

***Dementia Research: Responding to the Need Through Autonomous Choice***

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Mary Paul\*

ABSTRACT

Dementia is progressive and is characterized by fluctuating cognition, which presents challenges in the assessment of decision-making capacity and, ultimately, for informed consent. The responsibility for ethical research combined with the fluctuating cognition associated with dementia necessitates using a flexible decision-making and capacity assessment process that respects the autonomy of the participant, the uneven decline associated with the disease process, and responds to the urgent need for increased participation in studies.

**Keywords:** Dementia, Research Participation, Informed Consent, Decision-making, Exploitation

INTRODUCTION

Dementia, a common neurodegenerative disorder, is a leading cause of death worldwide and is estimated to affect more than 55 million people.<sup>1</sup> In the United States, 1 in 9 (6.7 million) people aged 65 and older have Alzheimer's disease—the most common type of dementia.<sup>2</sup> While dementia is a research priority and the National Institutes of Health funding for it exceeds \$3.7 billion annually, further clinical research and research participants are needed to understand and identify new approaches to prevent, diagnose, and treat dementia.<sup>3</sup> A significant barrier to research is the recruitment of persons with dementia as participants, specifically because of challenges in evaluating decision-making capacity and obtaining truly informed consent.<sup>4</sup>

Continued successful advocacy for additional dementia research requires more research at all stages of the dementia disease process<sup>5</sup> to better understand how and why the brain changes.<sup>6</sup> To reduce the physical, psychological, and financial impact on individuals and society, this research should include drug trials, medical devices, diagnostic tools, and both behavioral and lifestyle changes.<sup>7</sup> A potential ethical solution is

\* Mary Paul, D. Bioethics, Loyola University Chicago, MA, Clinical Ethics, Georgetown University, MA, Theology, Aquinas Institute of Theology

the use of a supported decision-making model for persons with dementia, which would not only reduce barriers to research participation but also promote individual autonomy.

## BACKGROUND

While dementia is progressive, it is also characterized by fluctuating cognition, which presents challenges in the assessment of decision-making capacity and, ultimately, informed consent.<sup>8</sup> Meaningful consent requires that the person providing it has the capacity to do so, yet these capacities may be reduced by the cognitive impairment and fluctuation associated with dementia.<sup>9</sup> Cognitive fluctuation means that decision-making capacity not only changes during different situations and over time but also may be time and task-specific.<sup>10</sup> The responsibility for ethical research combined with the fluctuating cognition associated with dementia necessitates the use of a supported decision-making and capacity assessment process that respects the autonomy of the participant, the uneven decline associated with the disease process, and responds to the urgent need for increased participation in studies.

### I. Research Participants and Barriers to Dementia Research

Increased investment in dementia research has increased the number of treatment, prevention, and care studies and has produced an urgent need to recruit and enroll participants in studies.<sup>11</sup> For example, Alzheimer's clinical trials are seeking more than 270,000 participants, with only one in ten persons screened being eligible for participation.<sup>12</sup> Research participation poses challenges, with the top barriers being the participant (study partner) burden and lack of awareness and resources among primary care physicians.<sup>13</sup> Many studies require participation by those who can provide informed consent and adhere to study procedures. Yet many caregivers of the patient, such as a spouse or family member, are reluctant to participate in studies due to extensive time commitments and unwillingness to authorize extensive screening tests that may not help the participant and may even cause discomfort or harm.<sup>14</sup> Furthermore, research participation may have risks of drug side effects. Additionally, physician offices may not be equipped to perform dementia-related diagnostic assessments and screening and may be unaware of opportunities for research participation.<sup>15</sup>

Informed consent and the recruitment of persons with dementia for research is complex because of fluctuating and progressively diminishing capacity of persons with dementia.<sup>16</sup> The inability to make one type of decision does not mean that there is an overall lack of ability to make decisions. Persons with dementia, for instance, may not have the capacity to agree to a complex treatment program or surgery, but they may have the ability to decide to take a new medication or to get a flu shot.<sup>17</sup>

