives, participants nevertheless found such directives attractive, and discussed ways to improve their use. However, this discussion also inevitably included the limitations of advance directives. The discussions on advance directives generally led to the conclusion that such directives could not by themselves solve the ethical dilemma of involving incapacitated persons in dementia research.

Improving Advance Directives—Participants discussed several ways to increase the use of advance directives. Some suggested encouraging individuals to complete advance directives as soon as they were diagnosed with dementia: "I keep coming back to the advanced directive. What if every person who is early … diagnosed with early Alzheimer's …What if they are immediately asked if they would consent?" (F45—participants are identified by gender and ID number). Other participants suggested that public awareness for the need for research advance directives could be raised through education: "It has to be education. It has to be lobbying efforts after the education. Most people aren't going to react unless it personally happens to them." (F50) Many participants suggested that research advance directives could be incorporated into other documents such as living wills, heath care durable powers of attorney, or even driver's licenses.

Limitations of Advance Directives—Despite the attractiveness of advance directives, the participants recognized that education and other efforts to increase their use may not be sufficient. One participant pointed out a number of reasons why she (despite being at risk for dementia) and many others fail to complete advance directives:

> F15: The reason the numbers are so low is because human beings by nature do not wish to think about our end times. I mean I have both parents gone from two different dementias. I don't have it yet. I've thought about it. Right now, I don't have the money to get it done. It has to be done with an attorney. I have to pick competent people.

Others pointed out the difficulty of anticipating the future when completing advance directives—both the content of future research as well as knowing what one's wishes might

be in the future: “Sometimes peoples’ thoughts change with time, and with the amount of pain they’re in or whatever” (M27) and “You don’t know the content of a study that might not be done until twenty years later. How could you know the content?”(M49) Another participant compared it to signing a Do Not Resuscitate (DNR) order in advance: “We all think we’re going to do that when we get to the end of our life, but none of us really wants to die and we don’t know …We might change our mind at the last minute, you know?”(F48)

Participants also pointed out that relying on advance directives may have negative consequences for future research since few people complete them.

> M63: If you limit it only to people who have advanced directives… there’s a great likelihood that we’re going to really limit the amount of research that can be done.

Challenges of Surrogate Consent—Having recognized the limitations of advance directives, there emerged a consensus that some form of surrogate consent is necessary:

> F23: In order to advance knowledge about Alzheimer’s, by definition, surrogate consent has to happen. It has to happen.
>
> F31: But if the answer is “no,” that surrogates can’t give consent, then there is no hope for ever getting anywhere. So the answer has to be in my mind, “yes.”

However, participants did not unquestioningly accept a policy of surrogate consent. Instead, they pointed out many challenges and potential abuses of such a policy. Participants were concerned about whether surrogates would be competent, knowledgeable, know the patient’s wishes, or have the patient’s best interests in mind.

> M26: Do they really understand that I wanted to do that? How forceful or how open was I with that statement and that choice? Are they informed of the research study and what it entails?
>
> M34: When you’re dealing with family members, not every family member may have that subject at heart. Do you know what I’m saying?…And a lot of them are just not smart enough… They’re not smart enough, educated enough, you know…

Many participants worried that surrogates may not have the best reasons for enrolling AD patients in research: “Would it be in the best interest of the person or is it monetary for them? Are they thinking of something else?” (F57)

It is clear that participants do not have unrealistic and rosy views of surrogate consent. They see the many challenges, even as they recognize that surrogate consent is necessary to move dementia research forward.

Safeguarding surrogate consent—Also, much like their discussion regarding advance directives, many participants went beyond a simple discussion of the pros and cons of surrogate consent, to seek solutions to improve and safeguard the process.

> F44: So it seems as though we almost have no choice but to have some form of surrogate consent, and our challenge is … How do we make it work? How do we build protections for, you know, the Alzheimer’s victim … the patients …

Participants discussed potential policies that would mandate safeguards such as third party oversight or some sort of vetting process to evaluate the competence, intentions, and appropriateness of the surrogate.

> M21: Let’s have some standards about who can and who can’t be a surrogate and for what reasons.

> F30: Allowing surrogate consent with certain safeguards in place…such as the person who is the surrogate is assessed. You know, you can do interview assessments that will tell you, you know …Using diplomatic questions that will allow you to obtain information …as to whether the person really not only understands what they're potentially saying "yes" to, but also whether they do have the best interest of the person at heart.
>
> M63: I think policymakers should consider the competency of the surrogate making this decision. There should be some sort of a test, some sort of questionnaire…

Small Group Deliberation: Specific Research Scenarios

In small group session 3, participants were asked to evaluate four specific research scenarios of varying risks and benefit and to decide whether society should have a policy that allows surrogate consent for each scenario.

