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Do Elderly Persons' Concerns for Family Burden Influence their Preferences for Future Participation in Dementia Research?

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BACKGROUND

Clinical dementia research often requires participation by cognitively impaired subjects for whom informed consent is provided by surrogates. Researchers encourage the use of various surrogate decision-making methods that are well-established in clinical care. These mechanisms, however, have been imported from the clinic with little modification, even though clinical care and clinical research differ in fundamental objectives (patient care versus developing new knowledge) and primary principles (beneficence versus truth), and the ethical and legal standards for informed consent for research are more rigorous than consent for treatment. Furthermore, surrogacy in clinical care is widely recognized as highly imperfect, and its validity in research is far less well understood.

Despite these conceptual issues, researchers promote the use of research proxies and research living wills to protect incapacitated adult subjects. Practical problems also exist, and well-known challenges that are associated with directives in clinical care are likely to be amplified when these are used for research. For example, few among the public complete proxy or treatment directive documents due to sociological, cultural, and other barriers.[1] Fewer still are likely to complete less essential and more complex directives for investigational interventions. Living wills frequently use ambiguous terms and criteria, and rely on "boilerplate" documents that dubiously represent patients' authentic wishes.[2] For logistical and other reasons, living wills are often ignored during actual decision making.[3] Furthermore, statements in these directives are unlikely to be specific enough, or well enough informed, to independently satisfy rigorous consent requirements for entry into research.[4]

Finally, the relatively few subjects who, while capacitated, complete research advance directives may ultimately bear a disproportionate share of the burden for research participation.[5] Such a skewed pool of research subjects may also threaten the validity of study findings.

Despite the promotion of research directives, research consent will likely remain the province of next-

of-kin who have little specific understanding of their relatives' preferences for participation in research. These surrogates typically employ the best-interest standard or the substituted-judgment standard for decision making, although neither relate easily to research.[6] Enrollment predicated on best interest is problematic, because subjects' best interests are often irreconcilable with the structure of clinical research, in which burdens fall squarely on subjects while benefits are intended for future patients.

More often, surrogates are encouraged to replicate patients' decisions by considering patients' preferences, values, and interests, in accordance with the substituted-judgment standard.[7] However, surrogates' treatment decisions are frequently inaccurate, and concordance is poorer still for decisions about research.[8] Nevertheless, patients, little troubled by this inaccuracy, continue to depend on surrogates for both clinical and research decisions. Patients may be more concerned with fidelity and with their surrogates' comfort with the decisions that are ultimately made.[9] Some patients do not expect surrogates to follow their precise wishes, and other patients alter their preferences in response to their family members' concerns.[10] Patients' concerns about the burdens that may be placed on their families influence their preferences regarding treatment, and some patients want their surrogates' decisions to reflect these concerns.[11] Unfortunately, patients' interests in family well-being is discounted in practice and in academic discourse.[12]

Empiric study of surrogacy in research, in general, is limited. In particular, there has been scant research on subjects' concern for family burden in decisions about research participation, despite ample evidence that family burden is a central concern among ill persons.[13] Because subjects' concerns for their family remain unexamined, surrogates may consider their own burden in their substituted judgments without reference to the way that the subject preferred to consider family burden.[14] If respect for autonomy requires an accounting of all important concerns of subjects, and concern for family burden is among these, then this should be an actively considered content area in substituted judgment for research (and for treatment).[15]

More empirical data on research surrogacy is needed to address the significant ethical gaps in widely held normative positions in which the ethical basis for consent to participate in research by a third party is not clearly defined.[16] Since conventional mechanisms for consent that attempt to replicate narrowly drawn preferences of subjects are ethically problematic, a more qualitative approach to determining subjects' preferences, one that integrates a greater range of subjects' concerns, may provide a valuable and more authentic basis for consent. For example, ethical surrogate decisions for dementia research should include decisions that subjects would embrace because their participation will advance their interest in attenuating the burden on their surrogates (for example, less emotional distress by exhausting all treatment possibilities, or by creating altruistic meaning from a devastating illness). A greater understanding of the ethics of surrogate consent for research must be developed to respect subjects, to promote appropriate research involving noncapacitated subjects, and to better ethically clarify surrogates' authority.

