As the population ages worldwide, a growing number of individuals suffer from diseases that impair their decision-making capacity. Over the years, researchers around the world have intensified their efforts to identify the causes of these diseases, develop effective treatments to slow their progression, and further our understanding of their impact on affected individuals and their families.

At the same time, there has been increasing recognition of the ethical dilemma that arises in conducting research on diseases that alter decision-making capacity. All research involving human subjects should be conducted in accordance with three cardinal ethical principles: justice, beneficence, and respect for persons. Respect for persons entails securing free and informed consent from potential research participants before their enrollment in a study. This requirement poses special challenges to investigators conducting dementia research on diseases that impair decisional capacity, such as advanced dementia. Subjects in the early stages of the disease may retain sufficient decisionmaking capacity to give informed consent for some studies. However, the irreversible and progressive nature of the illness ultimately robs its victims of the ability to fully appreciate the consequences of their involvement in research. Due to this distinguishing characteristic, decisionally-compromised subjects are viewed as a group particularly vulnerable to exploitation whose rights and welfare call for special legal protection.

Recognizing the need to produce knowledge that may lead to improved care for future incapacitated patients, many jurisdictions authorize the enrollment of subjects unable to consent themselves provided certain precautions are fulfilled. These often include the obligation to obtain the approval of an Institutional Review Board (IRB), the consent of the subjects’ legal representatives, and the subjects’ assent. Although a matter of some debate, these legal provisions are viewed by many commentators as a socially acceptable compromise between proceeding without any consent and foregoing all research on diseases that impair decisionmaking capacity.

In order to protect vulnerable individuals, these special provisions must be known and respected by...
all concerned, including researchers and IRB members. Recently, we conducted a postal survey in these two populations to assess their knowledge of the legislation that governs the process of consent for research on mentally incapacitated older adults. The survey was conducted in Quebec, Canada, where the law (Appendix A) prohibits enrolling such subjects in most experiments if they are not legally represented. Only emergency research is exempt from the obligation to obtain prior consent from the legal representative.

The study revealed a lack of knowledge in both groups, perhaps because the legislators failed to define the term experiment. As a result, there has been considerable debate surrounding the type of research to which the law applies. Interestingly, two-thirds of the respondents unaware of the law wrongly thought that a caring family member who was not legally appointed could provide a substituted consent for research on behalf of a mentally incapacitated relative, as is the case for consent to health care and emergency research. As part of the survey, we also asked the respondents who they thought should consent to research on behalf of an incapacitated person. Opinions varied with the degree of risk involved in the study. In the absence of risk, over 70% of the researchers and IRB members felt that the surrogate decisionmaker did not have to be legally appointed.

These findings suggest that researchers may be enrolling cognitively impaired subjects with the consent of someone who is not legally authorized to make a substituted decision. Moreover, the conduct of researchers may be sanctioned by their IRB, which provided prior approval of the research protocol. To our knowledge, no published study has examined the conduct of researchers and IRB members with respect to proxy consent.

This article reports data from the third component of our survey that was designed specifically to shed some light on this issue. We also report data on related issues, such as respondents’ views of the consequences and scope of current legislation governing substituted consent.

Survey of Researcher and IRB Conduct Involving Proxy Consent: Methods

Study Participants

The survey has been described in detail elsewhere. To summarize, we first designed, pretested and mailed a postal questionnaire to all researchers in aging from Quebec identified from the latest version of the Provincial Directory of Public Researchers (n = 160). With the objective of maximizing the response rate, we followed Dillman’s suggestions on how to design an attractive questionnaire, the ideal number of repeated mailings, and the content of each mailing. Potential respondents received a first copy of the questionnaire with a
personal covering letter that stated the objective of the survey and underscored the importance of their participation. The first mailing also contained a self-addressed and stamped return envelope, a letter of support signed by three well-known researchers from the fields of aging, mental health and ethics, and a postcard to be returned separately from the questionnaire. The postcard served to identify those who had returned the questionnaire while maintaining the anonymity of their responses. Two weeks later, a reminder postcard was mailed to all non-respondents. Lastly, two months after the first mailing, individuals who had not yet returned their questionnaire received a replacement copy and a new personalized letter. Ninety-eight researchers returned the questionnaire. Excluding ineligible researchers (n = 16), the response rate was 68.1%.

