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FEATURE ARTICLE

Surrogate Consent for Dementia Research:
Factors Influencing Five Stakeholder Groups from the SCORES Study

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Alzheimer's disease and other dementias are devastating neurological disorders with tremendous impact on affected individuals, their families, and health care systems. Over 37 million people worldwide are currently living with dementia, a number expected to reach 115 million by 2050. The total costs of dementia, estimated at U.S. $600 billion in 2010, will likely rise as the prevalence increases. Indeed, despite considerable scientific efforts, currently available drug therapies do not fundamentally alter the course of the disease.[1] There is thus a pressing need to identify modifiable risk factors of dementia and develop more cost-effective preventive and therapeutic interventions. Such research must in part be done with affected individuals, including those at later stages of the disease who may lack the decisional capacity to give valid consent to research.[2] Permission to enroll decisionally incapacitated subjects in research must then be provided by substitute decision-makers, usually family members.[3] Surveys conducted in North America have found broad support for relying on family surrogate consent for dementia research.[4]

Knowledge of the factors that influence surrogate consent is critical to successfully producing valid and reliable data from completed dementia studies. Low statistical power due to under enrollment, slow trial accrual that consumes scarce financial resources, and selective enrollment that yields biased samples can seriously undermine the validity and generalizability of clinical trial findings.[5] Factors investigated for their possible effect on participation in clinical research in the United States include characteristics of the surrogate and/or prospective subject, such as age, race/ethnicity, relationship, and health status, as well as the risk and nature of the study.[6] Most published studies, however, have involved patients who were able to consent to research by themselves or parents consenting for their minor child.[7] We know of only five studies aimed at uncovering factors that influence surrogates' decision to enroll their decisionally impaired relative in actual or hypothetical dementia research. Mastwyk and colleagues[8] based their study on a questionnaire completed by 25

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Table 1.
Characteristics of Respondents (n = 2,060)

	Older adults *n = 679*	*Caregivers* *n = 384*	*Physicians* *n = 495*	*Researchers* *n = 177*	*IRB members* *n = 325*
Age (years)	75.2 ± 6.9 (65 to 95)	65.6 ± 12.0 (31 to 88)	51.4 ± 11.6 (29 to 94)	49.8 ± 8.8 (28 to 73)	50.7 ± 11.3 (21 to 78)
Sex (female)	56.8	74.8	33.7	54.7	56.9
Religion					
Protestant	50.6	56.5	25.8	29.3	28.9
Catholic	22.1	25.4	21.4	14.4	21.9
Other religion	11.2	6.3	23.6	11.4	12.2
No formal religion	16.1	11.8	29.2	44.9	37.0
Education					
Less than high school	20.1	11.8			0
High school graduate	53.9	45.9			1.9
Professional school or college	14.0	20.3			22.7
University	12.0	22.0	100	100	75.4

Note: Data shown are percentages or means ± standard deviations (range) as previously reported in G. Bravo, Dubois MF, Cohen CA, et al. Are Canadians providing advance directives about health care and research participation in the event of decisional incapacity? *Canadian Journal of Psychiatry* 2011;56(4):209-218. Rates of missing data range from 2.1% (for sex) to 6.8% (for age).

patient caregivers enrolled in one of three dementia drug trials. The four other studies[9] were qualitative in nature, with findings based on interviewing Alzheimer's disease patients and family caregivers. Reasons for enrolling typically featured potential health benefits to the patient, a desire to help others by contributing to scientific knowledge, trust in investigators and their institutions, and desperation. Predominant reasons for not enrolling were the burden of participating in research and concerns that participating in a study would disrupt the patient's quality of life. Overall, risk involved in participating was infrequently mentioned as an influential factor in enrollment decisions. According to Sugarman and colleagues,[10] belief in the goodness of research and trust in those involved in the research enterprise minimized concerns about potential research risks and uncertainties.

These five studies are informative, but they were not designed to compare the views of older adults and caregivers or to quantify the relative importance of one factor over the others. Moreover, the views of others who may one day be a surrogate for a decisionally impaired relative—i.e., physicians, researchers, and institutional review board (IRB) members—were not explored. Knowledge of key stakeholders' perspectives on factors that may influence their decisions as surrogates regarding their relatives' participation in research could inform the design and conduct of future dementia clinical trials, as well as the informed consent process for those trials.

As part of a larger research project on substitute decision-making, we asked members of the five aforementioned groups to identify factors that would influence their decision about whether to enroll a decisionally incapacitated close relative in a hypothetical research study. Herein, we summarize and compare across groups their ranking of factors that would influence their decision-making. We also explore respondent characteristics associated with their rankings. Given the tendency of IRBs to be protective of research participants[11] and of study participants to be motivated by therapeutic benefits,[12] we hypothesized that IRB members would rank potential risks as more influential than potential benefits, while the reverse would be observed among laypersons (i.e., older adults and informal caregivers). No hypotheses were formulated relative to physicians and researchers, given the lack of prior research in these groups.

