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ISSUES RAISED BY RESEARCH USING PERSONS SUFFERING FROM DEMENTIA WHO HAVE IMPAIRED DECISIONAL CAPACITY

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INTRODUCTION

Two basic assumptions underlie this discussion: First, appropriately designed clinical research is an ethical activity. Research necessarily treats the individual as an object to be observed, measured, or intervened with, and it downplays or ignores the subjective aspects of the human experience. The only justification for conducting research in this manner is that research can ultimately benefit the individual participant or other human beings by increasing knowledge about the etiology, course, and treatment of human afflictions. For research to be justified, there must be no other way to gather the information, the design of the study must minimize the risks to the individual, the design of the study must be appropriate to answer the research question, and the research question should be one that is felt by the research and non-research communities to have a utility in being answered.

The second assumption of this discussion is that the Nuremberg Code,¹ its subsequent modifications and later implementing regulations form the basis of informed consent to participate in research.² The Code is frequently cited as the first statement of the concept of informed consent, and its principles generally underlie all subsequent documents and discussions of the topic.³ The Code requires that research participants be informed, comprehending, voluntary, and competent.⁴ Clearly, the decisionally incapacitated cannot meet these requirements. Therefore, only two options are available: First, do not allow any research in persons unable to meet these criteria, or second,

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1. The Nuremberg Code (1948) *reprinted in* The Nazi Doctors and the Nuremberg Code 2 (George J. Annas & Michael A. Grodin eds., 1992).

2. See Greg A. Sachs et al., *Ethical Aspects of Dementia Research: Informed Consent and Proxy Consent*, 42 CLIN. RES. 403 (1994).

3. See R. FADEN, A HISTORY AND THEORY OF INFORMED CONSENT 153, 154 (1986).

4. *Id.* at 155.

construct special criteria that offer added protections and restrictions to protect those who do not meet these criteria.⁵

Specific criteria which have been added to the basic principles of the code are the assessment of potential benefits (e.g., therapeutic vs. non-therapeutic; if therapeutic, low vs. high potential) and potential risks (graded as less than minimal, minimal or more than minimal).⁶ If added protections are needed to protect decisionally impaired individuals, then these risk and benefit criteria are likely to be a focus of the modifications.

Decisional Incapacity

Decisional capacity is defined here as an aggregate of the cognitive processes which underlie communication, judgment, and reasoning. Impaired decisional capacity can have many causes. For example, children are decisionally impaired by definition since younger children have not developed the capacities or maturity needed to make independent choices. The status of adolescents is under active debate since many do have some or all of the attributes identified by the Nuremberg Code,⁷ but at present, a single age, the age of majority, is used as the point at which decisional capacity is considered legally present. Nevertheless, children are not a focus of this article because the ethical issues are different than for adults and regulations for children exist that add protections.⁸

In adults, a variety of disorders can impair decisional capacity. Table 1 below organizes them into congenital and non-congenital disorders. These categories can be further broken down into focal brain injury (in which the impairments are limited to a single or small number of capacities) and generalized brain disorder, either delirium (a cognitive decline, usually of acute onset, accompanied by an altered level of consciousness) or dementia (a generalized cognitive decline occurring with the normal level of consciousness).

5. See Sachs, *supra* note 2, at 403.

6. *Id.*

7. See Nuremberg Code, *supra* note 1.

8. See Protection of Human Subjects, 45 C.F.R. §§ 46.401- .409 (1997).

DISORDERS ASSOCIATED WITH IMPAIRED DECISIONAL CAPACITY*

Disorder	Congenital			Acquired		
	Focal	Generalized	Focal	Delirium	Dementia	Generalized
Learning disabilities	Usually intact	Mental retardation	Focal <i>e.g.</i> , Aphasia, Agnosia	Delirium	Dementia	Major mental illnesses Schizophrenia; Mood Disorder
Decisional capacity	Usually intact	Usually intact	Variable	Usually impaired <i>temporarily</i>	<i>Often</i> impaired <i>permanently</i> May be intact	<i>Occasionally</i> impaired <i>Often</i> intact
Prior expression to participate in research	Unlikely	Not possible	Unlikely	Unlikely	Possible	Possible
Reversible	No	No	Possible	Possible	Rare	<i>Often</i>
Difficulty in determining decisional incapacity	Easy	Hard	Easier	Easy	Hard	Hard

