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Review Article

Consent and Capacity in Dementia Research: Rethinking Proxy Decision-Making

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ABSTRACT

Dementia research depends on enrolling people whose decision-making capacity is often partial, fluctuating, or absent, which places substantial strain on the standard model of individual informed consent.

This review examines how the field has tried to make research participation ethically defensible despite this strain, beginning with the difficulty of assessing decision-specific capacity that changes over time and by task.

It then surveys proxy or surrogate consent combined with ongoing assent and dissent monitoring, and the unresolved question of what standard a surrogate should apply when the research offers the participant no direct benefit.

We examine advance research directives as an alternative that lets a person specify research wishes while still competent, and the long-running philosophical dispute over whether such directives should bind a person whose values may have changed with disease progression.

We conclude that no single mechanism resolves the tension between honoring a person's present will and their prior wishes, and that defensible practice likely requires combining risk-sensitive capacity assessment, genuine attention to assent and dissent throughout a study, and legal recognition for advance research directives that stops short of treating them as automatically dispositive.

Keywords: informed consent; dementia research; decision-making capacity; proxy consent; advance directives

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INTRODUCTION

Dementia research occupies an uncomfortable place in

research ethics because the population it most needs to study is, by definition, the population least able to satisfy the standard model of informed consent. A

person with mild cognitive impairment may retain enough decisional capacity to weigh a study's risks and benefits in a meaningful way; a person with advanced Alzheimer's disease typically cannot. Between those two poles lies a long, uneven decline during which capacity fluctuates by task, by time of day, and by how a study's risks are explained, which makes any single yes-or-no capacity determination a crude instrument for a genuinely continuous condition [1]. Excluding everyone below some conservative capacity threshold would protect individuals from exploitation but would also make it nearly impossible to study the disease that most needs studying, since the trial population would systematically exclude the more advanced stages that carry the greatest disease burden [2].

The field's practical answer has been proxy or surrogate consent: a legally authorized representative, usually a spouse or adult child, consents to research participation on the patient's behalf, subject to the patient's own assent or lack of dissent. This arrangement is well established in clinical decision-making, where surrogates routinely authorize treatment for incapacitated patients, but its extension to research is more ethically fraught, because research, unlike treatment, is not undertaken primarily for the participant's own benefit [3]. A surrogate deciding whether to withdraw life support is applying a substituted-judgment or best-interests standard to a decision with a reasonably clear therapeutic stake; a surrogate deciding whether a relative with dementia should undergo a lumbar puncture for a biomarker study, with no prospect of personal therapeutic benefit, is doing something conceptually different, and the ethics literature has been correspondingly more cautious about it [4]. This review surveys how the field has tried to make proxy consent for dementia research defensible: through the assent/dissent framework, through advance research directives, and through ongoing empirical and philosophical debate over how much authority a person's past, competent wishes should retain once their values may have changed. Table 1 summarizes the main proxy-decision-making mechanisms this literature has produced, and Figure 1 offers a schematic view of how the tension between honoring the current person and the person's prior wishes shifts across these mechanisms and across the stages of the disease.

ASSESSING CAPACITY: A MOVING, NOT A FIXED, TARGET

The clinical and legal instruments used to assess decision-making capacity for research were largely developed with a single competent adult in mind, evaluated once at enrollment. Dementia does not cooperate with that model. Capacity is decision-specific rather than global -- a person may be able to understand and appreciate the implications of a low-risk observational study while lacking the capacity

to consent to a study involving an experimental drug with meaningful side effects -- and it can also fluctuate within the same day, particularly for people experiencing delirium-like states superimposed on an underlying dementia [5]. A widely cited framework from work on Alzheimer's clinical trials scored capacity along four legally recognized standards -- expressing a choice, understanding relevant information, appreciating the situation and its consequences, and reasoning about treatment options -- and found that impairment on the more demanding standards (appreciation and reasoning) appeared well before a person lost the ability simply to state a preference, meaning that a person who can clearly say "yes, I want to participate" may nonetheless be doing so without the reasoning capacity the law formally requires [6].

This has practical consequences for how institutional review boards and researchers actually operate. Some have proposed a sliding-scale standard, where the threshold for adequate capacity rises with the risk of the proposed research -- a lower bar for a survey, a higher bar for anything invasive -- rather than a single fixed threshold applied uniformly regardless of what is being asked of the participant [7]. Qualitative work with clinicians who conduct these assessments in practice has found persistent disagreement over how to operationalize "appreciation" in particular, since it requires a judgment about whether the person has genuinely internalized their own diagnosis and its implications, not merely whether they can repeat back the information they were just given [8]. The result is a domain where capacity determinations carry more clinical judgment, and more room for inconsistency across evaluators and sites, than the tidy language of "capacity" versus "incapacity" in most consent regulations tends to suggest.

