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Brief Communication

Advance Consent in Acute Stroke Trials: Survey of Canadian Research Ethics Board Chairs

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ABSTRACT: Advance consent could allow individuals at high risk of stroke to provide consent before they might become eligible for enrollment in acute stroke trials. This survey explores the acceptability of this novel technique to Canadian Research Ethics Board (REB) chairs that review acute stroke trials. Responses from 15 REB chairs showed that majority of respondents expressed comfort approving studies that adopt advance consent. There was no clear preference for advance consent over deferral of consent, although respondents expressed significant concern with broad rather than trial-specific advance consent. These findings shed light on the acceptability of advance consent to Canadian ethics regulators.

RÉSUMÉ : Le consentement préalable dans le cas d'essais cliniques portant sur les AVC aigus : une enquête auprès des présidents des Comités d'éthique de la recherche au Canada. Le consentement préalable pourrait permettre aux personnes présentant un risque élevé d'AVC de donner leur accord pour participer à des essais cliniques portant sur les AVC aigus, et ce, avant même d'être estimées admissibles. Cette enquête entend explorer l'acceptabilité de cette nouvelle modalité auprès des présidents des Comités d'éthique de la recherche (CER) canadiens qui évaluent les essais cliniques portant sur les AVC aigus. À cet égard, les réponses de 15 présidents de CER ont montré que la majorité d'entre eux se sentaient à l'aise d'approuver des études ayant adopté le consentement préalable. Aucune préférence nette pour le consentement préalable par rapport au report du consentement n'a émergé même si les répondants ont exprimé des préoccupations importantes à l'égard du consentement préalable général plutôt que spécifique à un essai clinique. Ces résultats mettent donc en lumière l'acceptabilité du consentement préalable au sein des organismes canadiens de réglementation de l'éthique.

Keywords: Consent; advance directives; research ethics

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Introduction

Informed consent is an integral part of both medical practice and clinical research, reflecting a respect for the rights of individuals to be involved in decisions regarding their own healthcare. There are several widely accepted elements to informed consent, including competence, disclosure, and voluntariness.[1] However, in some emergency conditions, such as an acute stroke, time, patient capacity, and other contextual limitations may prevent patients from either providing consent or from being enrolled into important and potentially beneficial clinical trials.[2] Advance consent could address these issues by identifying individuals at risk of stroke in stroke prevention clinics and allowing them to consent to research participation prior to experiencing a stroke that would limit their capacity to consent in the moment.

In this setting, patients identified to be at risk of stroke in a stroke prevention clinic would be invited to speak with a research coordinator about their willingness to provide advance consent. Patients who agree to give advance consent would have their

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Table 1: Demographics of survey respondents ($n = 15$)

		n	%
Age	40–49	3	20
	50–59	6	40
	60+	5	33
	Did not respond	1	7
Gender	M	8	53
	F	6	40
	Prefer not to say	1	7
Province of REB jurisdiction	Ontario	8	53
	Quebec	3	20
	British Columbia	2	13
	Saskatchewan	1	7
	Did not respond	1	7

consent documented in the electronic medical record which would be visible to the acute stroke team if the patient presented to the emergency department incapacitated with an acute stroke, streamlining that patient's enrollment process. Implementing advance consent in acute stroke trials would involve the participation of multiple stakeholders, including patients and their families, clinicians in the circle of care, researchers, and regulators who provide ethical approval for human subjects' research. Previous work has suggested that Canadian stroke physicians are open to the idea of enrolling patients into acute stroke trials using advance consent.[3] In this paper, we explore the perspectives of Chairs of Canadian Research Ethics Boards (REBs). Moving forward, we will assess the perspectives of people with lived experience of stroke and conditions that place them at risk of stroke.

We developed a 9-question online survey administered through the online platform Qualtrics® (Qualtrics International Inc., Provo, UT) to assess the acceptability of various approaches to advance consent from the perspective of REB chairs from across Canada. We were interested in establishing how comfortable respondents would feel with approving studies that adopted advance consent, and in particular, whether trial-specific advance consent would be a more acceptable model than broad advance consent, that is, consent not limited to a particular trial. Eligible candidates were chairs of REBs across Canada whose boards review at least one stroke trial per year. We chose to limit our study to the chairs of REBs that review stroke trials because our feasibility study will be limited to acute stroke trials.

Participants were identified using publicly available information; 54 REB chairs were invited to complete the survey via email between July 27 and September 15, 2022, with reminders sent out to all invitees one week and two weeks after the initial invitation. The survey was also advertised to the members forum of the Canadian Association of Research Ethics Boards and Clinical Trials Ontario. The research protocol was approved by the Ottawa Health Science Network Research Ethics Board. The survey was closed on October 11, 2022. Quantitative data were analyzed using Microsoft Excel Version 2205 (Microsoft Corporation, Redmond, WA).