This exploratory, qualitative study is a first step toward identifying elderly participants' specific preferences for research surrogacy and the importance of burden on surrogates in this decision-making process. The research sought to address three specific questions:

1. Do elderly persons presume that their health surrogates have authority over their entry into research, based on trust and fidelity, rather than on replicating specific choices?
2. Is concern for family burden a widely held central interest of potential subjects of dementia research?
3. Do elderly persons want this concern to be a major consideration in surrogates' decisions regarding participation in research made on their behalf?

METHODS

In-person, semi-structured interviews were conducted with 10 older adults. Participants were recruited from among patients in a suburban, hospital-based, geriatric medicine practice. All interviews were conducted by the first author. Interviews were tape-recorded and transcribed verbatim. Participants also completed a brief written questionnaire prior to each interview. Only demographic information from this questionnaire will be reported here.

THE SEMI-STRUCTURED INTERVIEW

Participants reported whom they would rely on as a health surrogate, whether or not they had formally appointed a healthcare proxy, and the reasons for choosing that individual or individuals. The interviewer assessed subjects' preferences for different levels of care and for participation in different types of research for hypothetical conditions of moderate and severe dementia. Subjects were reassessed for their preferences for treatment and for participation in research when decisions would be made by their surrogates. For preferences regarding participation in dementia research, participants were asked to describe: (1) their direct preferences for research participation, (2) their preferences for participation if their surrogate was responsible for the decision, and, finally, (3) their preferences for their surrogate's consent for research, should their surrogate find benefits through relief of emotional burden, financial burden, physical burden, and social burden. For each scenario, subjects were asked whether they would be willing to enroll (or would want their surrogate to enroll them) in each of the following types of research study: drawing blood only, physical exam only, taking a drug approved by the Food and Drug Administration (FDA) with a low risk of side-effects, taking an FDA-approved drug with a risk of serious or irreversible side-effects, or taking a nonapproved experimental drug.

Before asking about treatment preferences, the interviewer read a definition of moderate and severe dementia based upon Reisberg's Global Deterioration Scale for Alzheimer's Disease, so that each participant would use a consistent definition of these stages of dementia when answering the interview questions.[17] The interviewer also described four types of burdens on family that are common in dementia care—emotional, financial, physical, and social—so that participants would again use consistent definitions.

DATA ANALYSIS

The authors analyzed transcripts of a subset of interviews to identify common themes. From these themes, a coding scheme was developed. The authors analyzed a second subset of interviews using the coding scheme, discussing any discrepancies and revising the coding scheme, until 100 percent agreement was achieved. Finally, all interviews were re-analyzed using the revised coding scheme.

RESULTS

SAMPLE

Ten participants were recruited through a suburban primary care geriatric medical practice. Inclusion criteria consisted of English-speaking, older adults (aged 65 or older) without cognitive impairment. The sample consisted of two men and eight women with a mean age of 73.6 years (range 67 to 80). All were White and middle-class; eight subjects had graduate degrees. Six were married; four were no longer married, three due to death and one to divorce. All but one had children.

ADVANCE DIRECTIVES, HEALTHCARE PROXIES, AND RESEARCH SURROGACY

All 10 participants had some form of written advance directive in place and most (six) had both an advance directive and a healthcare proxy. All participants chose members of their immediate family as their surrogate. All married participants (six) chose their spouse as a first choice; the others chose an adult child. Only two participants mentioned more distant relatives or friends as surrogates, and these were alternates in case a spouse was incapacitated as well.

When asked why they chose a particular individual to act as their surrogate, participants overwhelmingly cited trust and family closeness. For many, trust was based upon their family member's performance in a past crisis: "Because they love me and they're close to me and they've helped me before in a very difficult situation." Another participant described a specific trauma from the past: "We went through the loss of my oldest son, their brother and he [the son chosen as proxy] was with him [the son who died] at the time."

For other participants, trust was based purely on the family relationship and the perception that the surrogate knew the subject well: "She's most familiar with what I want, as I am with what she wants. She's really the one I trust the most." As another respondent explained, "My husband or my cousin who has been listening to me for many years, so she knows where I'm coming from." Another man discussed his confidence in his wife to anticipate his wishes: "In other words I would want her to do what she thinks I would do, and I think she knows me well enough to know that."