* In adults

Another group of conditions in which decisional capacity is occasionally impaired consists of the major mental illnesses (schizophrenia and mood disorder). These disorders usually do not impair decisional capacity, but some severely ill individuals do develop incapacities to comprehend, communicate, and make judgments. These incapacities often resolve as the acute condition improves, but some severely and persistently ill individuals are permanently incapacitated.

Dementia as a Cause of Impaired Decisional Capacity

This paper will focus on dementia as a potential cause of impaired decisional capacity and will note relevant issues raised by other disorders that can impair decisional capacity. Dementia is a medical syndrome defined by three characteristics: a decline in cognitive ability, impairments in at least two distinct areas of cognition, and a normal level of alertness.⁹ Most dementias are irreversible, and many are progressive.¹⁰ However, a diagnosis of dementia does *not* necessarily indicate that decisional capacity is impaired because the cognitive impairments may not be of sufficient severity to abolish the capacity to make reasoned decisions or may not impair those abilities needed to make decisions. Nevertheless, many individuals with dementia, probably a significant majority, do have impaired capacity to consent to research.¹¹ An initial question, then, is whether research is justified in persons with dementia, and if so, is the inclusion of incapacitated individuals ever justifiable?

Justifications for Research into Dementia

There are several justifications for research into dementia. First, dementia is a prevalent problem, affecting 6-8% of individuals over the age of 65.¹² Second, the dementias cause serious morbidities in all those they afflict.¹³ These include multiple cognitive impairments and decrements in the ability to carry out everyday activities such as dressing, bathing, walking, and feeding.¹⁴ Hallucinations and delusions occur in 25-50% of individuals with dementia, aggressive and agitated behavior occur in 25-40% of individuals, and depression and

9. See AMERICAN PSYCHIATRIC ASS'N, DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS (4th ed. rev. 1996).

10. See Sachs, *supra* note 2, at 410.

11. See *id.* at 405-07.

12. See N. MACE ET AL., THE 36-HOUR DAY: A FAMILY GUIDE TO CARING FOR PERSONS WITH ALZHEIMER'S DISEASE, RELATING DEMENTING ILLNESS AND MEMORY LOSS IN LATER LIFE 7 (1981).

13. See *id.* at 7-10.

14. See *id.*

apathy occur in approximately 20% of individuals.¹⁵ Family and friends who care for individuals with dementia also experience morbidity.¹⁶ They experience emotional distress¹⁷ at rates two to three times higher than the rates seen in otherwise similar non-caregivers. Moreover, it is common for the caregiver to suffer social and financial difficulties.¹⁸ Clearly, dementia is an appropriate syndrome to research.

The next question is whether decisionally incapacitated subjects need to be studied. If the important research questions could be answered by studying individuals with intact capacity to consent, then decisionally incapacitated subjects should not be included. However, most of the important research questions about dementia require the participation of individuals who have dementia. They cannot be answered by studying cognitively intact individuals or by studying animal models. Of more relevance to this discussion, many research questions can be answered only by including individuals who have more severe forms of dementia — most of whom are decisionally incapacitated. One reason for this is that dementia is often difficult to diagnose until the symptoms become prominent,¹⁹ by which time many individuals have lost decisional capacity. Another reason is that the large number of subjects needed for some studies (such as treatment studies) requires the inclusion of decisionally incapacitated individuals. In addition, the care of the more severely incapacitated could not be studied without their participation. Thus, research with decisionally incapacitated individuals with dementia is necessary and appropriate.

