

Protection of Participants in Research

COMMON QUESTIONS

- Is it appropriate for surrogate decision makers to enroll a person with Alzheimer's disease in a research trial?
 - What is the appropriate level of risk to benefit when deciding to enroll a person with Alzheimer's disease in a research study?
 - What principles should guide the decisions of a surrogate?
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BACKGROUND INFORMATION

The Association believes that research to prevent, delay onset, or slow progression of dementia before the advanced stage is among the most pressing medical imperatives of the twenty-first century. It also believes that the protection of those who participate in such research is essential. Informed consent is a central means of protecting participants while allowing them to exercise self-determination. Cognitive disability, however, can make it impossible to obtain valid informed consent. In such cases, persons with Alzheimer's must rely on their surrogates—usually a spouse, child, caregiver, or other trusted individual—just as they eventually must do in all decisions of everyday life or medical care. Research participation is not an exception to this necessary and beneficial dependency on caregivers.

Most discussions about protecting participants in research address issues of risk. There is no single

standard about what constitutes “minimal risk” and “greater than minimal risk” research. The Alzheimer's Association believes that “minimal risk” includes routine observations, data collection, epidemiological surveys, diagnostic interviews, blood draws, and imaging scans. By almost all standards, any study involving surgery is “greater than minimal risk” in the case of Alzheimer's disease. However, the whole spectrum of risks is more difficult to define. Federal agencies exercise some control over defining risks, and patient protection committees at research institutions play a role in determining the risks of a particular study.

ASSOCIATION POSITIONS

The consent of the individual who is capable of making informed decisions should be the standard for participation in research. The Association affirms, however, that persons with Alzheimer's who are no longer able to provide informed consent should not be deprived of the potential benefits of promising research. Nor should they be denied the opportunity to make a contribution to science by participating in research that someday might help others. And surrogates should be able to make decisions regarding research participation without a formal legal device, as is the current standard of practice in dementia research programs.

The Association's statement, *Ethical Issues in Dementia Research*, was approved by its national board of directors on May 18, 1997. The statement can be summarized in three major points.

1. For minimal risk research all individuals should be allowed to enroll, even if there is no potential benefit to the individual. The consent of a surrogate is acceptable even if the individual with Alzheimer's did not address research participation in an advance directive, a legal document that allows a person to state wishes for future medical decisions.
2. If the research presents greater than minimal risk *and* if there is a reasonable potential for benefit to the individual, the enrollment of all individuals with Alzheimer's disease is allowable based on consent of the surrogate. The surrogate's consent can be based on either an advance directive about research participation *or* on the surrogate's judgment of the individual's best interests. The conversations of the Association's Ethics Advisory Panel indicate that this second guideline will be wide in scope, because most research on Alzheimer's does have potential benefits for participants, thereby allowing for surrogate consent. This reliance on surrogate consent in all research of potential benefit to the subject is standard practice in Alzheimer research programs across the United States.
3. If the research involves greater than minimal risk *and* if there is *no* reasonable potential benefit to the individual, only those individuals who (a) are capable of giving their own informed consent or (b) have executed a research-specific advance directive are allowed to participate. In either case, a surrogate must

be available to monitor the individual's involvement in the research.

Important considerations: Surrogates have a great responsibility overseeing the care of people with Alzheimer's disease. When making decisions regarding participation in research, surrogates should consider the following principles:

1. Surrogate consent should always be based on accurate facts about the risks and potential benefits of the clinical trial, rather than on understatement of risks or burdens and exaggerated claims of benefit.
2. Participants in all research should be protected from significant pain or discomfort. It is the responsibility of all researchers and surrogates to monitor a participant's well-being.
3. Surrogates must not allow their hopes for effective therapies to overtake their critical assessment of the facts or diminish the significance of a participant's expression of dissent.
4. A participant's dissent or other expressions of agitation should be respected, although a surrogate can attempt reasonable levels of persuasion. A participant with dementia, for example, may initially refuse to have blood drawn or to take medication, but he or she may be willing to comply once a family member helps calm the situation and explain things.
5. Continued dissent by the participant requires withdrawal from the study, even when surrogates would prefer to see research continue.