Second, we identified the 37 IRBs designated by the provincial Minister of Health and Social Services to review research protocols involving persons unable to consent for themselves. All these IRBs are affiliated with a university or health care institution. IRB chairpersons were contacted personally by phone to inform them of the study and solicit their participation as well as that of their members. One chairperson refused to participate. The others received a personalized introductory letter, a one-page questionnaire for them to fill out personally and the relevant number of a second questionnaire for distribution to the ethics committee members. Two months later, chairpersons and individual IRB members received a second letter reiterating the importance of their participation. Twenty-four chairpersons (64.9%) and 136 IRB members (34.6%) returned their respective questionnaires.

**The Questionnaires**

The data reported in this article originate from three different questionnaires investigating researchers’ and IRBs’ behavior regarding proxy consent. In the case of researchers, this was achieved through a series of questions regarding how they secure consent from incapacitated older adults for studies with minimal risk (Appendix B). The questions designed to assess ethics committees’ willingness to approve research proposals involving such individuals were addressed specifically to the IRB chairpersons. These questions were constructed using the same model as those addressed to the

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**Figure 2**

**Flow chart summarizing IRBs’ position in regard to substituted consent**

- IRB chairpersons who returned the one-page questionnaire
  - n = 24

- IRBs reviewing research proposals involving older adults unable to consent
  - n = 21

- Accept, under certain circumstances, that older adults unable to consent participate in research
  - n = 19

- Accept, under certain circumstances, that older adults unable to consent and not legally represented participate in research
  - n = 12

- Only in the context of emergency research
  - n = 4

- In other situations
  - n = 8

- If the research involves … *

- No serious risk but some personal benefits for the subject
  - n = 8

- No serious risk or personal benefit for the subject but benefits for others
  - n = 4

- Some risks but also personal benefits greater than the risks
  - n = 1

* More than one answer could be given
How Researchers and IRBs Obtain Proxy Consent: Results

Figure 1 gives an overview of the conduct of researchers regarding proxy consent. Sixty-four percent of the respondents answered that some of their research projects target older adults unable to consent for themselves. In the vast majority of cases, a member of the research team solicits the consent of the prospective subjects and judges whether they are able to consent, often after consulting with a health professional aware of the subject’s mental condition (data not shown). When encountering an incapacitated older adult, 3.4% exclude him/her immediately, 59.3% investigate the legal status of the prospective subject, and 37.3% solicit the consent of a proxy who may not have been formally appointed as the subject’s legal guardian. Among those who investigate the legal status of a potential subject, 37.1% will exclude a subject who is not legally represented, while the others will solicit the consent of a traditional surrogate decisionmaker. Overall, 74.6% of researchers do not comply with the law in effect in Quebec by recruiting decisionally incapacitated older adults on the basis of a consent given by someone who may not have the legal authority to do so.

Figure 2 summarizes the IRB chairpersons’ responses to the questions designed to assess their degree of permissibility towards substituted consent. Of the twenty-one IRBs that have reviewed proposals involving decisionally incapacitated older adults, two responded that such protocols would be rejected. Of the nineteen IRBs open to the recruit-
ment of older adults unable to consent, twelve accept that these individuals do not have a legal guardian, at least under certain circumstances. In one-third of the cases, these circumstances are restricted to emergency research. In the other two-thirds, all would approve a study that involved no serious risk for the prospective subject and could benefit him/her personally; one in two would support a study with no serious risk or benefit for the subject but that could benefit others; and one would approve a study involving some risks to the participants, provided the benefits for the subjects outweigh the risks.

Responses to the four questions submitted to both researchers and individual IRB members are shown in Table 1. In the opinion of the majority, the obligation to exclude incapacitated adults who are not legally represented impedes the advancement of knowledge, in addition to depriving these individuals of the benefits of being a research subject. One in five respondents believed that the legislation governing substituted consent does not apply to all types of research. Forty-five percent of researchers and 35% of IRB members admitted that they simply didn’t know.

Three common themes emerged from the content analysis of the researchers’ and IRB members’ definition of what constitutes an experiment. In both groups, 11% defined an experiment as an intervention involving some risks to the subject’s health. For example, one researcher wrote: “an experiment is an intervention that involves an aggressive physical or mental procedure (pain, risk of infection, discomfort).” Half alluded to an intervention in their definition, but without mentioning risk. Two examples are: “Process that requires a person to submit to specific conditions related to treatment or care which his/her condition does not necessarily require” and “Any intervention in regard to a person which has the potential to modify physical and/or psychological functions with the aim of developing scientific knowledge in a specific field.” Another 40% of respondents believed that the term experiment encompasses all types of research, whether or not an intervention is present, and whether or not risks are involved. The following definition proposed by a member of an IRB illustrates this view: “Any research project in which a person participates or is observed in order to test a hypothesis.”