Extra Protections

Since decisional incapacity is common in persons with dementia and research is justifiable, added protections are appropriate. One approach would be to ban the decisionally incapacitated from all non-therapeutic studies, that is, studies without potential direct benefit to that person. Arguably, this may be too restrictive because it limits some individuals from an act they might have chosen to do if they had the capacity. It would also prevent them from aiding others who have

15. See *id.* at 117-124.

16. See Peter V. Rabins et al., *The Emotional Impact of Caring for the Chronically Ill*, 31 *PSYCHOSOMATICS* 331 (1990).

17. See Peter V. Rabins et al., *The Impact of Dementia on the Family*, 248 *JAMA* 333 (1982).

18. See MACE, *supra* note 12, at 189.

19. See Stephen J. Anderer, *A Model for Determining Competency in Guardianship Proceedings*, 14 *MENTAL & PHYS. DISABILITY LAW REP.* 107, 109 (1990).

a similar disorder (a group with whom an individual might have a special affinity).

A less restrictive alternative would be to ban decisionally incapacitated subjects from "higher" risk research. This second approach offers some added protection but would still restrict individuals from participating in a study they might have chosen to participate in were they competent. If the argument that the individual may have wanted to participate in research is accepted, then there should be clear evidence that the person would have chosen to participate in any study, even one with a significant level of risk. Third, a reasonable accommodation would be to allow participation in non-therapeutic studies which carry more than minimal risk only if the person has expressed a prior wish to do so. This requirement adds meaningful protection but does not prevent an act that some individuals would have chosen to do, as long as there is convincing evidence that the person would have made the choice when capacitated.

Finally, most individuals who have impaired decisional capacity can give "assent" that is, they can indicate a willingness to go along with the research. The issue of assent needs to be studied carefully since it relies on observations that may well be unreliable and makes inferences from scant information. However, individuals who, by observable behavior or by verbal statements, indicate that they are in distress or discomfort should be considered to have expressed the desire to discontinue participation.

Research on the Consent Process in Persons with Dementia

While there is an extensive amount of literature on the assessment and determination of capacity to consent, most research based articles relate to the consent to treatment, not to participation in research.²⁰ To illustrate, Dr. L. Jamie Fitten and co-workers examined 51 residents of a Veterans Administration nursing home (many of whom suffered from dementia) and administered three vignettes that assessed the subjects' willingness to participate.²¹ Using a clinician's assessment as the standard for determining decisional capacity, they determined that approximately one-third of subjects had intact decision-making capabilities.²² Similarly, Dr. Cohen-Mansfield found that a majority of subjects with some degree of cognitive impairment understood the nature of questions about life-sustaining therapies and

20. See, e.g., L. Jamie Fitten et al., *Assessing Treatment Decision-Making Capacity in Elderly Nursing Home Residents*, 38 J. AM. GERIATRICS SOC'Y 1097 (1990).

21. See *id.*

22. See *id.*

gave internally consistent answers.²³ Dr. Thomas E. Finucane, Associate Professor of Medicine at Johns Hopkins University School of Medicine, found that a small sample of outpatients with Alzheimer's disease could discuss hypothetical situations about severe illness and life-sustaining treatments without becoming emotionally distressed.²⁴ Dr. Meghan B. Gerety, of the Division of Geriatrics and Gerontology, and Division of General Medicine at The University of Texas Health Science Center, and her colleagues concluded that many subjects with mild to moderate dementia had wishes similar to those of non-cognitively impaired individuals regarding treatment selections.²⁵ The cognitively impaired subjects were able to communicate their desires clearly and base their treatment decisions on prognostic information presented to them.²⁶ In addition, the cognitively impaired subjects were as consistent as the subjects with normal cognitive scores.²⁷ Dr. Greg Sachs reported that many of the patients with dementia whom they interviewed were able to communicate their values and preferences for enrolling in research.²⁸ Each of these studies demonstrates that some patients with dementia have the capacity to engage in meaningful discussions about their future care and have intact capacity to consent to treatment. It seems reasonable to extrapolate that some individuals with Alzheimer's disease also have the capacity to express preferences regarding participation in research.

