

# A Survey of Researchers Using a Consent Policy for Cognitively Impaired Human Research Subjects

by Philip J. Candilis, Robert W. Wesley, and Alison Wichman

Illnesses leading to some degree of cognitive impairment are a considerable health problem in the United States. These include Huntington's disease, cerebrovascular disease, psychiatric disorders, chronic alcoholism, and AIDS dementia complex. For many years, investigators at the Warren G. Magnuson Clinical Center (CC) of the National Institutes of Health have conducted research involving cognitively impaired subjects in order to investigate the etiology and treatment of these disorders. However, dementing and mental disorders may limit or destroy research subjects' abilities to give informed consent. Therefore, a challenge to all institutions and investigators conducting such research is balancing the scientific mandate to advance knowledge with the ethical requirement to protect the rights and safeguard the welfare of human subjects.

The Belmont *Report* interprets the relevant principle of respect for persons as incorporating two ethical convictions: that individuals should be treated as autonomous agents, and that persons with diminished autonomy are entitled to protection.<sup>1</sup> Also, protecting human subjects with diminished autonomy is addressed broadly in Department of Health and Human Services regulations: "where some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as persons with acute or severe physical or mental illness, . . . appropriate additional safeguards have been included to protect the rights and welfare of these subjects . . ."<sup>2</sup> In 1987, the CC adopted an informed consent policy that provides additional safeguards for research subjects who, because of their underlying diseases, are or are likely to become cognitively impaired during the course of the research. We report the results of a survey conducted in 1990 to address practices and attitudes concerning this policy. It is our intent that by presenting the experience with the CC policy, other IRBs and researchers will be encouraged to evaluate and formulate practical safeguards for cognitively impaired research subjects.

## Policy on the Consent Process in Research Involving Cognitively Impaired Human Subjects

The development of the CC policy is described in detail elsewhere,<sup>3</sup> with only a brief description given here. The policy was designed to strengthen the role of the CC's thirteen IRBs in safeguarding the rights and welfare of cognitively impaired human research subjects and to promote ethically appropriate research in disorders involving cognitive impairment. The policy contains two main features: (1) prior evaluation of proposed research studies by an IRB to allow the appointment of surrogate decisionmakers for subjects who are or may become cognitively impaired; and (2) an internal system of oversight and consultation once the appointment of surrogate decisionmakers is authorized by the IRB. The policy recognizes eight distinct clinical cases that require additional safeguards to the informed consent process.<sup>4</sup> The cases incorporate several considerations: (1) that assent of cognitively impaired subjects is necessary but not sufficient for participation in research; (2) that the protection should be proportionate to the risk involved, with the least protection required when research involves no more than minimal risk; (3) that the durable power of attorney (DPA) model for the appointment of a surrogate decisionmaker is the most ethically and legally supportable practice when future intellectual impairment of research subjects can be predicted on the basis of diagnosis or when existing cognitive impairment is still mild; and (4) that degree of cognitive impairment, level of research risk, and prospect of benefit to individual subjects determine whether DPA or other approaches, including court appointed guardianship, are used in selecting a surrogate decisionmaker.

## Report of Survey

The CC policy had been in existence for three years when this survey was conducted to determine practices and attitudes and to evaluate whether hospital educational efforts could be designed more effectively to improve its application.

### *Methods*

The four Institutes of the NIH that conduct the majority of research involving cognitively impaired subjects are the National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Mental Health (NIMH), the National Institute of Aging (NIA), and the National Institute of Alcohol Abuse and Alcoholism (NIAAA). Therefore, 317 questionnaires were sent to all principal/ associate investigators, registered nurses, and junior medical staff fellows working in these four Institutes.

The survey consisted of four sections. The first requested anonymous demographic information including Institute, years of employment, age, sex, and position title. Section two contained true/false questions designed to elicit knowledge about various aspects of the CC policy. Section three surveyed degree of agreement with 44 statements regarding attitudes toward the policy and use of DPA in clinical research. A multiple choice scale offered four ordered responses: strongly agree, somewhat agree, somewhat disagree, strongly disagree. Sections two and three included randomly embedded reliability test questions (e.g., "Current DPA policy impedes research"; "Current DPA policy facilitates research"). Section four solicited open-ended responses to specific questions of practice (e.g., "What role, if any, should DPA play in patients with psychiatric disorders?").

Descriptive rather than evaluative questions were used to elicit information on the practical application of DPA in a research setting and to prevent repetitive response patterns. Further efforts to avoid response bias included framing questions to elicit agreement or disagreement with equal frequency.