Study Methods

For our investigation we used data from the study Substitute Consent for Research in Elderly Subjects (SCORES), which explored issues surrounding substitute decision-making for research.

Table 2.
The Survey Question of Interest

Assume that a close relative of yours is no longer capable of making decisions and that you are asked to decide on their behalf whether they will participate in a study. Below is a list of seven factors that might influence your decision.

A. Inconveniences to you in letting your relative participate in the study (e.g., the need to accompany them to the research center for repeated testing)

B. The prospect of direct benefits to your relative

C. The reputation of the researcher conducting the study

D. Inconveniences to your relative in participating in the study (e.g., repeated testing)

E. The prospect of benefits to others suffering from the same disease

F. The possibility of serious side effects for your relative

G. The prospect of benefits to you (e.g., your relative may exhibit less disruptive behaviors as a result of being in the study)

Please select from this list the three factors that would most influence your decision. Write down below the letter for the factor you believe would be the most important, which would be the second most important, and which the third.

Most important factor ☐

Second most important factor ☐

Third most important factor ☐

Of the remaining four factors you did not select, which would least influence your decision? (Write the letter for this factor in the box below.)

Least important factor ☐

The SCORES study included an anonymous postal survey conducted with the following populations: 1) community-dwelling adults aged 65 and over, 2) informal caregivers of decisionally incapacitated older adults, 3) physicians, 4) researchers conducting studies on aging, and 5) IRB members. Potential participants were from four Canadian provinces (Nova Scotia, Ontario, Alberta, and British Columbia) of predominantly English-speaking Canada. They were selected randomly from various sampling frames (older adults, informal caregivers, and physicians) or comprised all researchers conducting studies on aging and IRBs registered on various Web sites (e.g., that of the Canadian Institutes of Health Research and the National Council on Ethics in Human Research).

The survey and postal questionnaires were designed according to Dillman's recommendations.[13] Survey packages contained a personalized letter describing the survey, the questionnaire, and a letter of endorsement from a relevant organization. Potential respondents were asked to complete the questionnaire and return it by mail in the enclosed self-addressed, stamped envelope. A thank you/reminder postcard was sent two weeks after the first mailing, and a second survey package two months later. In order to preserve the anonymity of their members, caregivers' associations and some IRBs handled the mailings themselves. Questionnaires were identical across groups except for the last section that collected demographic information about the respondents and various other group-specific data. Further information on the SCORES study and content of the questionnaires can be found in an article by Bravo and colleagues.[14]

■ *Statistical Analyses.* First, respondents' characteristics were summarized and compared with available census data. From these analyses, samples were deemed representative of their respective population, except for physicians. Physicians over 65 years of age are overrepresented in our sample. Accordingly, analyses involving physicians were weighted. Second, we tabulated respondents' rankings of the seven factors listed and compared rankings across groups with the chi-square test and follow-up contrasts. These contrasts mostly involved comparing laypersons (a term referring to the combined group of older adults and informal caregivers) with professional respondents (combining physicians, researchers, and IRB members). Given the relatively large sample sizes and number of comparisons involved, the significance threshold was lowered to 0.001 when emphasizing group differences. Lastly, we conducted exploratory analyses at the conventional 0.05 significance level aimed at identifying respondents' characteristics associated with their rankings. Characteristics investigated were extracted from the last section of the questionnaires collecting demographic and other group-specific information. Analyses were performed with SPSS version 18.0 (SPSS Inc., Chicago, IL).

Table 3.
Overview of Respondents' Rankings of the Influence of Factors A to G on Surrogate Decision-Making

Factor	*The most influential* %	*Among the three most influential* %	*The least influential* %
A: Inconveniences to proxy	2.9	13.6	42.2
B: Prospect of direct benefits to relative	55.8	88.6	0.7
C: Reputation of the researcher	5.1	24.5	24.0
D: Inconveniences to relative	2.3	33.5	4.0
E: Prospect of benefits to others	2.5	46.6	3.7
F: Possibility of serious side effects for relative	30.0	71.9	4.4
G: Prospect of benefits to proxy	1.4	19.4	20.9

Study Results

In total, 2,060 respondents returned the questionnaire (32.7%). Response rates ranged from 18.3% among physicians to 59.9% among informal caregivers. Selected characteristics of the respondents are presented in Table 1. More information is provided in a recent paper from the SCORES study.[15] Of the 2,060 survey participants, 161 provided inconsistent responses or did not answer at least one of the four subquestions. Of those, 104 (64.6%) were older adults and 23 (14.3%) were informal caregivers. Subsequent analyses were thus based on reduced samples.