### II. Capacity Assessment and Supported Decision-making

Decision-making capacity varies along a continuum and is affected by factors such as mood and motivation, yet the research review and approval processes require a categorical, binary determination about a continuous phenomenon.<sup>18</sup> Decision-making capacity is not always linear and includes factors such as mood, trust, and timing.<sup>19</sup> Informed consent and the associated assessment of decision-making capacity for research is determined by the investigator where the exposure to the potential participant over time is intermittent and limited, and where the researcher's goal is generalizable knowledge rather than treatment of the patient. Therefore, while the principal investigator should have the most comprehensive knowledge about the potential risks and harms of any drugs or procedures being performed as part of the research, the principal investigator might have limited knowledge of potential participant values, preferences, and goals and how the participant might view risks and harms.<sup>20</sup> Current literature demonstrates that while

researchers are willing to support the decision of persons with dementia to participate or not, researchers are not equipped to assist in decision assistance and concrete decision support measures.<sup>21</sup> Further, decision assistance by the researcher may not be appropriate and could create a conflict of interest.

Persons with dementia should participate in decision-making about research participation, although they may lack decisional capacity when it comes to other decisions, including other healthcare decisions, and they may need support in making those decisions. If they understand the risks and the responsibilities of the research study, then they should be able to decide, even if a surrogate decision-maker has been identified. Surrogate decision-makers can fail to incorporate the nuanced context related to fluctuating capacity. Clinicians, surrogates, or other legally authorized representatives are oftentimes “gatekeepers” to potential research participants and may not make a decision that reflects what the patient would want.<sup>22</sup> Institutional review boards provide inadequate protection from misaligned decisions by surrogates because they also lack knowledge of the participant’s current values and preferences.<sup>23</sup> Due to the slow, progressive nature of dementia and the need to assess decision-making capacity for medical treatments early in the disease process, the default position may be overreliance on surrogate decision-making throughout the disease process for all decisions, even when the individual has some capacity and desire to make decisions autonomously.<sup>24</sup>

Capacity assessment is not an all-or-nothing proposition, and supported decision-making could enable persons with dementia to retain their ability to make autonomous choices.<sup>25</sup> Supported decision-making is a structured yet flexible process that fosters independence. As of 2024, 18 states plus the District of Columbia have passed supported decision-making laws.<sup>26</sup> Trusted advisors, called supporters, often selected by the individual, help the person understand, consider, and communicate decisions about areas where decision-making assistance may be needed, such as research participation.<sup>27</sup> Supporters, for example, would gather relevant information, including from the researcher and care provider, and provide information to the potential participants, enabling them to make their own decisions. The research participants would make decisions about when, where, and how capacity tests would be performed in addition to decisions about their medical care and research participation. Ideally, the selected test would be relevant to the risk of the intervention, decisional complexity, and consequences of the intervention and should be performed under optimal circumstances and conditions.<sup>28</sup> Supported decision-making helps fulfill the researcher’s obligation to assure adequate consent with a process that promotes autonomous participant decision-making rather than defaulting to a proxy or surrogate.

This collaboration between supporters and research participants should enhance the participant’s understanding of the risks and benefits of the research. Working together, clinicians, researchers, research participants, and relatives can mitigate challenges such as stakeholder biases, role confusion, and paternalistic behaviors.<sup>29</sup> An estimated 75 percent of caregiving for a patient with dementia is provided informally by friends and family.<sup>30</sup> This already existing informal network provides the foundation for a more structured, supported decision-making model that recognizes the strengths and capacities of various stakeholders and trusted advisors, with an aim to promote participant autonomy. These trusted advisors should know the individual’s values and goals and should assist the potential participant to express, not construct, their decisions.

Structured, supported decision-making with trusted advisors can be implemented on a case-by-case basis for individuals determined to have dynamic functional impairments. Implementation begins with the identification of the areas of assistance needed specific to the research study under consideration. Next,

the persons who could serve as supporters should be identified. The individual should discuss the role with each potential supporter and any agreement should be documented.<sup>31</sup>

Supporters are selected by the beneficiary and are usually friends, family members, or experts who know and respect the individual's will and preferences. The role of the supporter is to provide information to the individual so that the *individual* can decide. For example, if the research is social or behavioral in nature, and involves physical activity or interaction with other individuals, a friend who has knowledge of the individual's daily activities could provide guidance as to an optimal time of day for participation. If the research involves medical testing, a family member could gather and present pros and cons of the procedure to the individual. Most importantly, supporters are people who know and respect the values of the potential participant and commit to assisting the individual in making their own decision.