Lower risk scenarios—In the lumbar puncture and drug study scenarios, low risk was the most commonly cited criterion for voting to allow a policy of surrogate consent. However, risk was not the only deciding factor. Participants also emphasized as important considerations societal benefit and the necessity of research, potential individual benefit (drug study), the importance of patient assent, and the value of monitoring for adverse events.

Societal and individual benefit: The participants distinguished between societal and individual benefits, and saw both as considerations:

> M34: I'd like to say one thing. Another reason why I say "allow" is because it says right here, "The study will not directly benefit the patient," right? But what it will do … It will lead to better understanding …understanding of the disease itself.
>
> F50: My way of looking at this is that it's one step in the chain towards a cure.

The drug study scenario had the additional appeal of potential direct benefit to AD patients who may enroll in such studies:

> F65: If a person does have Alzheimer's and the drug actually is a positive drug and it works, the person doing the test will actually benefit from it.
>
> F31: There is an additional reason. There's a chance it might help.

Importance of assent/dissent: Another important issue for participants was the concept of assent: even if the surrogates give permission, if AD patients refuse to participate, they have the final word.

> M21: As I understand it, if at any point in the process the patient says, "I don't want to do that." "I don't want to do it any more," or "I don't want to do it," to begin with, then the answer is already "no." No matter what the surrogate says, if the patient says "no," the answer is "no."

For many participants understanding assent was critical to their approval of surrogate consent. One participant stated in a later higher risk scenario, that her appreciation of the concept of assent was her "lightbulb" moment, when she became comfortable with surrogate consent (F23).

Value of monitoring adverse effects: Some participants who voted to allow surrogate consent mentioned the importance of close monitoring of subjects in research studies:

F39: I know when I was in one study, I had to report morning and night and answer all these questions. You know, very specific questions. So it's pretty well-monitored for safety reasons. So that's another reason I would allow it.

Higher risk scenarios—For the vaccine and gene transfer studies, not unexpectedly, the issue of risk was highly salient for participants. When voting whether to allow surrogate consent in these studies, it often came down to whether the level of risk was sufficiently offset by potential benefits.

Risks not offset by benefits: For participants who opted not to allow surrogate consent in the higher risk scenarios, they felt that there were simply not sufficient benefits either to patients or to society to make up for the high risks.

F30: I feel that way from a societal point of view too because we can't …. I mean each individual human life is important, and it has value… You still have to value the individual human life. Otherwise, you're on that slippery slope where you start evaluating human life and you end up with things like the horror stories that he told us about.

F56: I just think the risk/benefit ratio is not good. The chance of it helping anybody is pretty low.

However, for some participants, their concern was mainly a deep discomfort with surgical intervention into the brain.

F24: …any time you put foreign material into the brain, you are risking all kinds of problems in my opinion.

F42: I would not allow this. This just seems like spooky old school, creepy, witch doctor-type surgery.

Benefits to patient or society: For participants who would allow surrogate consent, the higher risk was offset by potential benefits to patient or society.

M20: What it might be is the fact that this is the first step towards something really promising. This may not be the end-all cure, but if we try this and it looks like this is actually having an effect, maybe now we can focus more research on this. In the end, we'll have a much huger positive impact.

F39: Yeah. Slightly helping …You know having someone be able to get dressed in the morning on their own can be huge for that person's state of mind and for the people who care for that person…Who knows? Maybe they're getting more improved, less side effects … You never know unless you allow somebody to make the choice to be a research patient.

Trust in the oversight system: During the session day, participants were presented with information about historical research abuses and current protections to prevent these abuses (see PDF, Supplemental Digital Content 1). We found that prior to the study, most participants had been unaware of the human subject protections system. The participants appealed to this new knowledge in supporting a policy of surrogate consent:

M36: That comes from pressures from society on how we behave. Like Tuskegee or any one of those experiments… There were a lot of things going on then that were acceptable that are not acceptable today… They're just not tolerated.

F41: I guess I have faith in how it was described earlier in how it went through these different boards and getting the study approved. I mean I put a lot of faith in

> that system… there aren't those Nazi doctors and some of those other things that we saw earlier. So, therefore, I have my confidence in that there aren't going to be butchers out there cutting open peoples' heads …

Trust in surrogates: Trust in surrogates was another salient theme for participants who voted to allow surrogate consent in the higher risk scenarios.