Proxy Consent

The most widely used method for obtaining consent to participate in research from individuals with impaired capacity is to utilize a proxy, usually defined as a person most authorized to act for another.²⁹ Dr. Dallas M. High of the Department of Philosophy at the University of Kentucky surveyed researchers at thirteen Alzheimer's disease research centers and found that consent was provided by fam-

23. Jiska Cohen-Mansfield et al., *The Decision to Execute a Durable Power of Attorney for Health Care and Preferences Regarding the Utilization of Life-Sustaining Treatments in Nursing Home Residents*, 151 ARCHIVES INTERNAL MED. 289, 293-94 (1994).

24. Thomas E. Finucane et al., *Establishing Advance Medical Directives with Demented Patients: A Pilot Study*, 4 J. CLIN. ETHICS 51, 52 (1993).

25. Meghan B. Gerety et al., *Medical Treatment Preferences of Nursing Home Residents: Relationship to Function and Concordance with Surrogate Decision-Makers*, 41 J. AM. GERIATRICS SOC'Y 953, 958 (1993).

26. *Id.*

27. *Id.*

28. Greg A. Sachs, *Advance Consent for Dementia Research*, 8 ALZHEIMER'S DISEASE & ASSOCIATED DISORDERS 19, 23-4 (Supp. 4, 1994).

29. THE AMERICAN HERITAGE DICTIONARY OF THE ENGLISH LANGUAGE (10th ed. 1981).

ily members for 75% of the subjects.³⁰ Forty-seven percent of the projects were categorized by the researchers as potentially providing direct benefit, but only 22% were thought to provide a potential "medical" benefit.³¹ Dr. High also found that most proxy consents were "informal," that is, were provided by a person with no legal standing as a substitute.³² Studies of proxy consent which focus on consent to treatment generally do find that concordance between patients and proxies on hypothetical scenarios is often low or no better than chance.³³ For example, Dr. Gerety found that agreement is best when the scenarios refer to the subject's current state of health or to a vegetative state whereas agreement is poorest in intermediate states.³⁴

Dr. John W. Warren, of the University of Maryland School of Medicine, surveyed proxies about their decisions to allow nursing home residents to participate in a minimal risk study.³⁵ Of the surrogates who believed the patient would have *refused* to be a subject, 31% consented to have the patient participate; that is, these surrogates frequently provided consent even though they believed that the consent did not represent the patient's wishes.³⁶ More recently, Dr. Sachs examined the level of agreement between dementia patients and their surrogates regarding the patient's preferences for research participation in four hypothetical studies.³⁷ Agreement between patients and their surrogates were modest at best.³⁸ Dr. Sachs found that, overall, surrogates give consent for their relatives to participate in research more frequently than that person would have chosen.³⁹ One explanation might be that surrogates are using a "best interest" standard rather than the "substituted consent" standard that is assumed by some to underlie proxy consent.

It could be argued that a mandate authorizing only legally designated proxies to give consent to research participation offers a higher

30. Dallas M. High, *Advancing Research With Alzheimer's Disease Subjects: Investigators Perceptions and Ethical Issues*, 7 ALZHEIMER'S DISEASE & ASSOCIATED DISORDERS 165, 168 (1993).

31. *Id.* at 171-72.

32. *Id.* at 169.

33. See, e.g., Joseph G. Ouslander et al., *Health Care Decisions Among Elderly Long-Term Care Residents and Their Potential Proxies*, 149 ARCHIVES INTERNAL MED. 1367 (1989); Allison B. Seckler et al., *Substituted Judgment: How Accurate Are Proxy Predictions?* 115 ANNALS OF INTERNAL MED. 92 (1991); Jan Hare et al., *Agreement Between Patients and Their Self-Selected Surrogates on Difficult Medical Decisions*, 152 ARCHIVES INTERNAL MED. 1049 (1992).