The survey obtained 28 responses, with 15 respondents (response rate of 53%) meeting eligibility criteria, with most respondents being located in Ontario (53%) (Table 1). As the total number of REBs who oversees clinical stroke trials in Canada is unknown, to calculate this response rate we utilized two metrics to estimate the prospective sample size. First, utilizing data from registered trials on clinicaltrials.gov, we found the total number of sites that were recruiting for stroke trials in Canada in 2023 (28). Then, acknowledging that one REB may oversee multiple sites, we compared this number with the number of REBs utilized by a major Canadian stroke trial (AcT). AcT utilized 22 sites with 11 different REBs. Given this smaller number of individual REBs, the 15 respondents for this survey suggest a higher participation rate than 53% though it cannot be accurately quantified.

Most respondents (60%) indicated that they would be either very (13%) or somewhat (47%) comfortable approving study protocols that adopted advance consent for participation in an acute stroke trial. Only 20% of respondents were somewhat (7%) or very (13%) uncomfortable with this approach. The remaining 20% expressed neutrality regarding advance consent.

Respondents were asked how they felt about trial-specific and broad advance consent. Trial-specific advance consent was defined as consent given in advance for a specific trial, whereas broad consent was consent given in advance for participation in any of a set of trials, without necessarily disclosing the details of any specific trial to which the participant might be enrolled. Only 33% of respondents indicated that they would feel extremely (7%) or somewhat (27%) likely to approve a study that utilized broad advance consent, while 87% responded that they would feel extremely (47%) or somewhat (40%) likely to approve a study that utilized trial-specific advanced consent (Table 2). These views were echoed in comments from several respondents who wrote statements such as "If the details of the study have not been provided to the participant, then it is hard to justify that the advanced consent is informed."

We then asked respondents if they would be more likely to approve a stroke study that used advance consent or one that used deferral of consent, in which a patient is immediately randomized with the intention of seeking consent once the patient regains capacity or a surrogate becomes available. When asked to imagine how likely they would be to approve two studies that were identical except that one enrolled by advance consent and the other enrolled by deferral of consent, 33% responded that they would be more likely to approve the study using deferral of consent, 40% were no more likely to approve either study, and 27% were more likely to approve the study using advance consent (Table 2).

This survey of chairs of REBs in Canada that review acute stroke trials suggests that respondents were open to considering acute stroke trials that would enroll patients by advance consent, particularly if that consent were trial-specific. This is in line with what we hypothesized, as conversations surrounding specific advance consent are beginning to gain in popularity in other medical settings. For instance, the feasibility of utilizing advance research directives for persons with dementia while still competent is being studied as a means to prioritize patients' autonomy.[4,5] Similar conversations are being had in trauma and emergency settings, where significant barriers limit the ability of researchers to obtain traditional informed consent.[6–8]

Despite broad consent being a standard approach for health data repository and biobank research[1], respondents expressed discomfort with broad advance consent for participation in acute stroke trials, expressing worries that the consent was not meaningfully informed. This position is in line with a recent clarification from Health Canada regarding blanket consent for

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Table 2: Survey responses measuring: **a)** comfort approving studies using advance consent, **b)** likelihood of approving studies using broad advance consent vs trial-specific advance consent, and **c)** likelihood of approving studies using deferral of consent vs advance consent

a.	Very comfortable	Somewhat comfortable	Neither comfortable or uncomfortable	Somewhat uncomfortable	Very uncomfortable
How comfortable would you be approving study protocols that adopt advance consent for an acute stroke trial?	13% (2)	47% (7)	20% (3)	7% (1)	13% (2)
b.	**Extremely unlikely**	**Somewhat unlikely**	**Neither likely nor unlikely**	**Somewhat likely**	**Extremely likely**
How likely would you be to approve a study that utilized broad advanced consent?	27% (4)	20% (3)	20% (3)	27% (4)	7% (1)
How likely would you be to approve a study that utilized trial-specific advanced consent?	0% (0)	0% (0)	13% (2)	40% (6)	47% (7)
c.	**Much more likely to approve the study using deferral of consent**	**Somewhat more likely to approve the study using deferral of consent**	**Neither more or less likely to approve either study**	**Somewhat more likely to approve the study using advance consent**	**Much less likely to approve the study using advance consent**
Suppose you have two stroke studies that are identical other than for the fact that one uses advance consent and the other uses deferral of consent. Which study would you be more likely to approve?	7% (1)	13% (2)	40% (6)	27% (4)	13% (2)

unspecified future research which they reiterate is not permitted under the Tri-Council Policy Statement (TCPS) due to its unrestricted nature.[1]

