Ethics and Research in Long-Term Care: A Position Statement from the American Medical Directors Association

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Background: This position paper expands upon the work of members of the American Medical Directors Association (AMDA) at the 1995 Consensus Conference on the Humanistic Aspects of Research in Long-Term Care.

THE IMPORTANCE OF RESEARCH INVOLVING HUMAN SUBJECTS

The best practice of medicine rests on sound clinical evidence, which emerges only through the careful study of human subjects. Without the use of human subjects in research, the safe development and employment of new diagnostic and therapeutic interventions, including medications, would be impossible. The US Food and Drug Administration requires that clinical trials of new therapies demonstrate their safety and efficacy before approving them for public use.1

In the past, women, older adults in general, and residents of long-term care facilities in particular, were not included in most clinical trials. Consequently, the safety and efficacy of many medications and other medical interventions have not specifically been evaluated in older people, particularly in those who are frail or cognitively impaired. Of necessity, clinicians have extrapolated findings from studies of healthy younger people (and, more recently, of healthy older people) to the needs of other groups, including the frail and cognitively impaired elderly, though these groups may differ physiologically in significant ways. Older people differ from younger people in the rate of metabolism and excretion of drugs in ways that may affect the safety and efficacy of medical treatments.

The growing and diverse population of long-term residents presents a special challenge in this regard. At present, knowledge is lacking not only about the effects of many medical, surgical, and diagnostic interventions on this population, but also about such basic epidemiologic issues as the incidence and prevalence of specific conditions, and especially about the interactions among their many and complex comorbid illnesses. For example, the relationship between dementia, which is highly prevalent among long-term care residents, and the course of other diseases common in old age is just beginning to be explored. Similarly, the growing numbers of children and young adults in long-term care also have specific needs. Other populations, such as those with human immunodeficiency virus (HIV) infection and cancer, may already be involved in continuing clinical research studies when they enter long-term care.

If clinicians are to have information that is specific about the course of disease and the effects of medical interventions on long-term care residents, such residents must be included in epidemiological studies and clinical trials. This is the only way an evidence-based body of medical knowledge about their needs will develop.2,3

THE DEVELOPMENT OF STANDARDS AND FEDERAL PROTECTIONS FOR SUBJECTS OF CLINICAL RESEARCH

Historically, concerns about research involving human subjects have focused on ethical conduct and on preventing harm. These concerns were aroused in part by specific research projects, both large and small, which appeared directly to cause harm, to neglect the safety of participants, or to proceed without subjects’ informed consent.4–6 As a result, safeguards were instituted to protect human subjects of research. In the past 30 years, several national commissions have convened to develop standards of conduct for research and to create mechanisms to protect human subjects participating in federally funded research.

In 1979, the Belmont Report, issued by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, outlined federal standards for conducting federally funded research projects involving human subjects.7,8 The Belmont Report, and subsequent federal legislation prompted by that report, defined three principles essential to the ethical conducting of research: informed consent, risk/benefit assessment, and the appropriate selection of research subjects.

The report mandated that each federally funded research project involving human subjects be approved by an independent Institutional Review Board (IRB) composed of scientists, clinicians, lay people, and community representatives. Each institution conducting federally funded research was required to create its own IRB that would provide initial approval for all projects and would periodically review studies in progress.
Since then, it has been standard practice in institutions conducting federally funded research on human subjects that any study performed on human subjects be approved initially and at intervals by the IRB, irrespective of the project’s source of funding. In addition to the federal requirements pertaining to IRBs, individual states may also have requirements that need to be fulfilled.

In 1994, the Clinton administration created the National Bioethics Advisory Commission (NBAC) to advise the federal government on bioethics and public policy issues related to research on human subjects. Prompted by continuing concern about the protection of human subjects, the commission resolved in 1997 that no person in the United States should be enrolled in research without the dual protections of informed consent by an authorized person and independent review of the risks and benefits of the research. A report by this commission in 1998 found that the legal protection of human subjects in research did not yet extend to all Americans and that federal protections did not always include specific provisions for especially vulnerable populations of research subjects. Residents of long-term care facilities were identified in this report as one such vulnerable population.

Many long-term care residents are physically frail, with less physiologic resilience than healthy adults. Residency in a long-term care facility by its very nature creates a special vulnerability, as residents depend upon others to meet their physical, emotional, and social needs. Because they cannot fend for themselves, they require protection by others from the risks inherent in participating in research. Cognitive impairment may prevent them from being able to describe distress caused by the research intervention itself. And for residents who cannot understand the goals of a particular research project, even such a small intervention as the sampling of oropharyngeal or nasopharyngeal secretions for the purpose of culture, or the drawing of blood, can induce fear or agitation that would not arise in a subject who understood the goals and the finite nature of the process. Cognitively impaired residents, if not protected, may also be subject to coercion.