Table 2 contains the survey question of interest for this study. The question was designed to measure the relative importance respondents attached to various factors in substitute decision-making for research participation. All respondent groups received the same question. Hence, IRB members, for example, were not asked to respond in that role, but rather as people who might someday assume the role of surrogate decision-maker for a decisionally incapacitated relative.

■ ***The Survey Question of Interest.*** Figures 1, 2, and 3 compare the selection of most and least influential factors across groups. Due in part to the large sample sizes, many between-group differences are statistically significant, even at the 0.001 level. Figure 1 shows that a slightly higher proportion of older adults (60.8%) chose the prospect of direct benefits to their relative (factor B) as the most influential factor, while the smallest proportion was found among researchers (47.4%). Conversely, laypersons less frequently chose the likelihood of adverse events (factor F) as the most influential when compared to professional respondents: 20.1% vs. 40.0%, $p < 0.001$. Also worth noting is factor C (reputation of the researcher), which was not chosen frequently overall as the most influential factor in surrogate decision-making, but was more frequently chosen by laypersons (8.6%) than by professionals (1.5%, $p < 0.001$).

With regard to Figure 2, three between-group differences are worth emphasizing. First, a much higher proportion of laypersons included the reputation of the researcher (factor C) and the prospect of benefits to themselves (factor G) among their three most influential factors than did the professionals combined (both p values < 0.001). Conversely, fewer laypersons gave a high ranking to factor F (the possibility of serious side effects for the relative) compared to their professional counterparts (56.9% vs. 86.9%, $p < 0.001$).

Table 3 shows how all respondents ranked the seven factors that might influence their decision about whether to enroll a decisionally incapacitated relative in a dementia study. For each of the seven factors listed, Table 3 reports the percentages of all respondents who ranked it as the most influential in their decision to allow their relative to enroll in a study, among the three most influential, and as the least influential. Just over half of respondents (55.8%) ranked the prospect of direct benefits to the decisionally incapacitated relative (factor B) as the most influential factor in surrogate decision-making, while nearly a third of respondents (30.0%) ranked the possibility of adverse events (factor F) as the most influential factor. Overall, 88.6% and 71.9% of all respondents included these two factors among their three most influential. Factor A (inconveniences to the substitute decision-maker) was the least influential factor (42.2% of respondents), followed by the reputation of the researcher (factor C; 24.0%) and prospect of benefits to the surrogate (factor G; 20.9%).

Interesting between-group differences also emerge from Figure 3 regarding the least influential factor. With regard to the four highly significant differences, it is notable that older adults' and informal caregivers' choices are similar, as are those of the professionals. "Inconveniences to proxy" (factor A) was endorsed more frequently as the least