34. See Gerety, *supra* note 25, at 956-57.

35. John W. Warren et al., *Informed Consent by Proxy*, 315 NEW ENG. J. MED. 1124 (1986).

36. See *id.*

37. See Sachs, *supra* note 2 at 404, 408.

38. See *id.* at 407-08.

39. *Id.* at 409.

degree of protection that is appropriate for research participation. However, this would require that the proxy be either a court-appointed guardian or have been given durable power of attorney for health care by the individual prior to losing capacity. This legal limitation would significantly hinder the research enterprise. For example, many individuals do not designate an agent via a durable power of attorney prior to losing capacity and, if they do, it does not typically apply to research participation. Further, the legal process of becoming a guardian is costly and time consuming.

Another proposed solution is the development of a new instrument—the durable power of attorney for research participation. This would designate an agent who would have power of attorney to consent to research participation if the individual became decisionally incapacitated. Such an instrument would strengthen the justification that the agent is acting for the subject. Moreover, since the majority of medical patients have not previously discussed their preferences for life-sustaining treatment with family members or their physicians,⁴⁰ it seems likely that even fewer individuals will have discussed preferences for participation in research before a dementia becomes symptomatic. While the recommendation has been made that physicians and investigators discuss possible future participation in research as well as potential proxies with patients while they have decision making capacity,⁴¹ the author knows of no data that demonstrate the effectiveness of such discussions. Therefore, even if it is desirable, the durable power of attorney for research is unlikely to be widely implemented.

Issues Unique to Dementia

The acquired dementing illnesses generally affect adults who have had intact decisional capacity for many years. These individuals have had the capacity and the time to develop wishes regarding willingness to participate in research. In contrast, adults with life-long mental retardation who presently lack decisional capacity are likely never to have had the capacity to consent to research.

Another difference between dementia and other disorders that cause decisional incapacity is that dementia is so prevalent in later life that many individuals will have a loved one or acquaintance who develops dementia. Such experiences could lead these individuals to consider the possibility of becoming afflicted with dementia them-

40. See Ezekiel J. Emanuel et al., *Proxy Decision Making for Incompetent Patients: An Ethical and Empirical Analysis*, 267 JAMA 2067, 2068 (1992).

41. See Warren, *supra* note 35; see also Sachs, *supra* note 2.

selves. Such a "personalizing" experience is much less likely in other acquired states of decisional incapacity such as those due to head trauma or delirium.⁴² (see Table I)

Furthermore, most dementias develop slowly and cause a gradual development of decisional incapacity. Since this occurs over a significant period of time, most individuals with early symptoms of dementia have intact capacity to consent to treatment and research. They may also have the capacity to consider whether they want to participate in research in the future if they become incapacitated.

Dementia differs from schizophrenia and mood disorders. These major mental illnesses infrequently cause decisional incapacity, onset often begins in adolescence or early adulthood and usually develop in an individual who has had no prior contact with another individual who has a mental illness.

Determining Decisional Incapacity

One of the challenges facing clinicians and researchers is determining the point at which decisional capacity is lost. The difficulty rests on a lack of agreement on the capabilities required for a person to have intact decisional capacity. The strategies proposed to assess capacity to consent range from in-depth neuropsychological batteries⁴³ to an enumeration of underlying principles without operationalization.⁴⁴ Recently, the MacArthur Treatment Competence Study developed several instruments that measure the capacities which underlie competency, and its participants are in the process of developing shorter instruments.⁴⁵ Whether instruments developed to assess a patient's competency to agree to treatment will be relevant to the capacity to consent to research remains to be demonstrated.

42. Delirium is an acute, usually reversible organic mental syndrome characterized by reduced ability to maintain attention to external stimuli and disorganized thinking as manifested by rambling, irrelevant, or incoherent speech. MILLER-KEANE ENCYCLOPEDIA AND DICTIONARY OF MEDICINE, NURSING AND ALLIED HEALTH (5th ed., 1972). Compared with dementia, which is an organic mental syndrome characterized by a general loss of intellectual abilities involving impairment of memory, judgment, and abstract thinking as well as changes in personality. See *id.*

43. See, e.g., Morris Freedman et al., *Assessment of Competency: The Role of Neurobehavioral Deficits*, 115 ANNALS INTERNAL MED. 203 (1991).