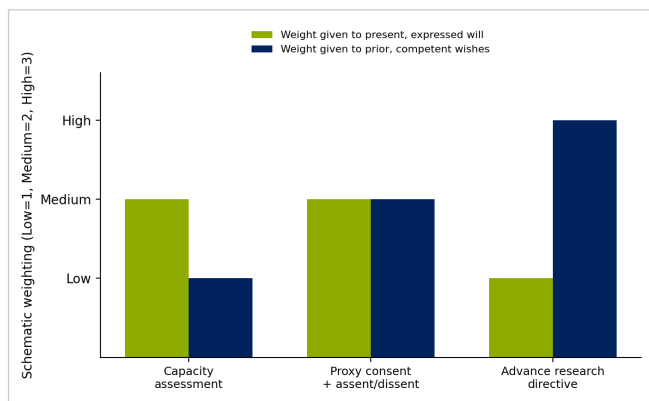
PROXY CONSENT, ASSENT, AND THE LIMITS OF SUBSTITUTED JUDGMENT

Once a person is judged to lack the capacity to consent independently, the default mechanism in most jurisdictions is proxy consent by a legally authorized representative, combined with an obligation to seek the participant's own assent and to respect any dissent they express, however impaired their formal decisional capacity may be. This assent/dissent framework is meant to preserve some form of participant agency even after legal capacity has been lost, on the reasoning that a person's expressed discomfort or refusal carries moral weight independent of whether it reflects a fully reasoned judgment [9]. In practice, this is harder to implement consistently than it sounds: research teams must decide how to interpret ambiguous behavioral signals -- resistance to a blood draw might reflect genuine dissent, or might reflect confusion, fear of an unfamiliar procedure, or simple discomfort unrelated to the research itself -- and different teams resolve that ambiguity differently [10].

Table 1. Mechanisms used to authorize dementia research participation, compared by decision-maker and the standard each is meant to apply.

Mechanism	Decision-maker	Governing standard	Main ethical limitation
Capacity assessment	Clinician/researcher, at enrollment	Decision-specific competence (choice, understanding, appreciation, reasoning)	Fluctuates over time and by task; does not itself resolve who decides once incapacity is found
Proxy/surrogate consent with assent-dissent	Legally authorized representative, with participant assent sought	Substituted judgment or best interests, moderated by observed dissent	Ambiguous behavioral signals; unclear whether an uncompensated surrogate is a legitimate proxy for non-therapeutic research
Advance research directive	The person's own prior, competent decision	The person's previously stated wishes	Uncertain authority once values or the sense of self may have changed with disease progression

Figure 1. Schematic comparison of how much weight each proxy-decision-making mechanism gives to a person's present, expressed will versus their prior, competent wishes (illustrative, not derived from a single empirical study).



Surveys of the surrogates who actually make these decisions complicate the picture further. A national survey of older Americans serving as potential proxies found that willingness to authorize a relative's participation in dementia research varied considerably by study risk and that many surrogates reported real uncertainty about whether they were applying the patient's own prior wishes, their own judgment of the patient's best interests, or some blend of the two that they could not clearly articulate [11]. Interview-based work with people actually serving as study partners for people with Alzheimer's disease has found that the assent/dissent process, and surrogate decision-making generally, can impose real emotional

burdens on the surrogate -- guilt over enrolling a relative in a study with no direct benefit, or conversely over declining a study that might contribute to future treatments -- that the research ethics literature has historically treated as a side issue rather than a cost to be weighed directly [12]. A separate body of work asks the harder normative question underneath these surveys: does a surrogate deciding about research participation for someone who cannot benefit from it function as an ethically legitimate decision-maker at all, or does the absence of any expected benefit to the participant strip the surrogate's authority of the moral basis it has in ordinary medical decision-making [3]?

ADVANCE RESEARCH DIRECTIVES AND THE PROBLEM OF CHANGED VALUES

If the difficulty with proxy consent is that a surrogate is guessing at what an incapacitated person would have wanted, one natural solution is to ask the person directly, in advance, while they still have capacity: an advance research directive, structurally parallel to an advance directive for medical treatment, in which a person specifies whether and under what conditions they would want to participate in research after losing capacity [13]. Early proposals for this instrument argued that it would resolve the guesswork inherent in surrogate decision-making by substituting the actual prior wishes of the person for a surrogate's best approximation of those wishes, and several US states and other jurisdictions have since developed legal mechanisms recognizing some form of research-specific advance directive [14].