Questionnaires were piloted with a dozen intramural and extramural experts representing potential respondents in neurology, psychiatry, nursing, and ethics. Surveys were subsequently mailed with a request for response within two weeks.

### *Statistical Analysis*

Statistical analysis correlating an ordered response (i.e., strongly agree) with an unordered category (i.e., respondent's Institute) employed a version of the Kruskal-Wallis test for contingency tables with ordered columns;<sup>5</sup> a two-sided  $p$  value ( $P_2$ )  $< .01$  indicates statistical significance. Correlation between ordered responses to related questions used Mantel's test for trend for contingency tables;<sup>6</sup> again, a  $P_2$  value  $< .01$  indicates statistical significance. For example: responses to "Current DPA policy impedes research" and "Current DPA policy facilitates research" correlate with  $P_2 = .009$ , indicating, as expected, that those disagreeing with one question agree with its antithesis. Mantel's test for trend was also used to assess the correlation of an ordered response with an ordered category (i.e., years of experience).

### *Results*

Forty-nine percent of principal/associate investigators polled returned questionnaires, as did 48 percent of RNs and 35 percent of junior staff fellows. The overall response rate slightly over 44 percent. Telephone follow-up revealed, however, that a number of potential respondents were off campus during the survey or had changed location since the latest personnel update. Given that only 25 of 30 telephone follow-ups represented accessible respondents, we estimate the true response rate to be approximately 53 percent.

Response by Institute indicated a 46 percent return rate from NINDS, 47 percent from NIMH, 40 percent from NIA, and 36 percent from NIAAA. Respondent sample was representative for MD/RN ratio (54:46) and sex (F:M::53:47). Respondents' ages ranged from 20 to over 60 years (majority, 30 to 39 years). Length of employment at the NIH ranged from less than one year to more than 10 years (majority, 2 to 10 years). Random telephone follow-up of survey recipients not returning questionnaires indicated that the sample was representative of the population targeted.

To determine whether the CC policy is perceived as an important safeguard for cognitively impaired subjects and to learn whether respondents believed the CC policy interfered with or promoted clinical research, relevant questions were randomly distributed within the survey. Ninety-three percent of respondents agreed (68% strongly) that “Safeguards for impaired research patients should be more stringent than those for routine clinical practice.” Indeed, 48 percent agreed that “To perform research with impaired subjects, safeguards must be improved beyond current standards.” Eighty-five percent believed “Current DPA policy facilitates research.” Further, 96 percent agreed (71 strongly) that “Preservation of the research subject's autonomy is worth the extra procedures of DPA.” Agreement that “DPA is an important element of patient rights” (94%), that “DPA is best signed early in a patient's research course” (96%), and that “The process of informed consent is vital to a patient's participation in clinical research” (95%) indicates that respondents view the CC policy as an important element in promoting the informed consent process. This view is further demonstrated by 84 percent disagreement (55% strong) that “The current informed consent process exclusive of DPA -- is sufficient to protect impaired research subjects,” and 87 percent disagreement (58% strong) that “Informed consent procedures used for unimpaired research patients are sufficient for impaired subjects.” These responses notwithstanding, 22 percent agreed that “A patient's participation in research is generally more important than that individual's autonomy.”

We also addressed respondents' views concerning the role of surrogates in research decisionmaking when subjects become unable to make their own decisions. Ninety-four percent agreed (59% strongly) that “the surrogate's role is to represent the patient's wishes even in the face of the medical team's objections.” Respondents agreed that surrogates do not usually make choices contrary to patient best interests (95%).

Respondents acknowledged the responsibility to involve the surrogate in the decisionmaking process. For example, 88 percent agreed that once DPA becomes effective, “surrogates must always be included in research decisions affecting their principals,” and 95 percent agreed that “in my experience, staff members follow a surrogate's requests.” Eighty-eight percent agreed that “the surrogate is a valued member of the decisionmaking team.” Responses correlate with  $P_2 < .001$  between the latter two statements as well as between the first and third.

Nonetheless, 19 percent of respondents agreed that “surrogates who make decisions consistent with patient wishes are often persuaded to change their minds by staff opinions.” Further, 32 percent agreed that “surrogates are not consulted when researchers anticipate a disagreement.” A correlation ( $P_2 = .0006$ ) between this last response and responses concerning selection of the proper surrogate suggest that those who believe surrogates are not consulted are those who think an improper surrogate has been appointed.