44. See generally Loren H. Roth et al., *Tests of Competency to Consent to Treatment*, 134 AM. J. PSYCHIATRY 279-84 (1977); Paul S. Appelbaum et al., *Assessing Patients' Capacities to Consent to Treatment*, 319 NEW ENG. J. MED. 1635 (1988); Anderer, *supra* note 19.

45. See, e.g., Thomas Grisso & Paul S. Appelbaum, *The MacArthur Treatment Competency Study III: Abilities of Patients to Consent to Psychiatric Medical Treatments*, 19 LAW & HUM. BEHAV. 149 (1990).

One difficulty with the search for neuropsychological indicators of decisional incapacity is that these tests are dimensional, that is, they make measurements on a continuous scale, while the concept of incapacity is categorical. Another problem is that several different cognitive processes underlie decisional capacity. Therefore, it is unclear whether all must be impaired, whether some are more crucial than others, and at what level each individual capacity must be impaired before the general capacity of decision making is absent. On the other hand, strengths of this method are the reliability of the measures and their ability to define a range within which the person moves from having decisional capacity to lacking decisional capacity.

Problems also arise when defining incapacity by relying on categorical criteria. For example, one criterion common to many definitions of incapacity is the presence of an "irrational" decision. Not only is this unreliable and difficult to operationalize, it conflicts with the principle of autonomy that supports the choice of foolish or unusual choices.

A recent study sought to combine the strengths of the categorical criteria approach and the neuropsychological approach.⁴⁶ They presented two vignettes to subjects with probable Alzheimer's disease and to "normal" elderly controls and rated competency to consent to medical treatment on five legal standards: evidencing choice, reasonable choice, appropriate consequences, rational reasons, and understanding choice.⁴⁷ The older controls scored as "competent" on 72 out of 75 choices and scored as "incompetent" for 1 out of 75.⁴⁸ Subjects with moderate Alzheimer's disease scored as competent on 28 out of 75 choices and "not competent" on 36 out of 75 choices.⁴⁹ The standard of "rational reasons" best distinguished between competent subjects and non-competent subjects, and this standard correlated with neuropsychological tests that measure "frontal lobe function" such as the Initiation/Preservation Scale of the Dementia Rating Scale. However, there are both technical (low reliability) and ethical objections to the rational reasons criterion (noted above). Therefore, no single standard is adequate to identify capacity to consent to medical treatment. This suggests that the determination of decisional ca-

46. Daniel C. Marson et al., *Neuropsychologic Predictors of Competency in Alzheimer's Disease Using a Rational Reasons Standard*, 52 ARCHIVES NEUROLOGY 955 (1995).

47. See *id.* at 956; see also Marson et al., *Assessing the Competency of Patients with Alzheimer's Disease Under Different Legal Standards: A Prototype Instrument*, 52 ARCH. NEUROL. 955, 956 (1995) (providing an empirical assessment of the competency of patients with Alzheimer's disease to consent to medical treatment under five different legal standards).

48. See *id.* at 957.

49. See *id.*

capacity should depend on a combination of objective data and an appreciation of the context in which the decision is being made.

Decisional incapacity is a fluid concept, the definition of which will change to reflect the values of society over time.⁵⁰ Its definition should rely on a combined judgment that includes the views of lay people, clinicians, researchers, and ethicists, and its determination should depend on neuropsychological and personal history data. Because it will remain difficult to identify the point at which decisional incapacity develops, as one gradually moves from a capacitated to an incapacitated state, researchers studying dementia must be cognizant of and vigilant for the development of decisional incapacity. Moreover, because the desire for treatment is almost universally shared, while the desire for research participation is not, society and researchers should err on the side of over-estimating decisional incapacity to consent to research and have less stringent criteria for supporting capacity to consent to treatment.