Several respondents spoke of a desire to avoid family conflicts in their choice of a surrogate. For example, one participant chose her husband, even though she felt that one of her sons would make better decisions on her behalf. She said that she wanted to avoid the appearance of favoritism of one child over the others: ". . . we've had these discussions, and I'll say to him, 'If anything happens to me I'll give you [her husband] three months to pull the plug.' He'll say, 'Don't pull the plug.' I think on the whole he would probably make the decisions, but I would have a talk with my son if things started, to watch over Dad. . . . We've been married 53 years, so we've developed a relationship; and with five boys, sometimes, even though there's the oldest, the other ones, I think, resent the oldest. So we have trouble: Which one do we ask to do something without upsetting the other ones? So we end up doing it ourselves."

Other respondents spoke about love and family closeness as the basis of their choice of surrogate. "They're the only ones I have. I'm a widow for 30 years and I'm very close to my girls."

Another participant combined all these concerns—love, trust, and avoiding conflict: "Even though she [her daughter] is very busy, she is very compassionate and thinks a lot like me and I feel most comfortable with her. . . . My son is very loving, too, but he's very demanding, and my youngest, who is 10 years younger than the other two, I had her 10 years later, she's too concerned about me. We are very close in a way, and she's too concerned. So that's why I picked the oldest. And being the oldest, you know the others cannot say, 'Why didn't you pick me?' I thought that would be the best."

When asked what they would want their surrogate to consider in making decisions for them, nine of 10 participants spontaneously mentioned the surrogate's welfare and burden as equivalent to, and sometimes exceeding, the subject's own welfare: "Well, I would probably want to go to a facility. I wouldn't want to be a burden." Another explained, "I would never want to be a burden to other people. That's what I dread the most. I always say, 'I hope I get hit by a truck and that's it.' " Others expressed the desire for their caregiver to go on with life: "I guess it depends on the severity of it. I would like her to not spend her every living minute worrying about caring for me. I'd like her to have somewhat of a life of her own."

Other major concerns included the participant's own quality of life and physical comfort, and a desire to maintain personal dignity. "Like I said, I made out the living will, and if I couldn't recover and live any kind of a life, I don't want anything done. I don't want any great precautions made if my heart stops beating. I don't want anyone to bring me back. I'd rather not live that way." Some participants expressed their trust in their proxy to see to it that they would be well cared for: "She would see to it that I wouldn't be in pain. . . . I know she would take care of that." As another put it, "He should think about my dignity, my good health, a safe environment, and hopefully being placed in a place where people are really caring for you in the proper way."

Participants also were asked whether they would be willing to participate in research, and why they would choose to do so. Four respondents had participated in a clinical study in the past, and another five had considered it. When asked about their reasons for considering clinical research, participants voiced two distinct considerations: altruism coupled with the possibility of personal or family gain. Nine cited the desire to help others or further scientific knowledge in general, and nine also described personal reasons, such as access to new medications or the importance of speeding the discovery process in chronic illnesses that ran in their own families. If they themselves could not benefit, they reasoned, then perhaps their children or grandchildren would.

When subjects were asked whether or not their health surrogate should also make decisions about research, all 10 subjects presumed that these individuals would. Subjects generally saw no clear line separating

acting as a health surrogate from acting as a research surrogate. One subject replied, "If I've designated him as my healthcare proxy, I'm incapacitated; it's his decision." Some subjects gave measured license to their surrogates, limiting decisions in various ways. For example, one subject gave his wife blanket authority over nontherapeutic research, while limiting her decisions about therapeutic research to lower-risk studies.

PARTICIPATION IN RESEARCH TO RELIEVE SPECIFIC BURDENS

The next set of questions asked participants whether they would want their surrogates to enroll them in dementia research if participation would relieve specific burdens for the surrogate. Table 1 shows the number of participants who were willing to be enrolled in each type of study under the various hypothetical circumstances.

The overwhelming majority of participants would be willing to have blood drawn, undergo a physical examination, or take an approved drug with a low risk of side-effects for research purposes, whether or not this participation would relieve their surrogate's level of caregiver burden. Overall, participants were reluctant to consider taking experimental drugs or those with serious known side-effects. However, some participants did express willingness to take such drugs, despite their concerns, if doing so would benefit their surrogates in some way. For example, only two would choose to take a drug with serious side-effects for research if they were making the decision themselves, and only three said they would be comfortable with their surrogate making such a decision. However, six respondents said they would definitely be willing to do so if participation in the study provided their surrogate with relief from the physical burden of caregiving, perhaps by offering some form of respite. Similarly, five participants would agree to take a drug if participation in the study relieved their surrogates' emotional burden, and four would take it to relieve social burden.