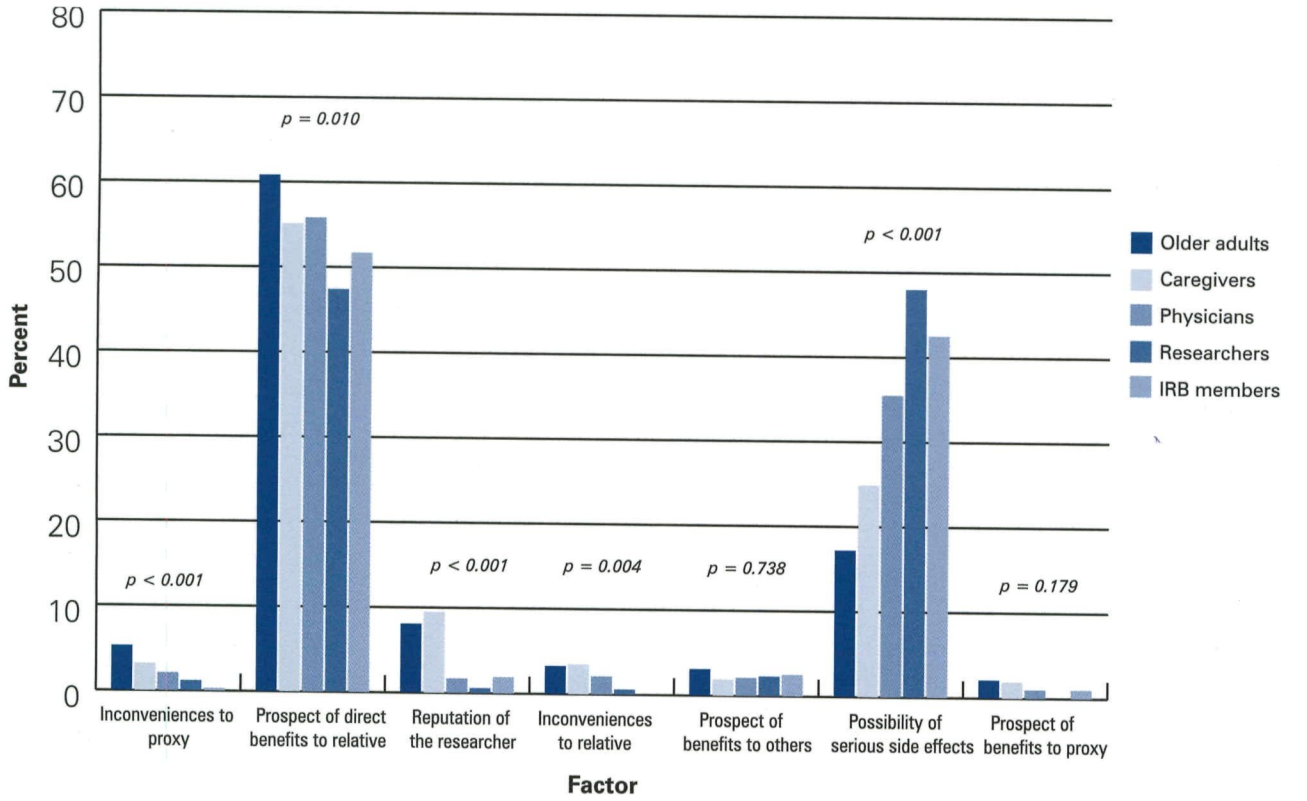
influential factor by laypersons than by professionals (51.6% vs. 32.9%, $p < 0.001$), as was the possibility of side effects for the relative (factor F) (7.9% vs. 1.0%, $p < 0.001$). The reverse is the case for factors C (reputation of the researcher) and G (prospect of benefits to proxy), which were more frequently chosen as the least influential factor by professionals than by laypersons (both p values < 0.001).

■ ***Correlates of Respondents' Rankings.*** We examined characteristics that distinguish three types of respondents (Figure 1): those that chose the prospect of direct benefits to their relative (factor B) as their most influential factor in making a surrogate decision, those that chose the possibility of serious side effects (factor F), and those that chose neither. Comparing respondents according to whether they differentially ranked potential benefits and risks is of great interest from a policy perspective, given the importance of these two factors in the ethics review process. Analyses were conducted separately in each of the five groups to explore a larger number of characteristics. These are listed in Table 4, together with the results of testing their bivariate relationship with the respondents' choice of the most influential factor.

Overall, few variables were found to be linked to the respondents' choice. None were found among older adults and physicians. Two were linked to informal caregivers' selection: age ($p = 0.006$) and relationship to the care recipient ($p = 0.028$). Informal caregivers who chose the possibility of serious side effects for their relative as the most influential factor in their decision were younger, on average, and more often a child than the spouse of the care recipient. When including both variables in a multinomial logistic regression, caregivers' age remained significant ($p = 0.036$) but not relationship to the care recipient ($p = 0.161$).

Having a medical degree was the only variable associated with the researchers' choice ($p = 0.002$). Researchers trained in medicine were less likely to choose the possibility of side effects as the most influential factor in surrogate decision-making. Discarding the eight researchers who selected another factor as the most influential led to the same result: having a medical degree was the only variable distinguishing the researchers who selected the prospect of direct benefits from those

Figure 1.
The Most Influential Factor*



* For each of the seven factors listed, percent of respondents who chose that factor as the most influential, had they to make a surrogate decision about research participation.

Table 4.
Bivariate Analyses Linking Respondents' Characteristics to Choice of Most Influential Factor on Surrogate Decision-Making