The Issue of Multiple (or Conflict of) Interests

One issue that has received more attention in recent years is the multiple conflicts of interest between those designing, implementing, and participating in research. A recent editorial concerning these conflicts of interest concluded that the issue is more appropriately called "dual" interests.⁵¹ I would broaden this further and suggest that most individuals have "multiple interests." A researcher, for example, might be simultaneously interested in furthering knowledge, furthering career, obtaining future funding to continue research, enhancing his or her reputation in order to get promoted, making a patentable discovery that will provide financial rewards, and feeling good about contributing to humankind. Persons who believe that researchers are abusing subjects also have multiple interests. They may be motivated by a desire for public recognition, payment for writing articles, revenge against perceived perpetrators of inhumane practices, status as an advocate for the downtrodden, and feeling good about contributing to humankind.

The best we can do is to recognize that multiple interests are often at work and to make public those interests which involve personal financial gain. Experience teaches that most participants are

50. See FADEN, *supra* note 3, at 200-01. (A discussion of the evolution of federal policy governing human research).

51. Richard Horton, *Conflicts of Interest in Clinical Research: Opprobrium or Obsession*, 349 THE LANCET 1112 (1997).

primarily motivated by positive, desirable motives, and this should be presumed unless evidence is developed to demonstrate otherwise.

CONCLUSION

Research involving decisionally incapacitated individuals is ethically justifiable, but persons at risk and with decisional incapacity need added protections. Therefore, there should be stricter standards for the inclusion of decisionally impaired subjects in research than exist for research subjects in general. In studies of persons with high-risk disorders such as dementia, ongoing monitoring is necessary to determine if and when decisional incapacity develops.

Studies including decisionally incapacitated subjects with dementia should be done only to answer important questions that cannot be adequately answered in persons who have intact capacity. If the study presents more than minimal risk, then the appropriate reviewing agency must determine that this risk is justified in relationship to the knowledge to be gained. Close scrutiny of these questions is necessary in patients with decisional incapacity because proxy consent is less desirable than individual consent. Therefore, added expectations should be placed on IRBs⁵² to determine that any research project with the decisionally impaired is necessary and that studies with higher than minimal risk require that proxies have direct knowledge of the person's prior values. These higher standards protect subjects at risk but allow research to go on.

The degree of capacity necessary to participate in research can vary with the degree of risk of the study. Research which carries more than minimal risk can be carried out in persons with dementia who have intact decisional capacity just as they are in other individuals with intact capacity. Subjects who have consented to participate and then developed incapacity should be allowed to continue in the study as long as they "assent" and their proxy agrees that the person would want to have continued. However, it is too restrictive and unrealistic to require that a decisionally impaired person have expressed wishes specifically related to research because this would eliminate many individuals who would have participated. While there is no "right" to participate in research, it seems wrong to establish a blanket prescription against the participation of individuals who have not expressed a desire to participate in research while capacitated. However, individuals who no longer have intact decisional capacity should be included

52. IRBs are institutional review boards charged with the responsibility of monitoring research for the purpose of protecting research subjects.

in studies with more than minimal risk only if the individuals will receive potential therapeutic benefit, have chosen a proxy prior to incapacity, or have indicated by written document that they would have wanted to participate in such a study.

The proposed durable power of attorney for research is an attractive solution. It has the benefits of determining that an expressed prior wish to participate existed and of allowing the persons to choose an individual who would make decisions for them. However, it is unlikely to be widely utilized and is, therefore, too restrictive to be the only means for research participation by the decisionally impaired.

Christine Cassell argues that paternalism is appropriate in some circumstances and that the social value of research should be considered in supporting the research enterprise.⁵³ She concludes that "ethical caution" is necessity but that "flexibility and caution must go hand in hand."⁵⁴ The challenge facing the researcher, proxy, ethicist, and legislator is providing appropriate solutions without undue restrictions.

53. See Christine Cassel, *Research on Senile Dementia of the Alzheimer's Type: Ethical Issues Involving Informed Consent*, in *Alzheimer's Dementia: Dilemmas in Clinical Research* 99, 103-07 (V.L. Melnick & N. Dubler eds., 1985).

54. *Id.* at 107-08.