Non-Compliance with Legal Requirements: Possible Explanations and Discussion of Implications

Improving the patient’s condition is the sole aim of clinical care. In contrast, research is conducted to produce knowledge that may lead to improved care for future patients. As in many jurisdictions, Quebec authorizes a close relative or friend to consent to health care required by an incapacitated patient when a legal guardian has not yet been appointed. Turning to families for assistance with health care decisionmaking is a common practice among medical practitioners. It is also widely accepted by the general population. Surveys have repeatedly shown that most people would trust their families to make medical decisions on their behalf when the need arises. Despite potential conflicts of interest and strong empirical evidence of significant discrepancies between patients’ treatment preferences and proxies’ perception of those preferences, the family continues to be viewed as the most concerned for the welfare of a decisionally-compromised patient.

Recognizing the distinctions between health care and research, some jurisdictions chose to limit authority for research decisionmaking to the legal guardian when the prospective subject is unable to decide him/herself. Stricter regulations are justified by the need to protect vulnerable individuals from the risk of being exploited in the name of science. But they must be respected. The data reported in this article show that this is not the case, at least in the province of Quebec. Three out of four researchers on aging admitted soliciting the consent of a traditional proxy, half without first determining whether the potential subject has a legal representative. Moreover, a number of IRBs approve non-emergency research involving incompetent older adults without legal representation.

Different hypotheses could explain the conduct of researchers and ethics committees. First is their lack of knowledge of the legislation. Investigators and IRB members should be familiar with the laws that apply in their jurisdictions. Educational efforts to enhance awareness of legal aspects of research consent are still in an embryonic state. Second is the ambiguity of the law itself, which does not specify the type of research to which it applies. As a result, the interpretation of the law varies within the group of researchers as well as among ethics committee members (Table 1). Thus researchers conducting intervention trials without risk to the subjects’ health may proceed with the consent of traditional proxies simply because they think the law does not apply in that case. IRB members may approve such protocols for the same reason. Given the ambiguity of the law, researchers and IRB members should not be criticized for not complying with the legislation governing surrogate consent for research.

A third explanation lies in the belief that the current legislation is inadequate, for several reasons. Most would agree that cognitively impaired subjects deserve special legal protection. But complete exclu-
sion of all those without legal representation may deprive them of the health benefits of research participation, a view shared by the majority of respondents in our survey (Table 1). These benefits may include access to a promising treatment, enhanced medical attention, or increased social and emotional support. Many people and families also take comfort and find hope in being able to help increase knowledge about currently incurable conditions such as Alzheimer’s disease.

In addition to discriminating against non-legally represented incompetent individuals, the obligation to exclude them makes adequate recruitment difficult, skews the population being studied, and limits the generalizability of the results. Despite widespread professional and public endorsement of advance planning, few people have appointed an agent to make decisions on their behalf in the event of incapacity. Those who have are known to differ from the general population, particularly with respect to their socioeconomic status. Limiting enrollment to cognitively impaired subjects who are legally represented could thus lead to unrepresentative samples. These considerations may have motivated a majority of researchers and IRB members to respond that the current legislation inhibits scientific progress (Table 1). Given the modest impact of interventions designed to promote advance planning for health care and research, the number of legally represented older adults is unlikely to increase significantly in the near future.

The picture we have presented of the conduct of researchers and ethics committees reflects a widely endorsed practice that involves obtaining informed consent from a proxy for the subject, whether or not this person has been legally designated as a guardian, along with the subject’s assent. Our finding that the Quebec legislation is often violated does not imply that impaired older adults in this province are exposed to greater risks since the questions put to the researchers were restricted to studies with minimal risk. Furthermore, to our knowledge there is no empirical evidence that legal guardians afford better protection to cognitively impaired adults than caring family members without legal authority. To allow the latter to consent on behalf of relatives with diminished mental capacity would move research decisionmaking from the courtroom to the common practice of clinical decisionmaking. In the clinical setting, when patients are incompetent and lack a formally appointed surrogate, physicians turn to the patient’s family for insight into treatment preferences. Patients who do not have the ability to make complex decisions may still have decisionmaking capacity to choose a trusted surrogate.