Selected characteristics		*Most influential factor*			
		The prospect of direct benefits	*The possibility of side effects*	*Other*	*p value*[1]
Older adults (n = 605)		**n = 368**	**n = 104**	**n = 133**	
Age (in years)		74.9 ± 7.1	74.0 ± 6.3	75.5 ± 6.8	0.268
Sex (female)		54.9	59.4	54.3	0.687
Religion (some)		82.3	91.8	86.2	0.063
Education:	high school or less	72.5	70.0	73.4	
	professional or college degree	16.1	14.0	13.3	
	university degree	11.4	16.0	13.3	0.731
Knows someone unable to make decisions		43.2	44.4	38.1	0.546
Informal caregivers (n = 370)		**n = 204**	**n = 92**	**n = 74**	
Age (in years)		66.0 ± 12.4	62.4 ± 10.9	68.3 ± 11.8	**0.006**
Sex (female)		74.9	78.9	70.8	0.498
Religion (some)		90.1	82.4	93.0	0.073
Education:	high school or less	60.9	50.0	3.5	
	professional or college degree	15.1	26.7	28.2	
	university degree	24.0	23.3	18.3	0.073
Relationship to the care recipient:	spouse	57.6	40.2	56.9	
	child	35.0	44.6	37.5	
	other	7.4	15.2	5.6	**0.028**
Physicians (n = 485)		**n = 270**	**n = 172**	**n = 43**	
Age (in years)		52.0 ± 11.7	49.9 ± 11.4	53.1 ± 11.8	0.130
Sex (female)		33.2	32.5	35.7	0.926
Religion (some)		68.9	72.3	80.0	0.324
Family physician		52.0	54.2	43.6	0.489
Years in practice		25.4 ± 12.3	23.9 ± 12.0	28.2 ± 12.4	0.131
% of patients unable to make decisions		13.0 ± 22.2	14.8 ± 23.6	15.1 ± 24.2	0.688
Involved in research in the last five years		39.4	38.0	53.7	0.174
Member of an IRB in the last five years		2.2	3.6	0	0.369
Researchers of aging (n = 171)		**n = 81**	**n = 82**	**n = 8**	
Age (in years)		49.3 ± 8.7	50.1 ± 9.2	51.4 ± 4.9	0.734
Sex (female)		51.3	62.5	25.0	0.075
Religion (some)		62.8	48.7	37.5	0.125
Has a medical degree		35.0	12.3	37.5	**0.002**
Years in research		14.1 ± 7.8	15.8 ± 9.1	16.3 ± 6.6	0.405
Conducts clinical research		63.8	49.4	50.0	0.173
Conducts research with subjects unable to consent		48.1	42.7	37.5	0.710
Member of an IRB in the last five years		12.5	9.8	25.0	0.425
IRB members (n = 315)		**n = 163**	**n = 134**	**n = 18**	
Age (in years)		51.1 ± 11.2	49.4 ± 10.9	54.5 ± 15.2	0.163
Sex (female)		57.3	56.9	52.9	0.942
Religion (some)		66.5	58.1	66.7	0.333
Education (university degree)		78.6	72.9	64.7	0.304
Years on the IRB		5.1 ± 4.6	4.4 ± 4.6	6.2 ± 8.1	0.219
Appointed as ...	a researcher	31.4	46.9	50.0	**0.018**
	a physician	23.9	28.9	22.2	0.588
	an ethics expert	13.2	10.2	0	0.216
	a layperson	26.4	9.4	22.2	**0.001**

Note: Data shown are percentages or means ± standard deviations, except last column.
[1]Derived from an analysis of variance when the variable is continuous, and a chi-square test when it is categorical. Values in bold are significant at the 0.05 level.

who selected the possibility of side effects as the most influential factor ($p = 0.001$).