A supported decision-making model will not only increase much-needed research participation but will also promote the autonomous decision-making of the participant. This model for research participation decision-making shifts the process from a traditional assessment of decisional capacity to a study-specific assessment that engages trusted stakeholders earlier and throughout the participation period and assesses capacity with a relevant task at an optimal time.

### III. Counterarguments to Supported Decision-making

Despite its benefits, supported decision-making has its limits and its risks. First, while dementia is characterized by fluctuating capacity, dementia is progressive and may require other surrogate approaches to decision-making, especially in the late stages of the disease. Surrogate or proxy decision-making may be appropriate for persons who consistently lack capacity, and the appropriateness of supported decision-making for persons with fluctuating capacity must be regularly evaluated and modified as needed. Second, no systematic method for determining whether a supporter has offered non-biased or non-controlling advice to the individual or if the individual's decision has been properly represented or communicated has been identified. These challenges are not unique to supported decision-making, however. For example, surrogates may not easily identify or prioritize the relevant values associated with a particular decision, such as quality versus quantity of life. Further, a surrogate may make decisions based on personal desire for patient survival. Frameworks for value-based decision-making have been developed to support surrogates and to manage biases.<sup>32</sup> These frameworks could serve as a model for trusted stakeholders to adopt as part of the supported decision-making model. Third, the processes and roles of the stakeholders remain somewhat vague. The determination of which supporter is assigned to which decision or topic can be complex and requires good collaboration and communication among supporters and researchers. Through a supported decision-making model, an opportunity exists to blend the skills, expertise, and knowledge of all parties toward the benefit of appropriate research along with an effort to reinforce, rather than override, individual autonomy.

### IV. Counterarguments to Encouraging Research Participation

There is a growing need to include persons with dementia in research. At the same time, many people may believe that research on individuals with diminished decisional capacity can place this vulnerable population at risk of physical, social, and psychological harm.<sup>33</sup> Further, this research may lead to drugs for future patients rather than the research subjects, many of whom would be nearing the end of life. Research undertaken with any vulnerable population raises concerns about how human dignity is both promoted and protected. However, failure to include this population in appropriate research can also contribute to the harm of individuals by slowing the development of evidence-based interventions.<sup>34</sup> Representation of

the interests of individuals with dementia, along with the protection of their rights, is paramount when ensuring research is ethical. Researchers, institutional review boards, and individual decision-makers must adhere to ethical research practices. Rather than posing unacceptable risks to research participants, low-risk research performed ethically could benefit patients by allowing them to contribute to solutions. While research is generally for the good of others or society, some research would increase the possibility of new treatments during the research subject's lifetime.

## CONCLUSION

Research to prevent, diagnose, and cure dementia remains a national priority due to both the human and societal impact of dementia as well as the direct and indirect costs associated with dementia care. Research funding toward these ends continues to increase at a rate that exceeds available participants.<sup>35</sup> Research participation is always a choice. Informed consent is the gold standard by which researchers protect participant autonomy and prevent coercion and biases so that the potential participant can make an informed choice. The progressive and fluctuating capacity associated with dementia poses significant and unique challenges to informed consent and associated decisional capacity assessment. A principal investigator's determination that a research protocol is minimal risk increases the likelihood that the research can ethically proceed, yet that determination has risks and challenges.

The fluctuating and, at times, impaired decisional capacity of persons with dementia makes recruiting participants difficult.<sup>36</sup> Different circumstances or conditions may demand different functional abilities—different tests of capacity based on risk.<sup>37</sup> Promoting autonomous decision-making in participants with impaired capacity does not necessarily require an alternate decision-maker but a supported decision-making structure that can adapt to the fluctuating capacity and risk of the decision.

A supported decision-making model that honors professional obligations and responsibilities, and brings together researchers, clinicians, caregivers, family, and friends in response to the fluctuating capacity of the potential participant is one way to increase research participation while respecting individual autonomy. The goal is to prioritize improved, autonomous decision-making for as long as possible so that persons with diminished decisional capacity can participate in dementia research—the right research at the right time with the right participant.

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