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Ethical considerations for decision making for treatment and research participation

John D. Fisk[a,*], B. Lynn Beattie[b], Martha Donnelly[c]

[a]QE II Health Sciences Centre; Department of Psychiatry, Department of Medicine, and Department of Psychology, Dalhousie University, Halifax, Nova Scotia, Canada

[b]Department of Medicine, Division of Geriatric Medicine, University of British Columbia, and the BC Network for Aging Research, Vancouver, British Columbia, Canada

[c]Division of Community Geriatrics, Department of Family Practice, and Division of Geriatric Psychiatry, Department of Psychiatry, University of British Columbia, and Geriatric Psychiatry Outreach Team, Vancouver Hospital, Vancouver, British Columbia, Canada

Abstract Here we review issues of patient decision-making and consent to treatment and research by persons with cognitive impairment and dementia. Clinicians and researchers must recognize their primary duty to care for the individual and must clearly distinguish their role as a clinician and/or researcher. Distinctions between standard care and research must be clearly understood by everyone, as must the clinician's role in each. Both actual and perceived conflicts of interest must be avoided. At present there is insufficient evidence to recommend specific methods for determining competency for decision-making, but a diagnosis of cognitive impairment or dementia does not preclude such competence. Competency is not a unitary or static construct and must be considered as the ability to make an informed decision about participation in the particular context of the specific treatment or study. Clinicians and researchers should consider consent as a process involving both the patient with cognitive impairment and his or her family/caregiver, particularly given the potential that competency for decision-making will change over time. As the availability of advance directives remains limited, clinicians and researchers must make efforts to ensure that decisions made by proxies are based on the prior attitudes and values of the patient.

Keywords: Alzheimer's disease; Dementia; Decision-making; Competency; Ethics

For the current revision of the Canadian Consensus Conference on Dementia (CCCD), the emergence of improved methods for early diagnosis of dementia as well as the availability of approved symptomatic treatments for Alzheimer's disease meant that the issues of patient decision making for treatment and research required discussion. The ethical considerations surrounding these issues had not been included in previous CCCD guidelines [1]. Not only did these issues seem of greater current priority, but also the ethical issues of decision making seemed to represent a logical extension of the discussions and recommendations surrounding the issue of diagnostic disclosure. Both have the issue of patient autonomy at their center. For this review, the PubMed and Embase databases were searched for articles with the keywords "Dementia OR Alzheimer's disease AND ethics AND competency." For discussion, preference was given to publications between 1996 and 2006. We also examined Canadian and international guidelines on the ethics of research, with particular attention to issues relevant to the participation of individuals with cognitive impairment and dementia in research.

We review and discuss issues on consent to treatment in clinical practice and consent to research participation by persons with cognitive impairment and dementia. We also review studies that have examined patient decision making for treatment and the participation of persons with dementia in research. Although attempts have been made to draw distinctions between the ethics of clinical care and the ethics of the conduct of research [2], this view is strongly opposed

*Corresponding author. Tel.: (902) 473-2581; Fax: (902) 473-7166.
E-mail address: John.Fisk@cdha.nshealth.ca

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by many [3] and is inconsistent with most national and international ethical guidelines for research [4,5]. Thus many of the same principles apply, regardless of whether treatment or research participation is the issue of discussion. For this reason, we have chosen to discuss these issues together in a single document and have combined the discussions and recommendations regarding treatment decision making and research participation decision making.

Although there might not be clear distinctions between the ethical issues that clinicians and scientists must consider, there are nonetheless clear distinctions between the roles of clinician and scientist. Specifically, appointments, investigations, and data collection that represent managment of an individual's health care must be clearly distinguished from similar activities that represent the conduct of a clinical trial for the research participant. Clinicians need to be keenly aware of the ethical issues, such as conflicts of interest, that they are likely to face when they conduct clinical trials. They must also be aware of the values and beliefs on which their own decision making is based. However, although research involving patients with cognitive impairment and dementia presents its own particular challenges, the ethical considerations themselves are not unique to dementia.

In 1997 the Alzheimer Society of Canada's ethical guidelines document [6,7] addressed both autonomy in decision making and participation in research. Even though the lack of available symptomatic treatment in Canada at that time limits their current applicability to some extent, these guidelines illustrate an important point. Specifically, they illustrate the differences that can emerge between general international guidelines on the ethical conduct of research and guidelines that are developed by individuals who are affected by specific medical conditions and their representatives. Individuals affected by specific medical conditions and their advocates, while continuing to point out the importance of protecting the rights of vulnerable individuals, generally place greater emphasis on ensuring that the potential to benefit from participation in research is not denied to specific groups of individuals. This inclusive stance toward research participation by persons with dementia has been articulated by High et al [8]: "To deny persons access to research participation out of fear of exploitation of specific groups of persons is to avoid rather than accept and practice ethical responsibility."

The principles that best describe ethical decision making regarding research participation are those articulated in the Belmont Report, produced by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research [9]. These include the principles of respect for persons, beneficence (ie, the obligation to do no harm and to maximize the potential for benefit while minimizing the potential for harm), and justice. These principles, in turn, are applied to clinical research through consideration of informed consent, assessment of risks and benefits, and the selection of subjects. In Canada, research on human subjects conducted at institutions that receive support for federal funding bodies must be conducted in accordance with guidelines established jointly by the Canadian Institutes for Health Research, the Social Sciences and Humanities Research Council, and the National Science and Engineering Research Council [10] that are largely based on these same ethical principles. The same principles are present in most international regulatory research guidelines such as the World Medical Association's Declaration of Helsinki [11], the Ethical Guidelines for Biomedical Research of the Council for International Organisations of Medical Sciences (CIOMS) [5], and the Council of Europe's Convention on Human Rights and Biomedicine [12]. Internationally accepted guidelines for the conduct of clinical trials are published in the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use Harmonised Tripartite Guideline (ICH) [13]. Unlike the ethical guidelines for research, these guidelines, often referred to as the "good clinical practice" (ICH-GCP) guidelines, were produced as a joint regulatory and industry project "to facilitate the adoption of new or improved technical research and development approaches which update or replace current practices, where these permit a more economical use of human, animal and material resources, without compromising safety" [13]. Given their origins and mandate, it is perhaps not surprising that despite recognizing the need to address issues specific to the conduct of clinical trials in elderly populations and reference to research on Alzheimer's disease [14], ICH-GCP guidelines provide no insight into the specific ethical issues that arise in those contexts. As with all guidelines, the challenge becomes how to find the right balance when attempting to apply the general principles to the specific ethical dilemmas that arise.

Perhaps the most obvious ethical dilemma associated with clinical trials for cognitive impairment and dementia is balancing respect for the autonomy of the individual with the protection of vulnerable persons. Most ethical guidelines regarding research focus on the individual in terms of the analysis of risk/benefit ratios and the consent process. Guidelines developed for persons with Alzheimer's disease, however, also acknowledge the need to consider the consequences of research participation on families and the importance of involving the caregiver/family in the consent process [8,15]. Even for individuals with Alzheimer's disease who are competent to provide informed consent, consent might be required of their caregiver/family. Typically it is they who will be expected to bring the person to scheduled appointments; observe the subject for adverse events, including those that should be reported immediately to the research team, as well as those of less urgent nature; ensure that the subject takes medications as required; observe and report possible treatment benefits; relay to the investigators the subject's continued assent to participation; and take part