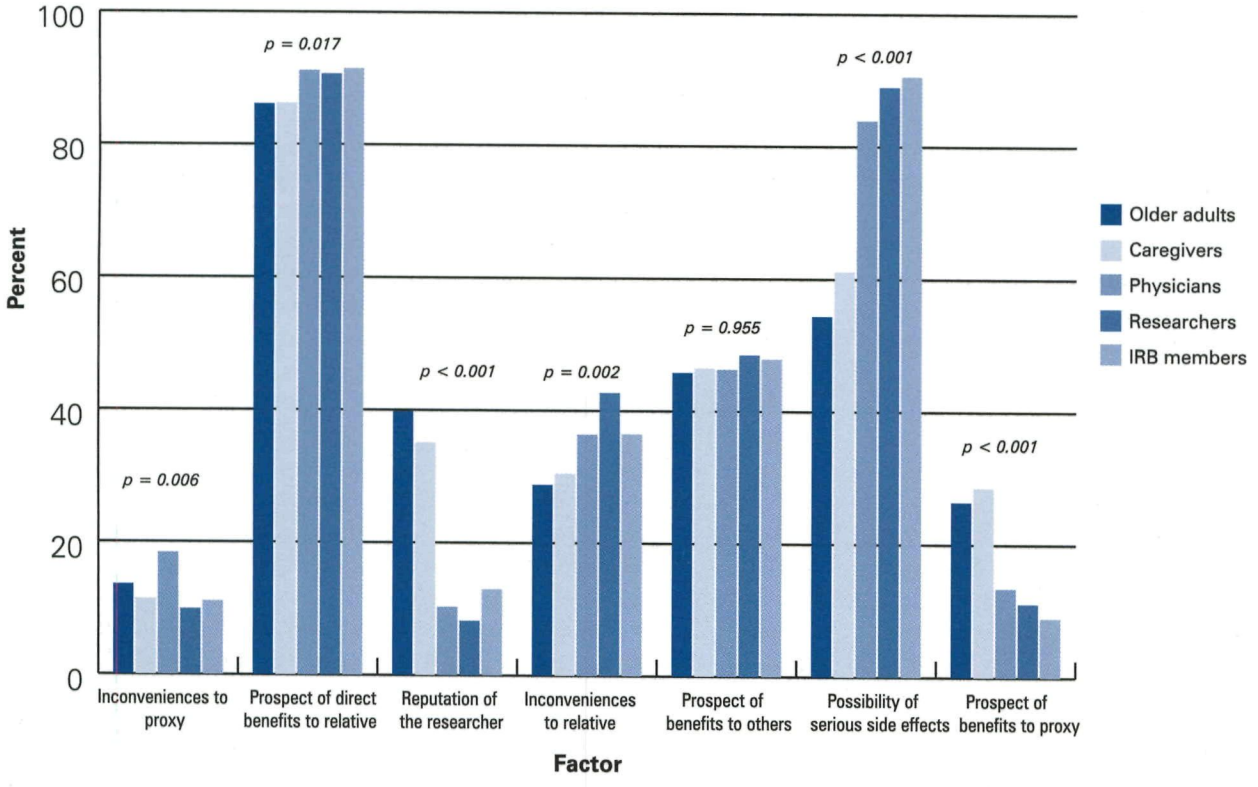
Lastly, whether an IRB member was appointed as a researcher ($p = 0.018$) or as a layperson ($p = 0.001$) affected their selection of the most influential factor. Researchers on the IRB were less likely to select the prospect of direct benefits as their most influential factor, with little difference in the proportions of those who selected either the possibility of side effects or another factor. Conversely, lay board members were less likely to select the possibility of side effects, with little difference in the proportions of those who selected either the prospect of direct benefits or another factor. Because only five IRB members indicated having been appointed as both a researcher and layperson, there was no point in examining the independent effect of these two variables in a multivariable model. Discarding the small subgroup of 18 IRB members who selected another factor as the most influential yields identical results: being appointed as a researcher ($p = 0.010$) or as a layperson ($p < 0.001$) were the only variables distinguishing the IRB members who selected the prospect of direct benefits from those who selected the possibility of side effects as the most influential factor.

Discussion

When a prospective research participant lacks decisional capacity, the decision about whether to participate in the study must be made by a third party on the participant's behalf.[16] Next-of-kin are generally considered appropriate substitute decision-makers, on the presumption that they are likely to promote their relative's best interests and welfare.[17] Decisions by surrogates should ideally be based on the potential participant's preferences and values, but those are often unclear or unknown, especially in regard to research participation.[18] Moreover, most people would grant their surrogate considerable leeway over expressed preferences in making important decisions for them.[19] In all likelihood, decisions made on behalf of a decisionally incapacitated individual will—at least in part—be influenced by factors valued by the surrogate decision-maker.[20]