> M17: I would allow it and, once again, placing your trust in the surrogate being someone who loves you, somebody who has your best interest at heart and …may know what you would have wanted.

> F48: We can trust our surrogate, like you said, so whatever the test is, they will … They are the rational minds, and they'll look it over and decide if this is something that they're willing to put you through.

Societal versus individual perspective: Participants who voted to allow surrogate consent in the higher risk scenarios also moved beyond a simple risk/benefit calculation to articulate the distinction between societal policy and the individual choices of surrogates:

> M36: By voting "nay" against surrogate empowerment, what you're essentially doing is voting "no" on every other family. You're putting yourself in a position of impacting every family who has an Alzheimer's patient. On the other hand, by giving the surrogate power in all cases, then it becomes a singular family issue, or a singular person issue.

DISCUSSION

Several studies have shown that there is considerable layperson support for allowing surrogate consent for dementia research.(12–14, 26) Among our participants, we found that the older general public strongly supports a policy of surrogate consent for dementia research and that this support increased after in-depth education and peer deliberation; for example, at baseline, support for a policy of surrogate consent for a dementia research protocol involving gene transfer neurosurgery increased from 56% to 68% after deliberation. (22) Our thematic analysis of participants' deliberations provides important insights into what this overall support means.

The attitude reflected in the deliberations can best be described as "cautious pragmatism." The participants reasoned their way through the complex ethical issues, aware of both the pros and cons of policy options, while maintaining their focus on practical solutions. They were strongly attracted by the potential of advance directives and tried to remedy their inherent shortcomings. These ideas included not only the expected "public campaign" type solutions but also the idea of obtaining a directive very early on in the course of dementia, which has recently become a focus of discussion.(27)

The participants' acceptance of the need for surrogate consent for dementia research was not an unthinking or idealized endorsement. They clearly recognized the potential pitfalls of such a policy and focused on providing practical safeguards. Their approach was, in effect, "trust but verify"—surrogate consent implies a trust in the surrogates to do the right thing, but procedures should be in place that maximize the likelihood that they can do the job of a surrogate. For example, the idea of conducting a screening interview, or even a capacity assessment, of the potential surrogates may in fact be justifiable (especially for high risk studies) on the grounds that although most adults when acting on their own behalf may deserve the presumption of capacity, when they are acting on behalf of others for decisions that are not inherently in their interest, the weight of that presumption can be less.

In their deliberation over specific research scenarios, we found that the participants, not surprisingly, weighed potential benefits against the risks of harm inherent in research protocols. But the details of their deliberations reveal that the participants were able to incorporate new materials into their reasoning process. They were able to distinguish between societal and individual benefits, use concrete examples of how research monitoring works, use the idea that a person might be incompetent to provide informed consent and yet be able to express meaningful preferences through assent or dissent, and understand that historical abuses have led to an extensive research oversight system. They also evaluated the implications of policy, e.g., they recognized that a policy that disallows surrogate consent is "essentially… voting 'no'" for all families whereas a policy which allows it makes research participation "a singular family or a singular person issue."

There are, however, important limitations to our analysis. First, the DD sessions require a considerable time commitment and there is likely unavoidable self-selection. For example, the high level of trust that most participants showed in the human subject protections system may reflect the fact that people who are willing to attend DD sessions are more likely to engage with "the system." Second, we used only 9 of the 27 transcripts for our qualitative analysis, allowing for the possibility that these were not representative of all session participants. However, after coding seven groups, we were not uncovering new codes, and coding of an additional two groups confirmed saturation. Third, we stratified our coding to have an over-representation of groups that had voted against allowing surrogate consent for at least one research scenario, and this may have led to under-representation of pro-research viewpoints.