**ETHICAL PRINCIPLES RELATING TO RESEARCH IN LONG-TERM CARE FACILITIES**

The Belmont Report and the NBAC suggest ethical principles for researchers to address in order to perform ethical research: informed consent, risk/benefit assessment, autonomy, beneficence, substituted judgment, selection of subjects, and best interest. They are outlined below.

**Justice and the Selection of Research Subjects**

The principle of justice requires that the benefits and burdens of research be allocated equally and fairly among all members of society and that standards for the protection of human subjects also be equally applied. Until recently, concerns about justice have focused on the risks assumed by participants in research. In the past two decades, however, the focus has been more on the need to include groups that were previously excluded from participating in research, such as women and the elderly, so that they, too, can reap its benefits. The principle of justice thus suggests that residents of long-term care, including the mentally incapacitated, be allowed to participate in research studies relevant to their needs, and that research be done for their benefit. At the same time, federal and state-mandated protection of research subjects must extend to these residents, in recognition of their vulnerability.

Existing guidelines and commentaries, such as those proposed by the NBAC, the National Institutes of Health (NIH), the Maryland Attorney General’s Office, and an advisory group of the New York Department of Health, differ about how to protect vulnerable groups, especially those unable to provide informed consent, from exploitation while simultaneously ensuring that their conditions be addressed rather than neglected by research. One recommended approach is to exclude potential subjects who are unable to give consent when the condition in question can be studied in subjects who can give consent. Other recommendations are to allow those people to be studied only when the proposed research pertains directly to the condition responsible for their subjects’ incapacity, or to a condition with similar manifestations. For the long-term care population, however, restricting research in people who are unable to provide informed consent could inhibit investigators’ learning more about the interactions among their comorbid illnesses, including dementia.

**Autonomy and Informed Consent**

The principle of autonomy requires that anyone consenting to participate in research be free from coercion or undue influence, and have the decision-making capacity to consent to or refuse participation. Residents who are capable of making decisions about whether to participate in research may base a decision to do so on the principles of their own best interest, social justice and beneficence (see below). Because decision-making capacity may deteriorate, or even improve, over time, however, it should be periodically reevaluated. In long-term care facilities, many residents lack decision-making capacity. When a resident is unable to provide informed consent, a designated surrogate decision maker must provide that consent in writing. Residents have the right to refuse to participate in research at any time, however, even when surrogate decision makers have given permission for their participation.

What surrogate decision makers are allowed to, or should, consent to for adults lacking decision-making capacity remains controversial (see sections on risk, best interest, and beneficence, below). For consent to be truly informed, the investigators must fully disclose the nature of the proposed research, including its procedures, risks, and benefits. For long-term care residents who lack decision-making capacity because of dementia, this disclosure must include not only medical risks and benefits but also consideration of the components of the research that might cause the resident distress, whether from fear, the disruption of schedule, or an unaccustomed kind of examination or observation. Protection of privacy, like confidentiality, is important in long-term care.
**Substituted Judgment**

When it is possible, surrogate decision makers should be guided by the principle of substituted judgment. That is, they are expected to base decisions on what the incapacitated person would have chosen. Written advance directives provide a vehicle for communicating wishes directly, and the idea of advance consent for participation in research, particularly in research about dementia, has been proposed.24 In practice, written advance directives rarely address the idea of participation in research, however, and preparing an advance directive that could meaningfully address participation in a particular study would be extremely difficult.

It is unusual for people to discuss the question of research with designated decision makers before becoming incapacitated, and many studies have shown that surrogate decision makers’ assumptions about what others would have chosen are often inaccurate.25 When they do have knowledge about a specific person’s attitudes toward research, they may be able to infer whether that person would have wanted to participate in a particular study. Otherwise, they must be guided by ethical principles other than substituted judgment.

**Best Interest**

Lacking information that would allow an accurate substituted judgment, surrogate decision makers are expected to make the best and most reasonable decision for the resident that is possible given the information available. Depending on the nature of the proposed research and the risk it poses for subjects, the decision maker must decide whether participation is in the resident’s best interest. Existing guidelines do not fully agree either about how to describe and categorize risk or about what constitutes acceptable risk for this population.19–23 Observational studies in which there are no medical interventions, for example, usually provide no direct benefit to the participants, but they also pose only minimal risk.

Clinical trials involving the administration of medications might confer direct benefit to the subjects, but the risk of harm is no longer considered minimal. Some guidelines suggest that subjecting an incapacitated subject to more than minimal risk, in the absence of the possibility of direct benefit, may be unethical.

