

Ethical Issues in Dementia Research (with special emphasis on “informed consent”)

Protecting individuals with dementia who participate in research, and encouraging dementia research to go forward, are twin goals of the Alzheimer's Association. These goals have not been adequately addressed by previous national commissions or federal regulation on research. Making matters worse, the courts and some state governments are scrutinizing research and often complicating rather than clarifying issues surrounding the involvement of human subjects in research, especially if those subjects are unable to give informed consent because of a cognitive or mental impairment. If this trend continues, it could seriously slow down advances in scientific knowledge at a time when research is making enormous progress toward bringing Alzheimer's and other dementias under control.

Critical elements in dementia research

The Alzheimer's Association believes the following variables should be used to assess research protocols involving people with dementia and to develop policies to protect such individuals:

- Risk — is the risk to the individual minimal? Or, is it greater than minimal: (Note: These are “terms of art” used in practice by institutional review boards and ethicists.)
- Potential benefit — is there potential benefit to the individual (therapeutic value)? Or, is there no possibility the research will be of direct benefit to the individual (nontherapeutic)?
- Decisional capacity — is the individual able to make a decision about participation?
- Advance consent — did the individual state his/her preferences about research prior to becoming impaired?
- Available proxy — is a proxy decision maker, such as a family member/caregiver, available?

For minimal risk research all individuals should be allowed to enroll, even if there is no potential benefit to the individual. In the absence of an advance directive, proxy consent is acceptable.

For greater than minimal risk research and if there is a reasonable potential for benefit to the individual, the enrollment of all individuals with Alzheimer's is allowable based on proxy consent. The proxy's consent can be based on either a research specific advance directive or the proxy's judgment of the individual's “best interests.”

For greater than minimal risk research and if there is no reasonable potential for benefit to the individual, only those individuals who (1) are capable of giving their own informed consent or (2) have executed a research specific advance directive, are allowed to participate. In either case, a proxy must be available to monitor the individual's involvement in the research. (Note: This provision means that individuals who are not capable of making their own decisions about research participation and have not executed an advance directive and do not have a proxy to monitor their participation, cannot participate in this category of research. Also, see “A concluding note” below re: definitions of risk.)

In all types of research the following conditions hold:

- A proxy may refuse to enroll a “decisionally incapacitated” individual if that proxy believes that research protocol is not in the best interests of the individual, even if such a decision conflicts with the individual’s advance directive.
- An individual who is not capable of deciding whether to participate in research always retains the right to refuse to participate. The possible exception to this would be if the research has a very high potential benefit and very low risk, where such research is the only way an individual could receive the beneficial treatment, where a proxy gives consent, and where other safeguards are put in place by an institutional review board.
- The involvement of people with dementia in grounds that such individuals are the only appropriate research subjects for answering a specific research question.
- Decision-making capacity is task-specific. Therefore, some cognitively impaired individuals retain the ability to make informed decisions for themselves about participating research.

Other research-related issues supported by the Alzheimer’s Association

Advance Directives for Research: The Alzheimer’s Association encourages the use of formal advance directives for research, especially those that designate a proxy who would be empowered to provide consent for research when the impaired individual is no longer capable of doing so. Such research advance directives would be especially useful for research that has no direct therapeutic value for subjects, a situation in which a normal advance directive for health care might not apply.

Institutional Review Boards (IRBs): The Alzheimer’s Association endorses the continued active involvement of the IRBs as the proper bodies for weighing issues for particular research projects, such as categorizing projects by level of risk, balancing risks and benefits and deciding what additional safeguards a project might require, such as a consent monitor or an independent monitor for the research project.

Community Involvement: Increased community involvement in IRB activities and in establishing values for the larger research enterprise is encouraged.

Clarification of Laws and Regulations: The Alzheimer’s Association calls upon state and federal authorities to clarify existing laws and regulations as they relate to research on people with cognitive impairments. Such clarifications should address the use of advance directives for research and the status of proxy consent in the absence of advance directives and incorporate the principles in the above position statement on protecting individuals with dementia research. The Alzheimer’s Association welcomes, and is well-positioned for, participation in discussions and debates on the policies governing research ethics.

A concluding note:

Definition of Risk: There is considerable disagreement in the ethics literature and in regulatory and statutory language about definitions of risk. In addition to the two polar definitions, “minimal risk” and “greater than minimal risk,” there are also various gradations, such as “minor increase over minimal risk.” The Alzheimer’s Association has chosen not to draw these finer distinctions in its position statement. However, this should not be construed to mean that the Association necessarily opposes involvement of decisionally impaired individuals in all nontherapeutic research involving minor increments over minimal risk. The degree of risk is a judgment call frequently and appropriately made by IRBs. The Association wishes to ensure proper safeguards are in place when risk to the individual is involved, however that risk is defined.

- Adopted by the Alzheimer’s Association National Board of Directors, May 1997