A widespread concern among respondents is proper preparation of surrogate decisionmakers for their duties. Ninety percent agreed (24% strongly) that “counseling of surrogates in the responsibilities of their role can be improved.” Thirty-nine percent believe that surrogates are not “adequately prepared for their role.” When coupled with responses to open-ended questions regarding who should lead DPA discussions, the overwhelming response (90%) indicated a wider role for the CC physician.

Respondents considered appointed surrogates better qualified to make decisions for cognitively impaired subjects than either the research team or the clinical center ethicist. However, respondents expressed a marked preference for next-of-kin as surrogate decisionmakers. For example, in the open-ended query, “Would you prefer to work with a next-of-kin decisionmaker or an appointed surrogate?” 60 percent preferred the former choice over the latter (19%), with 21 percent expressing no preference or indicating the two coincided in their experience. When associated, however, with the 80 percent agreement that “potentially impaired research subjects have the right to assign any surrogate decisionmaker they choose” a contradiction can be seen between respondents' preferences for the next-of-kin assignment and the belief in patients' right to choose whomever they prefer.

Because the CC policy was enacted in 1987, we addressed whether respondents knew such a policy existed. Only 59 percent of the respondents passed the screen question: “Are you aware a . . . DPA policy exists?” Awareness of the policy correlated with increased experience in the CC ( $P_2 = .003$ ), and was distributed

evenly among junior, senior, and nursing staff. Awareness of the policy is not consistent among Institutes, however, varying from 50 percent to 100 percent of the respondents. Also, 65 percent agreed that “researchers in my branch are not always sure when to use DPA” as stipulated in the CC policy. Seventy-one percent did agree, however, that ultimately DPA is applied consistently in similar cases and that the respondents are comfortable with its use (81%, 41% strongly). A trend test of  $P_2 < .0001$  indicates that, despite not always being sure when to use it, the same respondents believe DPA is consistently applied.

We were interested in how informed consent and the CC policy, particularly the use of the DPA, were viewed in the context of research involving individuals with psychiatric illnesses. In response to “What role, if any, should DPA play in psychiatric disorders?” 40 percent suggested applying DPA on a case-by-case basis, 36 percent supported a greater role for DPA for research subjects with psychiatric disorders, and another 24 percent supported a role commensurate with its use in other disorders. The differences in responses to this question are not statistically significant.

Difficulties in obtaining valid informed consent from some individuals with mental disorders was a concern for respondents. Sixty-three percent agreed (20% strongly) that “clinically depressed patients are often too impaired to give truly informed consent.” Responses did not vary by Institute ( $P_2 = .15$ ), but did vary by occupation ( $P_2 = .014$ ). Junior staff and nurses believed more strongly that depressed patients specifically are often too impaired to give informed consent.

However, perceived difficulties in the process of informed consent were not limited to depressed patients. There was further correlation between all responses and the view that informed consent is difficult under many circumstances ( $P_2 = .012$ ). Seventy-six percent agreed (30% strongly) that “I often question whether even competent patients understand the interventions they receive.”

The interaction of cognitively impaired research subjects with the health care/research team was explored also. Respondents agreed (93%, 62% strongly) that “Cooperation of the impaired research subject is necessary to facilitate research” and yet were less convinced that this cooperation was possible: 42 percent agreed that “Cooperation of the impaired research subject is not possible in clinical research.” Other cross-tabulations do not clarify whether this means some impaired subjects are unable to cooperate physically with research procedures or that they are incapable of providing valid consent.

## **Discussion**

There is general agreement that cognitively impaired individuals may be vulnerable to coercion or undue influence because of real or potential limitations to their ability to participate in informed decisionmaking.<sup>7,8</sup> Ethical guidelines and regulatory requirements for research involving human subjects stipulate that vulnerable subjects be afforded appropriate protections. Our study provides further information on specific protections that can be implemented in the research setting.

This survey was conducted for several reasons. The Clinical Center is a large clinical research hospital with 550 beds and 13 out-patient units in which the 900 to 1,100 research physicians change frequently. In addition, there are large numbers of nonphysician health care professionals who conduct clinical research. We wanted to investigate attitudes concerning informed consent in this research setting. Also, we were interested in respondents' specific knowledge of and attitudes toward the policy so that we could develop more effective educational strategies for research and clinical staff, research subjects, and their surrogates.

The survey serves to highlight various attitudes about informed consent. Most respondents consider the process of informed consent vital to participation in clinical research and believe strongly that safeguards for cognitively impaired research subjects need to be more stringent than in routine clinical practice. Respondents consider the appointment by research subjects of surrogate decisionmakers through the DPA mechanism to be an important protection of subjects likely to become cognitively impaired. Viewed by respondents as an extension of the informed consent process, its use is perceived to honor patient self-determination as well as to promote the institutional commitment to clinical research.