Participants were not willing to consider participating in a risky study solely for financial gain to the caregiver. Some reported that they had already planned for their own financial futures, so that their care would be covered financially. Another expressed the fear that their children would actually increase their sense of burden of guilt if they accepted money for a parent's or spouse's research participation: "But then she feels like I'm a guinea pig."

Overall, when compared to subjects' direct preferences for research participation, six of 10 subjects were prepared to accept additional research-associated risks specifically to attenuate some type of family burden.

Table 1
Number of Participants Who Would Want to be Enrolled as Subjects in Dementia Research under Various Hypothetical Conditions

	Blood Test		Physical Exam		Low-Risk Drug		High-Risk Drug		Experimental Drug	
Query Re: Type of Participation	Yes	Maybe	Yes	Maybe	Yes	Maybe	Yes	Maybe	Yes	Maybe
Would you enroll?	9	0	10	0	8	1	2	2	4	2
Should surrogate enroll you?	10	0	10	0	9	0	3	1	3	1
To relieve surrogate's emotional burden?	10	0	10	0	9	0	5	1	6	1
To relieve surrogate's physical burden?	9	0	9	0	9	0	6	2	4	3
To relieve surrogate's social burden?	9	0	9	0	9	0	4	2	4	2
To relieve surrogate's financial burden?	8	0	8	0	7	0	2	1	2	1

DISCUSSION

These findings represent a first step in documenting the strong preference of older adults to have their decision-making surrogates consider their concerns for family burden when making choices about participation in dementia research. Overwhelmingly, participants expressed the primacy of close family ties grounded in love, trust, and mutual concern. Participants were adamant that they would not want to be a burden to anyone, should they become physically or mentally incapacitated. They plainly expressed their desire for their surrogates to take their personal needs into account along with the patient's.

Overall, these individuals felt comfortable with the idea of participating in low-risk dementia research, either for possible benefits to themselves and their families or for altruistic reasons. They were more hesitant to become involved in research that involved greater risk that could worsen their condition or cause them pain or discomfort. However, a surprising number of participants were willing to take on these same risks if their surrogate could derive some benefit. They expressed trust that their surrogate would continue to watch out for them, while also voicing the desire that the surrogate not find his or her duties personally overwhelming.

Given the fact that older adults, at least in this sample, consider family burden an important consideration in clinical care and research participation, how can this knowledge inform researchers and ethicists as they develop guidelines for surrogate decision making? If substituted judgments require surrogates to identify what these individuals would want if they were able to make the decision themselves, surrogates should account for subjects' concerns for family burden. Researchers may be reassured by elderly subjects' faith and trust in their family members to make these decisions. Our subjects considered themselves embedded in a family network, and saw the possibility of future incapacity and their loved ones' responsibility for their care as an integral part of that family connection. While each one expressed it differently, all of them indicated that "what is best for my family is also best for me." As one participant put it in discussing her considerations for future treatment: "What am I concerned about? That she [her oldest daughter] takes away from her own family. I know my son-in-law deals very, very badly with sicknesses. My youngest would just be worried sick and wouldn't be able to do her job. She's not married yet. So they would take turns, I know that. And I would want to make it as easy for all three of them as possible." A second woman talked about the importance of her daughters tending to their own young children and busy professional careers, as well as considering their mother's medical condition and quality of life, in making decisions on her behalf. She concluded, "Well, I trust their decisions. They can make any decisions they want. I'll leave it to them."

LIMITATIONS

The generalizability of our study is limited for several reasons, in addition to the small size of the subject group. The participants represent a convenience sample drawn from a White, middle-class, and well-educated community. All participants already had completed one or more advance directive documents. Our subjects were atypical in that nearly all of them had participated in research or had considered doing so. Preferences and beliefs are sure to differ in the general population. Future studies should draw from a wider range of ethnic, religious, and socioeconomic groups to insure wider generalizability. We suspect that, among some minority ethnic groups in which identification with family is stronger compared to the dominant culture, preferences to participate in research may be more highly influenced by concerns for family burden.

The small number of participants makes it impossible to conduct statistical analyses. Therefore, we cannot determine whether the increased number of participants willing to participate in greater risk research to alleviate family burden is a reliable finding or due to chance.

Despite these limitations, these data offer insight into the importance of family concerns in making research and treatment decisions among older adults. Future research should explore these values with larger and more diverse samples. This information is crucial in order to strengthen our understanding of the ethics of third-party consent for research.

NOTES

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