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Letter to the Editor

Developing a Model of Advance Consent for Participation in Acute Stroke Trials

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Dear Sir:

While consent is a cornerstone of modern research ethics, the need for innovation on the topic of consent for participation in acute stroke trials has been widely recognized. Standard approaches to consent have significant limitations. Requiring research participants to provide their own consent is often impossible due to the symptoms of stroke, and has been shown to bias enrollment against those most severely affected.[1] Obtaining consent from a substitute decision-maker adds 20–30 minutes to door-to-randomization times,[2] a cost that is prohibitive in stroke research. Moreover, data suggest that substitute decision-makers' choices may not reflect the decisions of the participants themselves.[3] While the option to enroll patients into trials without prospective consent is allowed in some jurisdictions, this is not universally acceptable or consistently applied, and comes with the risk of enrolling participants against their wishes.

In this scientific note, we present a novel model of consent for acute stroke trials: advance consent. In advance consent, a participant can provide consent—or decline consent—for a given trial prior to experiencing an acute stroke and hence meeting eligibility criteria for a research trial (Figure 1). Research ethics guidelines in many jurisdictions—including in the United States and Canada—permit such an approach, though it has never been implemented in acute stroke research. Therefore, we have launched a feasibility study of advance consent based in a stroke prevention clinic at a comprehensive stroke center that participates in many acute stroke trials.

To assess the feasibility of advance consent, we first had to develop the model of advance consent that would be tested. In other words, we had to define the who, what, when, and how of advance consent. We report on the process of integrating data from surveys, focus groups, and consultation with ethics oversight bodies to develop the model of advance consent that is being tested in a real-world feasibility study.[4] We have also reported our findings from each of our stakeholder consultations, including a survey of Canadian stroke physicians,[5] a survey of Canadian Research Ethics Board (REB) chairpeople,[6] and focus groups held with patients with lived stroke experience.[7]

Who should be invited to give advance consent? We sought to define a population of people who would be at increased risk of stroke, either ischemic or hemorrhagic. For that reason, we chose to define our eligible participants as those who had been diagnosed with any of the following: ischemic stroke, transient ischemic attack (TIA), asymptomatic carotid stenosis, intracerebral hemorrhage, or amyloid angiopathy. From a review of our local data, selecting patients with a diagnosis of stroke or TIA reflects about 40% of the patients seen in our stroke prevention clinic, of whom approximately 7% may present to the emergency department as a "stroke code" within 1 year of their clinic visit.[4]

Who should seek advance consent? A research coordinator is embedded in the stroke prevention clinic as part of our study of advance consent. At our comprehensive stroke center, as at many other centers around the world, the same physicians who work in our stroke prevention clinic also provide on-call coverage for acute stroke care and, hence, tend to be familiar with the enrolling acute stroke trials to which eligible participants

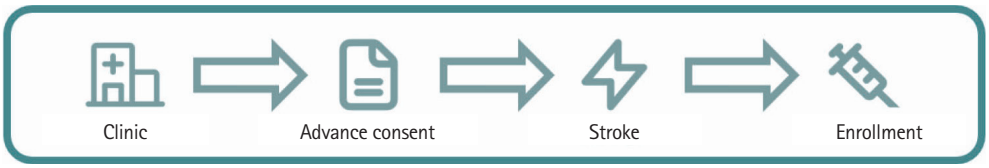

Figure 1. The flow of advance consent.

could consent in advance. When patients come in for their appointments, there is often sufficient time between assessments by the nurse specialist and the stroke physician for a research coordinator to speak with the patient for 10–20 minutes to explore trial details. We explicitly explored this question in a survey of Canadian stroke physicians, the vast majority of whom felt it would not significantly impact clinic flow to seek advance consent at the time of the clinic visit.

What information should be provided as part of advance consent? We considered whether advance consent should be tied to specific trial protocols or whether it should be broad and applicable to any potential future acute stroke trial. In 2023, Canadian research ethics guidelines issued a clarification that consent could not be generic and must include details about the research trial.[8] People with lived experience expressed concern about considering too many trials at any one time,[7] and therefore, we limited the number of potential trials to be considered to two at any one time. The two trials that we are currently including in this model are: (1) EASI-TOC (Endovascular Acute Stroke Intervention-Tandem OCclusion Trial),[9] a trial of acute cervical internal carotid artery stenting during endovascular thrombectomy for anterior circulation stroke, and (2) FASTEST (Recombinant Factor VIIa [rFVIIa] for Hemorrhagic Stroke Trial),[10] a study exploring if getting recombinant factor VIIa within 2 hours of hemorrhagic stroke can improve patient outcomes.

When should advance consent be sought, and how long should it last? American and Canadian research ethics guidelines make clear that consent is a process and not an event. Moreover, we heard from participants in our focus groups that they wanted to have the ability to revoke their advance consent at any point, should they choose to do so. We also heard from our REB that they were concerned about our ability to capture any changes in opinion among the participants who had offered advance consent. Therefore, we chose to limit the term of advance consent to one year. Upon further consultation with the Panel on Research Ethics, the body of the federal government that drafts the TriCouncil Policy Statement on Research Involving Humans (TCPS2), which governs research in Canada, we added a check-in at 6 months with participants who had given advance consent to confirm their ongoing comfort with advance consent. Participants were also informed that they could contact us at any point should they change their minds about ongoing consent. As part of our feasibility trial, we have just completed 6-month follow-ups, and all participants have confirmed their ongoing consent.