As pointed out by some authors, it makes little sense to allow a proxy to withdraw or withhold artificial nutrition or hydration but not to consent to blood drawing for research purposes, a brain autopsy, or medication trial for dementia. Many people likely share these views. In a recent telephone survey, 88% of interviewees supported allowing their family to make research decisions for them in the absence of prior specifications on their part. Moreover, 80% stated that their families could enroll them in research that offers a potential for medical benefit even when their advance directives opposed research participation. Strong support for allowing traditional proxies to consent to research that involves little risk was also observed in our survey. These results attest to the confidence older adults place in their close relatives to make decisions on their behalf, whether legally appointed or not. Of course, changes to the current legislation should be accompanied by educational efforts designed to enhance researchers’ and IRB members’ awareness of the rules governing substituted consent for research.

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References


8. At a symposium held in June 2002 and organized by the authors, lawyer Marie Josée Longtin, Director General, Legislative Affairs, Quebec Ministry of Justice, stated that the term experiment encompasses all types of research, medical as well as psychosocial. Proceedings of the symposium entitled “Consent to research on incompetent persons: Can we reconcile ethical, legal and scientific issues?” (translation from French), ISBN 2-875; McKneally MF, Singer PA. Bioethics for clinicians: 25. Teaching bioethics in the clinical setting. Canadian Medical Association Journal 2001;164:1163-1167.
18. See ref. 7; Bravo et al. 2003.
29. See ref. 10, Bravo et al. 2003.
APPENDIX A

Article 21 of the Civil Code of Quebec

[…] a person of full age who is incapable of giving consent may not be submitted to an experiment if the experiment involves serious risk to his health or, where he understands the nature and consequences of the experiment, if he objects.

Moreover, a person of full age who is incapable of giving consent may be submitted to an experiment only if, […] it has the potential to produce results capable of conferring benefit to other persons in the same age category or having the same disease or handicap. Such an experiment must be part of a research project approved and monitored by an ethics committee. The competent ethics committees are formed by the Minister of Health and Social Services or designated by that Minister among existing research ethics committees; […]

Consent to experimentation may be given, […] in the case of a person of full age incapable of giving consent, by the mandatary, tutor or curator. Where a person of full age suddenly becomes incapable of consent and the experiment, insofar as it must be undertaken promptly after the appearance of the condition giving rise to it, does not permit, for lack of time, the designation of a legal representative, consent may be given by the person authorized to consent to any care the person requires; […]

APPENDIX B

Questions addressed to the researchers:

1. Are older adults who are unable to consent for themselves sometimes targeted by your research projects?
   - No, never → Go to question 4.
   - Yes

2. What do you do when a prospective subject has been judged unable to consent for him/herself to research involving no serious risks for his/her health?
   - I exclude him/her → Go to question 4.
   - I immediately ask a significant other (spouse, close relative, etc.) to provide substituted consent → Go to question 4.
   - I check the prospective subject’s legal status.

3. What do you do when a prospective subject who is unable to consent for him/herself to research involving no serious risks is not legally represented?
   - I exclude him/her.

   - I ask a significant other to provide substituted consent.

Questions addressed to the IRB chairpersons:

1. Are older adults who are unable to consent for themselves sometimes targeted by research protocols submitted for approval to the Review Board you chair?
   - No, never → Please return the questionnaire in the enclosed envelope.
   - Yes

2. Does your Review Board accept, under certain circumstances, that older adults who are unable to consent for themselves participate in research?
   - No, never → Please return the questionnaire in the enclosed envelope.
   - Yes

3. Does your Review Board accept, under certain circumstances, that older adults who are unable to consent for themselves and are not legally represented participate in research?
   - No, never → Please return the questionnaire in the enclosed envelope.
   - Yes

4. Under what circumstances does your Review Board allow a close relative of an incompetent older adult who is not legally represented, to decide on his/her behalf whether or not to participate in a research project? (Check all circumstances that apply.)
   - If the research does not involve any serious risk for the prospective subject’s health and could benefit him/her personally.
   - If the research does not involve any serious risk for the prospective subject’s health and will not benefit him/her personally but could benefit others.
   - If the research involves some risks for the prospective subject’s health but also potential benefits that are greater than the risks.
   - If… Please specify: ______________________