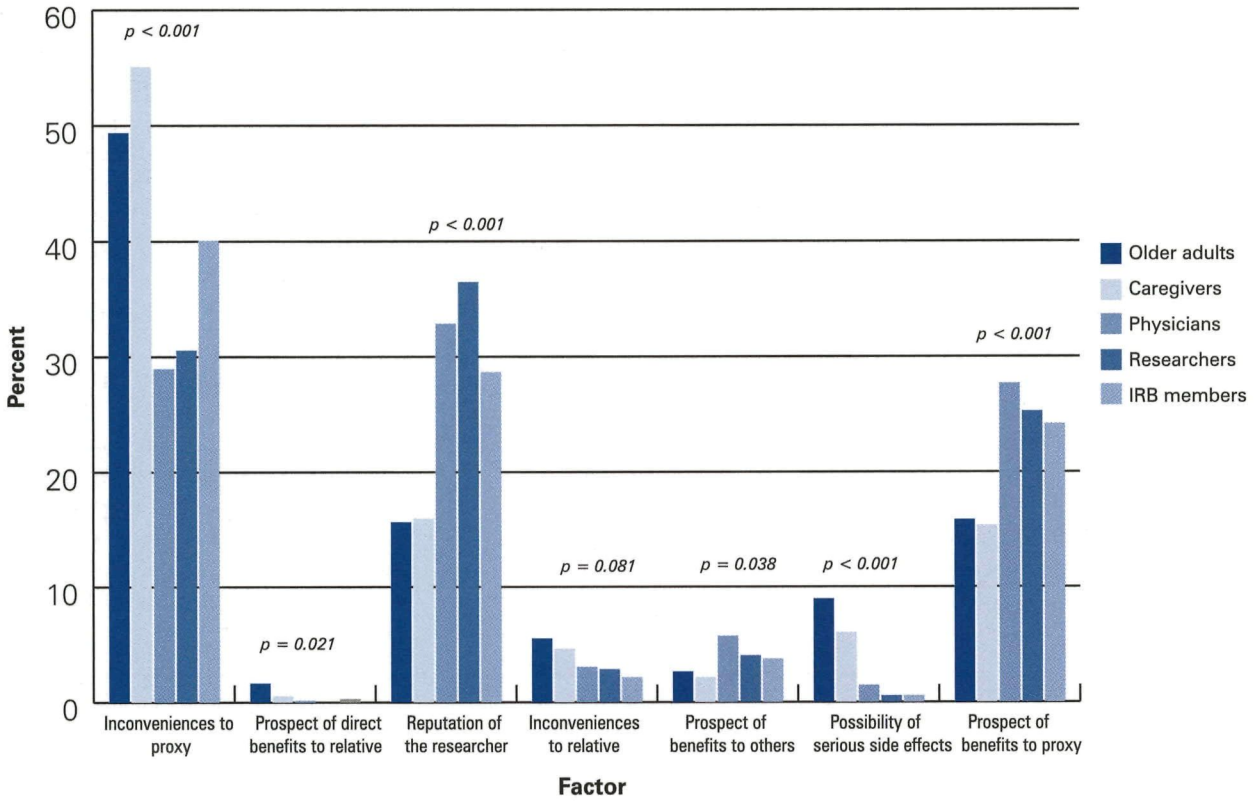
In this study, we explored these factors in five groups of people linked in some way to the research enterprise, either as potential research subjects (older adults) or

Figure 2.
Among the Three Most Influential Factors*



* For each of the seven factors listed, percent of respondents who chose that factor among their three most influential, had they to make a surrogate decision about research participation.

Figure 3.
The Least Influential Factor*



* For each of the seven factors listed, percent of respondents who chose that factor as the least influential, had they to make a surrogate decision about research participation.

surrogate decision-makers (informal caregivers) or as persons who might refer decisionally incapacitated patients to studies, conduct research on that population, or assess the ethical acceptability of such studies. We chose to ask the same question to all five groups of respondents, thereby avoiding the possibility that variation in wording accounts for part of observed differences. As a result, all respondents were asked to put themselves in the position of someone who is called upon to make a decision about research participation on behalf of a close relative who is no longer able to do so on their own. For some respondents, the depicted situation was purely hypothetical; they had never been in that position before. Others might have had some experience as a surrogate decision-maker in the research context. In our survey, only informal caregivers were asked whether they had made a research-related decision in the last five years on behalf of the person in their care. One-fifth (21.5%) indicated that they had. This covariate was not related to the caregivers' selection of the factor they considered most influential ($p = 0.507$). Nonetheless, as in any vignette-based survey, we cannot rule out the possibility that factors influencing a surrogate's decisions about research participation might be evaluated differently when confronted with the actual decision of allowing a close relative to participate in a study. Alternatively, we could have asked professional respondents what they believe *should* weigh more heavily in a surrogate's decision to enroll her decisionally incapacitated relative in a study or what, in their opinion, *does* influence such a decision. Whether the results under these two alternative formulations would have been different from those observed in our survey is unknown and could be explored in future studies.

Our study has a number of strengths, including its random samples, relatively large sample size, and the care taken in designing the questionnaires and implementing the survey. The response rates were low in some groups, but there is no evidence that participants formed a biased sample within their respective population, except for physicians, who were subsequently weighted. Moreover, as the question analyzed in this paper was one among many, there is little reason to believe that a person's decision not to return the questionnaire was

influenced in some significant way by that specific question.

Study limitations must also be acknowledged. First, findings are based on a Canadian sample and extension to other countries must be made with caution. Second, we imposed a list of factors to choose from and did not offer respondents the possibility of identifying other factors that they considered important in substitute decision-making. Third, we asked a broad question that provided little detail about the hypothetical study for which respondents had to make a decision on behalf of a decisionally incapacitated relative. Sugarman and colleagues[21] have found factors influencing research-related surrogate decisions depend in part on whether the study has a therapeutic orientation. Future studies could examine whether status of the factors varies with study type. Fourth, we did not define key terms such as inconveniences, benefits, or serious side effects, but rather gave examples in parentheses. These examples might have influenced respondents' answers. Fifth, responses may have been biased to some extent by social desirability—for example, when respondents asked to portray themselves as surrogate decision-makers chose inconvenience or the prospect of benefits to themselves (factors A and G) as the least influential factors (Table 3 and Figure 3). On the other hand, the relatively low weight respondents placed on these two factors is in line with prior findings that people tend to be protective of their charges and unlikely to put their own welfare ahead of their loved ones.[22]