The principle of best interest, when narrowly construed or considered in isolation, appears not to encourage surrogate decision makers to consent to participation by mentally incapacitated persons in research when the study intervention will not be of direct benefit to its subjects. Indeed, state laws may differ about which kinds of research they allow surrogate decision makers to consent to. Some projects appear to involve too much risk to be permissible for mentally incapacitated subjects. For this reason, court-appointed surrogate decision makers who are not family members (eg, public guardians) may be prohibited from giving consent for participation in specific types of research, or even research in general.

Surrogate decision makers may feel that, in the absence of any anticipated direct benefit from participation, their overriding responsibility to protect the incapacitated person from even minimal risk supersedes any other consideration. The benefits of research (unlike the risks) often all accrue to future populations. More broadly construed, best interest can allow participation in research, in the sense that the opportunity to contribute to medical knowledge can be in the best interest even of the mentally incapacitated.

**Beneficence and the Assessment of Risks and Benefits of Participation in Research**

Best interest might appear to conflict with beneficence, which is defined most simply as “doing good,” and which encompasses acts of kindness or charity that go beyond strict obligation. Beneficence extends beyond the best interest of the individual research subject. Though the ultimate benefits of a particular research project may not be realized by any of the study’s participants, the research provides benefits to society in the form of knowledge. Some guidelines suggest that, in the absence of direct benefit to participants, it is ethically unacceptable to subject mentally incapacitated subjects to more than minimal risk. All drug trials are considered to involve more than minimal risk. Even observational studies of behavior should raise concern when potentially dangerous situations may be observed but not corrected during observation periods.26

**INSTITUTIONAL RESPONSIBILITY**

IRBs have the responsibility of ensuring that the research projects they approve be ethically conducted and that they not subject participants to risk that is unreasonable in relation to potential benefits.23 The special vulnerability of nursing home residents, particularly those who are mentally incapacitated, requires that extra measures be taken for their protection. Long-term care facilities have an additional responsibility to ensure that research taking place in their facilities be of high quality and that it be conducted in an ethical and safe manner.

Each facility should have a consistent mechanism for addressing proposed research: how and on whom it will be conducted, how the facility’s staff will (or will not) be involved, and how the research process will be overseen. Some facilities designate special committees for this purpose; others use a previously constituted ethics committee; yet others arrange for an ad hoc group consisting of the director of nursing, the facility administrator, and the medical director to review all research projects involving the residents.

All proposed research in a nursing home should be reviewed by the facility’s medical director. IRB approval is not an adequate substitute for approval by the medical director. This is especially important when the institution planning to perform the research—and thus the IRB’s home institution—is not the long-term care facility but rather a different kind of institution such as a university. In this situation, the medical director’s particular expertise will allow him or her to weigh the potential benefits of the research and the appropriateness of the research design as well as its risks to the residents. This entails consideration of residents’ privacy, potential discomfort, disrupted schedules, and anxiety.16

Whenever a resident is involved in a study that influences his or her medical care, the investigators should discuss the research project with the attending physician. The attending
physician may be aware of specific risks to the resident of participating in a particular study. And without the knowledge and cooperation of the attending physician, there may be interactions between the research intervention and elements of the resident’s regular medical care.

Another responsibility of the institution is to eliminate the potential for conflicts of interest in research, particularly in studies funded by industry. This important issue will be examined in further detail in a future position statement.

POSITION STATEMENT: AMDA’S RECOMMENDATIONS

1. The Need for Research involving Long-Term Care Residents

The mission of the American Medical Directors Association (AMDA) is to improve the care of residents of long-term care facilities. Because there is still much to learn about residents’ special needs, physiology, responses to medication, and responses to diagnostic and therapeutic procedures, research on long-term care residents is essential for improving their medical care. Long-term care is not just for the elderly alone; these recommendations pertain equally to children and younger adults in long-term care. Each research project must be designed well enough to answer the research question, and the question must be worth investigating.

- AMDA strongly supports the involvement of residents of long-term care facilities in responsible, ethical and well-designed research.

2. Protection of Human Subjects

Residents of long-term care facilities should receive all protections required by federal and state statutes and regulations involving research in human subjects, irrespective of the source of funding for the proposed research. Because of the residents’ vulnerability, the standards for their protection should be higher than for persons without cognitive impairment and for persons living independently in the community. Protection can be ensured by scrupulous oversight that involves the medical director.

- Any research project involving residents of a long-term care facility should be approved both by an IRB and by the medical director of the facility.
- Any research project involving residents of a long-term care facility should be subject to ongoing review by the facility and IRB.
- Residents or their surrogate decision makers have the right to consent or refuse to participate in research.
- Informed consent must be obtained from all subjects or their surrogate decision makers before participation in research projects.
- Consent to participate can be revoked by the resident or surrogate decision maker at any time.
- Residents have the right to refuse to participate in research at any time, even when a surrogate decision maker has given permission for participation.
- The risk to participants in research should be reasonable in relation to its potential benefits.