Deferral of consent, an exception to consent allowed under Article 3.8 of the TCPS-2, is currently a common practice in the conduct of acute stroke trials in Canada but is not widely adopted in Quebec nor allowed in the United States.[9] We would have expected REB respondents to prefer advance consent over deferral of consent, in that participants have an opportunity to provide or decline informed consent before enrollment in a trial, though this was not the case. The results of our survey show no clear preference for the use of advance consent over deferred consent, with comments emphasizing the importance of the study's context when choosing between both approaches. Further discussion with people with lived experience of acute stroke may shed more light on the relative acceptability of these approaches and could impact how REB Chairs consider them.

There are several limitations to our study. Studying advance consent for participation in acute stroke trials mean that we were particularly interested in the perspectives of REB Chairs who oversee boards that review at least 1 acute stroke trial a year, a criterion that diminished the overall sampling population. Despite our small sample size ($n = 15$), we believe that we were able to capture responses from most chairs of REBs that review acute stroke trials in Canada based on acute stroke trial data obtained from the clinicaltrials.gov registry. These data obtained from the registry showed that that all registered active, recruiting, and completed acute stroke trials are frequently conducted in 1 or more of 28 institutions across Canada, including in jurisdictions like Alberta and British Columbia that have consolidated REB networks. In the absence of an analogous population, and in order not to bias our potential sample, this survey was not pilot tested but was adapted from a previously pilot-tested survey assessing clinicians' attitudes toward advance consent. We chose to focus exclusively on Canadian REBs, as it is our aim to develop an advance consent model in the Canadian regulatory environment, and therefore these results may not be generalizable to other jurisdictions. Additionally, we recognize that REB chairs' perspectives on advance consent may depend on trial-specific details, which were not provided in our survey questions.

Advance consent has the potential to allow persons with stroke – those who would otherwise be incapacitated at the time of treatment – to be in control of their research participation. Advance consent might be a preferable option to deferred consent, in which participants would not have a say in their research participation, but concerns around the ethical validity of both approaches are still being debated. This study sheds light on the acceptability of advance consent to ethics board chairs and opens the possibility of its adoption not only in acute stroke trials but also in other emergency conditions in which at-risk patients can be identified in advance of suffering a sudden and incapacitating event.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/cjn.2023.247.

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Competing interests. Dr Shamy and Dr Dowlatshahi report grants from Canadian Institutes for Health Research and the Government of Canada's new Frontiers in Research Fund for the conduct of the study. Dr Shamy reports a seed catalyst grant and a National New Investigator award from the Heart and Stroke Foundation of Canada; he is a member of the DSMB for the FRONTIER Trial and is Co-Chair, Writing Group, Canadian Stroke Best Practices Guideline on Acute Stroke Care. Dr Poppe reports consultancy fees and honoraria from Roche Canada; reports grants from Stryker and the Canadian Stroke Consortium-Brain Canada-Heart and Stroke Foundation of Canada; he is a member of the FLOW Trial DSMB and reports payment for an expert report for the Canadian Medical Protective Association. He is the program chair of the National Stroke Fellowship for the Canadian Stroke Consortium. Dr Fahed reports consultancy fees from Stryker Neurovascular, Yocan Medical Systems, Cerenovus, and Medtronic; he also reports a travel grant from Vena Medical. Dr Nicholls receives royalties from a book titled "Childhood Obesity: Ethical and Policy Issues." Dr Swartz. reports a grant from Sandra Black Centre for Brain Resilience and Recovery (CBRR) and a New Investigator award from the Heart and Stroke Foundation of Canada; he owns stock in FollowMD Inc. Dr Perry received a Mid-Career Salary Award from Heart and Stroke Foundation Ontario. Dr Hill reports grants from Canadian Institutes for Health Research, Alberta Innovates, NoNO, Biogen Inc., Boehringer-Ingelheim and Medtronic, outside the submitted work; reports consultancy fees from Sun Pharma Brainsgate Inc; reports 2 patent issued to US Patent office Number 62/086,077 and US Patent 10,916,346; owns stock in Circle Inc. and PureWeb Inc; is the President of the Canadian Federation of Neurological Sciences and a Board Member of the Canadian Stroke Consortium; is a member of the DSMB for the ARTESIA Trial and the BRAIN-AF Trial; chairs the DSMC for the RACECAT Trial, Oncovir Hiltonol trial, and the DUMAS Trial.

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