Lastly, very few variables among those explored were significantly linked to respondents' choice of the most influential factor in surrogate decision-making. A number of explanations come to mind. First, covariates such as race/ethnicity and risk tolerance were not included in the questionnaire but have been found, in studies conducted in the United States, to influence decisions to participate in clinical research.[23] Second, true correlates of respondents' choice may be hard to grasp through self-administered questionnaires and be more amenable to qualitative interviews. Third, our inability to differentiate respondents who selected the prospect of direct benefits to their relative as the most influential factor from those who selected the possibility of serious side effects or another factor may reflect measurement unreliability. Respondents were forced to rank order the listed factors, yet some may see potential benefits and side effects as equally important in surrogate decision-making or would feel comfortable with interchanging their rankings of these two factors. Most respondents did rank these factors among their three most influential (Table 3). Ranking instability introduces noise in the dependent variable—i.e., misclassification—which limits the possibility of linking it to other variables.

Nonetheless, there is some concordance between the results of comparing groups and those of exploring correlates of respondents' answers, especially among IRB members. Contrary to our hypothesis, more IRB members chose the prospect of direct benefits to their relative than the possibility of serious side effects as the most influential factor (Figure 1). However, IRB members appointed as researchers *less* frequently chose potential benefits over side effects as the most influential (Table 4), thereby confirming what we see in Figure 1 among the researcher group. Figure 1 also supports our hypothesis that for laypersons, the prospect of direct benefits is more important than risk in the decision to allow a close relative to engage in research, a result concordant with that reported on the last line in Table 4. Research ethics committees are composed of a variety of individuals, some of whom place more emphasis on the prospect of direct benefits, while others place more emphasis on risks. IRBs' tendency to be protective of research subjects may reflect researchers' greater influence on committee deliberations or the fact that they outnumber lay members on committees. Like all survey participants, IRB members were asked to select influential factors from a personal perspective—i.e., assuming that they had to make a research-related decision on behalf of a close relative. Arguably, that perspective may determine how they respond during a convened meeting—e.g, expressing support to approve or disapprove a protocol, or requesting modifications to it.

Whether an IRB member was appointed as a physician was not found to be associated with his or her selection of the most influential factor in surrogate decision-making (see last panel of Table 4, $p = 0.588$). However, focusing on the physician group in Figure 1 or, alternatively, on the third panel of Table 4, one notes that a higher proportion of physicians selected the prospect of direct benefits to their relatives over the possibility of serious side effects as the most influential factor in surrogate decision-making. Physicians' belief that decisionally incapacitated individuals could benefit from participating in research may—at least in part—be what motivates them to refer even vulnerable patients to studies. As we did for IRB members, we acknowledge, though, that extrapolating responses from physicians who were asked to imagine themselves as surrogate decision-makers to physicians who refer patients to clinical trials must be done with caution.

Overall, study findings indicate that potential benefits are more influential than risk, in particular for potential research subjects, informal caregivers, and physicians. Some may see the therapeutic orientation of some respondents as increasing the likelihood for therapeutic misconception.[24] It is reassuring, then, that other respondents,

notably researchers, tended to place greater weight on risks, thereby possibly counterbalancing potential participants' and surrogate decision-makers' therapeutic orientation. An alternative interpretation is that laypersons and physicians share a common motivation: welfare of research participants. Researchers, on the other hand, may be more concerned with scientific advances and minimizing harm, since risky therapies, even if effective, are less likely to be useful to future patients. Our survey thus shows the overall tendencies in how individuals perceive research studies. Older adults, informal caregivers, and physicians tend to see therapeutic opportunities; researchers tend to see research's long-term goals. This finding underlines the importance of having representatives of all stakeholders on IRBs, including older adults and informal caregivers, and respecting diverging opinions about reasons for allowing a decisionally incapacitated adult to participate in dementia research.

In conclusion, this study shows that across five stakeholder groups, potential research benefits and risks are the most significant considerations that would influence a decision to provide surrogate consent for a decisionally incapacited relative to participate in a dementia study. The study confirms findings from previous ones, but also expands on them through its unique ability to compare potentially influential factors across several groups and against each other. Given that older adults and informal caregivers were found to focus more on potential benefits, it is especially important that IRBs and review processes ensure that study risks are minimized and justified. Moreover, researchers and physicians should highlight potential research risks when approaching prospective research participants or their surrogate decision-makers about participating in research.

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