The advance directive solution runs into a deep philosophical problem that has occupied bioethicists for decades: whether the wishes a person expressed while cognitively intact should bind the person they become after dementia has substantially altered their personality, preferences, and apparent quality of life. Ronald Dworkin's influential distinction between a person's "experiential interests" (their moment-to-moment comfort and preferences) and "critical interests" (their considered judgments about what makes their life as a whole go well) argued that critical interests, including those expressed in an advance directive, should generally take priority even after dementia has eroded the capacity to hold or express them [15]. Critics have responded that this treats the person with dementia as a mere vessel for the wishes of their former, competent self, discounting the moral standing of the person who is actually alive now and who may, in an important sense, no longer be the same person who wrote the directive [4]. A related line of argument holds that even severely impaired individuals retain a capacity to value experiences and relationships in the present, and that respecting this present-tense agency sometimes requires overriding a prior directive rather than mechanically enforcing it [16]. More recent philosophical work has tried to move past this binary by asking under what conditions value

change in dementia should be understood as authentic development of the person, deserving deference, versus a symptom of the disease that a prior directive was specifically meant to guard against [17]. A parallel legal literature, drawing on the more developed practice around advance euthanasia directives in some European jurisdictions, has argued that research advance directives deserve similarly explicit legal status rather than remaining an ethical aspiration with no binding force in most legal systems [18].

For non-therapeutic research specifically -- studies offering no prospect of benefit to the participant, such as many biomarker or natural-history studies -- the case for advance consent is often considered stronger precisely because there is no competing therapeutic interest to weigh against the person's prior wishes, but this is also where the changed-values problem bites hardest, since these are exactly the studies a once-competent person is least likely to have anticipated in concrete detail [19].

REGULATORY VARIATION AND THE RISK OF PROTECTIVE EXCLUSION

Countries differ substantially in how they regulate research involving adults who lack capacity to consent, and these differences have real consequences for what gets studied and where. Regulatory frameworks written to protect a historically vulnerable population from exploitation can also function, in practice, to exclude that population from research entirely, producing what has been described as an "evidence-biased" medicine in which treatment guidelines for dementia are extrapolated from studies that structurally excluded the people the guidelines are meant to help [20]. A UK-based analysis of clinical trial recruitment found that adults lacking capacity to consent were substantially underrepresented in trials relative to their share of the relevant patient population, and argued that this gap reflects institutional caution and administrative burden as much as it reflects a considered ethical judgment about acceptable risk [21].

Alzheimer Europe's 2020 report on legal capacity and decision-making surveyed considerable variation across European jurisdictions in how "capacity" is defined and adjudicated, and in what legal mechanisms exist for supported or substituted decision-making, concluding that this patchwork makes multinational dementia research more procedurally complicated without necessarily making any single jurisdiction's protections more coherent [22]. There has also been a shift in emphasis toward involving people with dementia and their care partners directly in the design of studies and consent processes, on the view that much of the difficulty surrounding consent stems from research procedures designed without input from the population they are meant to include, and that public and patient involvement can surface friction points -- confusing language, poorly timed consent conversations,

assumptions about what participants can and cannot understand -- that a purely regulatory approach to capacity assessment tends to miss [23].

CONCLUSION

No single mechanism -- capacity assessment, proxy consent with assent/dissent monitoring, or advance research directives -- fully resolves the ethical difficulty of enrolling people with dementia in research that does not always serve their own interests. Each mechanism addresses part of the problem while leaving another part exposed: capacity assessment tells us when a substitute decision-maker is needed but not how that decision-maker should decide; proxy consent supplies a decision-maker but raises hard questions about what standard that person should apply and what burden the role places on them; and advance directives let people speak for their future selves but cannot fully settle whether that voice should still govern once the person's values may have genuinely changed. What the recent literature converges on is not a formula but a set of practical commitments: capacity assessments that are decision-specific and risk-sensitive rather than binary; genuine, sustained attention to assent and dissent throughout a study rather than only at enrollment; legal recognition for advance research directives sufficient to give them real weight without treating them as automatically dispositive; and a regulatory posture that treats exclusion of people with dementia from research as a cost, not merely a safety default. Getting this balance wrong in either direction has a real cost -- either a research base that continues to underrepresent the population dementia treatments are meant to help, or a research enterprise too permissive about whose voice actually governs the decision to participate.

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Conflict of Interest

The authors declare no conflicts of interest relevant to this work.

Author Contributions

Sigrid Dvorak conceived the review and drafted the sections on capacity assessment and proxy consent. Carla Nowak conducted the literature synthesis on advance research directives and the philosophical debate over changed values, and critically revised the manuscript. Fredrik Nielsen contributed the section on regulatory variation and protective exclusion and

provided final approval of the submitted version. All authors read and approved the final manuscript.

Ethics Statement

As a literature review synthesizing previously published, publicly available research and policy analysis, this article did not involve new data collection from human participants and did not require institutional ethics committee approval.

Data Availability

No new data were generated or analyzed for this review. All sources discussed are cited in the reference list and are publicly available through their respective publishers.

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