However, responses occasionally demonstrate a tension in attitudes. For example, some respondents indicate that subjects' participation in research may be more important than their autonomy. This view is ethically problematic particularly when subjects are participating in research that, while it may further knowledge about their disease, offers no prospect of direct benefit to them. Also, some respondents expressed little confidence in the process of informed consent, suggesting that even cognitively intact people have difficulty understanding their research care. While these attitudes were voiced by a minority of respondents, they underscore the need for ongoing educational programs and empirical research on improving the process of informed consent.

For surrogate decisionmaking, CC practices call for the use of the standard of substituted judgment. Because this standard requires that the surrogate "stand in the shoes" of the incapacitated individual (and make decisions the patient would make if able to do so), investigators are encouraged to recruit subjects who are not too impaired to appoint a surrogate. Research subjects then can be informed of the criteria for choosing a surrogate (i.e., the need to be available for consultation with the research team, the willingness to serve). Early appointment allows subjects time to inform their surrogates of their preferences for participation in research and therefore promotes the use of the substituted judgment standard. Also, early appointment allows time for the subject and surrogate to be educated by the research team and others about the surrogate's role and responsibilities.

Respondents expressed considerable concern that surrogates may not be prepared adequately for their role in research decisionmaking. Most respondents believe that surrogates need more education about their responsibilities and favor an increased educational role for the CC physician in consultation with others on the health care team—nurses, social workers, ethicists. Effective methods of education would include discussion of DPA early in the hospitalization, ward orientation sessions that include surrogates even before DPA takes effect, and discussions with subjects in the surrogate's presence. Such practices may smooth the transition of decisionmaking when subjects are determined to be incapable of making their own decisions.

Although respondents generally concerning the CC's policy on the expressed confidence in surrogates' informed consent process in research abilities, occasionally surrogates may be bypassed when researchers anticipate disagreement. Respondents who indicated that this occurs believed that improper surrogates have been assigned. Nonetheless, this reasoning is not sufficient to override the surrogate in the decisionmaking process. Respondents may need more guidance on effective ways to resolve disagreements. For example, if a situation arises in which a surrogate makes decisions known to be contrary to previously stated wishes or there is reason to question the ability of the surrogate to make decisions based on the substituted judgment standard, consultation with others (e.g., the Bioethics Program) is appropriate.

We did not pursue what respondents meant by "improper" surrogates. However, although respondents recognize the subject's right to appoint freely, they do express a preference for next-of-kin surrogates. It is clear that the primary emphasis needs to be placed not on who acts as the surrogate but on whether that individual is willing and able to fulfill the responsibilities. Since enactment in 1991 of the Patient Self-Determination Act, which requires health care institutions to inform patients of their right to participate in and direct health care decisions by implementing advance directives, respondents may have gained more experience and comfort with surrogates who are not next-of-kin.

Many respondents also thought that depressed subjects, specifically, may be unable to give valid informed consent. There is need for further discussion of which safeguards, including DPA, may be appropriate and practical for psychiatric subjects, particularly given the fluctuating nature of many mental disorders and the authority of medical staff in declaring incapacity.

Finally, responses focus attention on the need for improved dissemination of information concerning this policy. Differences among Institutes in awareness of the various protections for cognitively impaired research subjects identify areas for improved education and emphasize the usefulness of this type of survey tool in clarifying ambiguities.

## Conclusion

We present the results of a survey concerning the CC's policy on the informed consent process in research involving cognitively impaired subjects. The intent of the policy is to promote ethically permissible clinical research in disorders involving cognitive impairment. The survey has identified some of the strengths and weaknesses of the policy and its implementation and the results will be used in planning ongoing efforts to educate the CC clinical research staff. Investigators and institutions engaged in research involving cognitively impaired or potentially impaired subjects have a responsibility to maintain a balance between the goal of advancing science on the one hand and the ethical mandate to protect the rights and welfare of human subjects on the other. Rigorous evaluation by IRBs of the scientific aspects of such studies combined with practical institutional policies designed to protect the rights and safeguard the welfare of the cognitively impaired subjects is one way to help maintain this balance.

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**Philip J. Candilis, MD**, is a resident in psychiatry, Massachusetts General Hospital, Boston, Mass.; **Robert W. Wesley, PhD**, is chief of data management and PC applications, Medical Information Systems, Warren G. Magnuson Clinical Center, National Institutes of Health; and **Alison Wichman, MD**, is director of education, Office of Human Subjects Research, National Institutes of Health, Bethesda, Md.

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