Where will advance consent be documented? Participants will sign the standard informed consent form (ICF) for the trial(s) to which they have consented. The signed ICFs will be included in the standard regulatory binders for the trials. However, the consent form will only become valid should the participant have a qualifying event, such as an acute ischemic or hemorrhagic stroke. Therefore, the consent form will be signed when the participant is assessed in the clinic, but it will only be considered active should the participant become eligible in the future and will be re-dated at that time. Participants' wishes about participation in a given clinical trial will also be recorded in the patient's electronic medical record in a dedicated research note. Because a research coordinator is present at every stroke code to screen for trial eligibility, that coordinator will incorporate into their routine the step of checking the patient's medical record for any documentation of advance consent.

How will the participant's legally authorized representative be informed of advance consent? On the advice of our research ethics board, any participant who has offered advance consent will be given specific documentation to share with their legally authorized representative (LAR) to ensure that this person is made aware of their wishes, and to have as a reference should the participant become eligible for trial participation. At the time of enrollment into an acute stroke trial, any present LAR will be informed of the fact that their loved one has become eligible for enrollment into the trial for which consent had previously been given. The LAR will be asked whether they have any reason to believe the person's opinion has changed about having given advance consent. However, the LAR will not be asked to provide surrogate consent in the emergency setting, as this will already have been given by the potential participant. Should the LAR express a difference of opinion from the signed consent, the participant's consent will trump the LAR's opinion unless the LAR makes it clear that the participant had communicated a change of mind. Focus group participants who had themselves consented to research participation on behalf of loved ones expressed relief at being freed of the burden of making emer-

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gency decisions about research participation and affirmed their trust in the patient's decision-making.

In conclusion, the model of advance consent developed for this study could improve current consenting practices by better reflecting participants' wishes and maximizing trial recruitment, thus further contributing to the improvement of patient-physician relationships and patient outcomes. This model could also serve as the basis for further research in other conditions that cause sudden incapacitation, such as status epilepticus or cardiac arrest, as well as in perioperative, peripartum, or critical care settings.

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Conflicts of interest

The authors have no financial conflicts of interest.

Author contribution

Conceptualization: RS, DD, MS. Study design: RS, DD, MS. Methodology: BD, MF, SN, VS, DD, MS. Data collection: UU, EC, BD, MS. Investigation: RS, DD, MS. Statistical analysis: BD, DD, MS. Writing—original draft: RS, UU, BD, MS. Writing—review & editing: all authors. Funding acquisition: DD, MS. Approval of final manuscript: all authors.

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References

1. Tu JV, Willison DJ, Silver FL, Fang J, Richards JA, Laupacis A, et al. Impracticability of informed consent in the registry of the Canadian stroke network. *N Engl J Med* 2004;350:1414-1421.
2. Lindley RI, Kane I, Cohen G, Sandercock PA. Factors influencing the use of different methods of consent in a randomized acute stroke trial: the third international stroke trial (IST-3). *Int J Stroke* 2022;17:553-558.
3. Shalowitz DI, Garrett-Mayer E, Wendler D. The accuracy of surrogate decision makers: a systematic review. *Arch Intern Med* 2006;166:493-497.
4. Shamy M, Dewar B, Niznick N, Nicholls S, Dowlatshahi D. Advanced consent for acute stroke trials. *Lancet Neurol* 2021;20:170.
5. Udoh U, Dewar B, Nicholls S, Fedyk M, Fahed R, Perry J, et al. Advance consent in acute stroke trials: survey of Canadian stroke physicians. *Can J Neurol Sci* 2024;51:122-125.
6. Seeger R, Udoh U, Dewar B, Nicholls S, Fedyk M, Fahed R, et al. Advance consent in acute stroke trials: survey of Canadian research ethics board chairs. *Can J Neurol Sci* 2024;51:285-288.
7. Udoh U, Seeger R, Cummings E, Dewar B, Nicholls S, Fedyk M, et al. Advance consent for participation in acute stroke trials: a focus group study with people with lived experience of stroke. *Can J Neurol Sci* 2024 Oct 15 [Epub]. Available from: https://doi.org/10.1017/cjn.2024.302.
8. Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada. Tri-council policy statement: ethical conduct for research involving humans – TCPS 2 [Internet]. Ottawa: Government of Canada; 2022 [accessed February 9, 2023]. Available from: https://ethics.gc.ca/eng/policy-politique_tcps2-eptc2_2022.html.
9. Poppe AY, Simon N. Endovascular acute stroke intervention - tandem occlusion trial (EASI-TOC) [NCT04261478]. In: ClinicalTrials.gov [Internet]. Bethesda: U.S. National Library of Medicine; 2020 [accessed September 18, 2024]. Available from: https://clinicaltrials.gov/study/NCT04261478?term=EASI-TOC&rank=1.
10. Broderick J, Grotta J. Recombinant factor VIIa (rFVIIa) for hemorrhagic stroke trial (FASTEST) [NCT03496883]. In: ClinicalTrials.gov [Internet]. Bethesda: U.S. National Library of Medicine; 2018 [accessed September 18, 2024]. Available from: https://clinicaltrials.gov/study/NCT03496883?term=FASTEST&rank=1.

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