Despite these limitations, the results of our analysis are clear. It is possible to elicit highly informed and reasoned public opinions regarding the ethics of surrogate consent for dementia research and these opinions can inform the creation of policy. The public's generally positive view of surrogate consent should not, however, be taken as unalloyed, idealistic trust in science. Rather, the public appears willing to support a policy of surrogate consent, all the while recognizing the potential pitfalls of entrusting the scientific process (which includes an oversight mechanism) and future surrogates to do the right thing. This trust, based on a cautious pragmatism, will likely be dynamic, open to fluctuations that depend on how responsibly our society manages the involvement of vulnerable, incapacitated subjects in research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Plenary Introduction	• Lay out agenda for the day
Small Group Session 1	• Ice-breaker exercises • Video presentation of background on Alzheimer's disease • Discussion focusing on reactions to the video
Plenary Session 1	• The audience is encouraged to ask questions during and immediately following each presentation. Each presentation along with questions and answers takes an hour, for a total of two hours of interactive plenary presentations. (See PDF, Supplemental Digital Content 1) o Presentation and Q&A: "Alzheimer's Disease Clinical Research" o Presentation and Q&A: "Ethical Issues in Surrogate-Based Research"
Small Group Session 2	• Participants are given a chance to reflect upon and discuss the 2 plenary presentations. This allows for reactions and corrections to each other's understanding of the materials presented and to discuss the overall ethical dilemma of surrogate consent for dementia research.
Plenary Session 2	• Question and answer session with the two experts, framed around the scientific and ethical issues regarding the four research scenarios (lumbar puncture study, new drug randomized clinical trial, vaccine study, gene transfer study).
Small Group Session 3	• Participants are asked to reach a group decision for each scenario, by consensus or majority, by answering: "If patients cannot make their own decisions about being in studies like this one, should our society allow or not allow their families to make the decision in their place?" The groups are also asked to provide their rationale: "Why should surrogate consent be allowed or not allowed?"

Figure 1. Sequence and content of the DD session day[a]

[a]To maintain balanced expert responses to all questions, the two experts (AD clinical researcher and bioethicist) are available and travel together from table to table to answer questions throughout the day. Breaks and meal times are not shown.

Lumbar puncture study	Researchers want to study the fluid that surrounds the brain in patients with Alzheimer's. The fluid is removed by a process called a lumbar puncture. In a lumbar puncture, a doctor inserts a long needle through the lower back into the spinal canal. The patients are given numbing medicine but they may experience a small amount of pain. About 5% of patients get headaches that go away with Tylenol. About 1% get a severe headache that requires a procedure which involves inserting a needle into the lower back again. The study will not directly benefit these patients. But it may lead to better understanding of Alzheimer's disease that may help future patients.
New drug study	Researchers want to test a new drug to see how well it treats Alzheimer's disease. One half of the subjects will receive the new drug, and the other half of the subjects will get a sugar pill (that has no drug in it). The subjects will be randomly assigned (by chance, like flipping a coin) to get either the drug pill or the sugar pill. The new drug can cause upset stomach in some people, and in rare cases, bleeding in the stomach. The study may benefit some of these patients if the drug proves to be safe and effective. On the other hand, the drug may not work and it has the risks mentioned above.
Vaccine study	Researchers are developing a vaccine for Alzheimer's disease. It involves getting one shot every three months (for a total of five shots) and two lumbar punctures (in which a long, thin needle is inserted into the lower back to obtain fluid from the spinal canal).

	In a previous study, 18 out of 300 persons (or 6%) who got the vaccine developed brain inflammation. This brain inflammation caused one or more of the following symptoms: confusion, headache, sleepiness, vomiting, seizures, and difficulty with balance and speech. 7 of the 18 persons had permanent problems. However, in 60 out of 300 persons (or 20%), the vaccine seemed to help their symptoms slightly. Researchers have now changed the vaccine to try to make it safer.
Gene transfer study	Researchers want to begin testing a treatment for Alzheimer's disease where doctors insert genetic material (DNA) into the brains of Alzheimer's patients using brain surgery. This is to be the first study of this kind involving humans and the main purpose is to test its safety in just a few people, before moving on to larger studies. One risk of brain surgery is a 1-4% chance of bleeding into the brain. This is usually minor, but rarely it can cause serious harm. It is possible that gene transfer could make Alzheimer's symptoms worse, cause brain tumors or cause brain inflammation. No one knows how likely these risks are.

Figure 2.
Four Alzheimer disease clinical research scenarios discussed during deliberation.

Table 1

Participant characteristics, n=160.

Demographics	n (%)[a] or Mean±SD
Female	97 (61)
Age (years)	63±8
What is your current marital status?	
Single	13 (8)
Married	103 (64)
Divorced	26 (16)
Widowed	17 (11)
Are you Hispanic or Latino/Latina?	
Yes	1 (1)
What is your race?	
White	143 (89)
Black or African-American	16 (10)
Other	1 (1)
What is the highest level of education you have completed?	
Less than college	81 (51)
College	39 (24)
More than college	40 (25)
In general, how do your finances work out at the end of a typical month?	
Some money left over	110 (69)
Just enough to make ends meet	37 (23)
Not enough to make ends meet	8 (5)
Do you have any relationship with an Alzheimer's patient?	
Primary Caregiver/Decision-maker	46 (29)
Close to someone with AD	70 (44)
No relation	43 (27)

[a]Some percentages do not add to 100 because not all participants answered the question.