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Advance Consent for participation in Acute Stroke Trials (ACTION): protocol for a feasibility study

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ABSTRACT

Introduction Obtaining informed consent for research from patients in medical emergencies remains a challenge, particularly in acute stroke care as treatment must be administered quickly and patients often arrive in the hospital in a state of incapacitation. Adaptations to standard consenting approaches—such as the use of surrogate consent or deferral of consent—have significant limitations. This feasibility study aims to test a new consenting approach in acute stroke care that we call advance consent. Advance consent has the potential to render emergency trial enrolment faster, fairer and more transparent, leading to more generalisable results.

Methods and design We will conduct a five-part study at The Ottawa Hospital, a quaternary care stroke centre: (1) administering questionnaires in the Ottawa Hospital Stroke Prevention Clinic that will examine patients' perspectives on research participation and advance consent; (2) inviting participants to consent in advance to any or both currently enrolling acute stroke trials; (3) tracking patient enrolment into these trials over 1 year; (4) administering a follow up questionnaire to participants at 1 year and (5) administering a questionnaire to participating hospital staff in order to interrogate their experiences with advance consent. Outcomes include but are not limited to eligibility rate, recruitment rate, withdrawal rate and the proportion of patients whose advance consent results in trial enrolment.

Conclusion This study will test the feasibility of enrolling patients at risk of stroke into acute stroke trials using advance consent.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Obtaining informed consent for research from patients in medical emergencies remains a challenge, especially in acute stroke care as treatment must be administered quickly and patients often arrive in the hospital in a state of incapacitation. Adaptations to standard consenting approaches have significant limitations.

WHAT THIS STUDY ADDS

⇒ Advance consent refers to the practice of obtaining a patient's preference for participation in a clinical trial before meeting inclusion criteria. This study defines advance consent in a novel way. It will then assess the feasibility of implementing advance consent as a method of obtaining consent from patients who may be eligible to participate in acute stroke trials.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Determining whether advance consent is feasible, or if it is not, will be an important finding for the way research is organized for acute stroke trials and potentially for clinical trials in other emergency conditions.

INTRODUCTION AND RATIONALE

Informed consent is a standard component of participation in modern randomised clinical trials. Unfortunately, obtaining informed consent is challenging in acute stroke research for several important reasons. First, decision-making needs to happen very quickly: 1.9 million neurons are dying per minute, and treatment must occur as quickly as possible to achieve the best possible outcomes.[1] Second, patients suffering from stroke (including acute ischaemic stroke and intracerebral haemorrhage) are often unable to speak or are unconscious and so are almost never capable of providing informed consent even if time were not an issue.[2 3] Empirically, in the MR CLEAN Trial, up to 96% of patients with large-vessel occlusions (a common stroke presentation) were unable to provide their own consent at the time of presentation due to the severity of their deficits.[4] Similar issues arise for patients with other neurological emergencies such as status epilepticus and subarachnoid haemorrhage, though they occur less commonly than stroke. Third, even capable patients can find consenting to participation in research to be overwhelming, particularly in the acute stroke setting.[5] Many of these issues are applicable to other emergency,[6 7] critical[8] and time-sensitive situations.[9]

The concept of advance consent presents a possible solution to the issues identified above

by inviting patients at risk of stroke to consent in advance of being eligible for trial enrolment. Advance consent refers to the idea of identifying people at risk of an emergency condition, and obtaining their consent to participate in a research trial in advance, should they meet eligibility criteria in the future. This approach is specifically allowed under American and Canadian research guidelines. For example, Article 3.8 of the Tri-Council Policy Statement on research involving humans, which speaks to consent under emergency conditions, specifically allows for 'procedures to identify prospective participants in advance so that consent may be sought prior to the occurrence of the emergency situation'.[10]

In a newly developed model,[11] patients in a stroke prevention clinic will be invited to speak with a member of the research team about providing advance consent. They will review a trial's full informed consent form, and at their convenience decide whether they would wish to participate or not. This decision would then be documented in the medical records and in the trial's documentation. For patients who do consent to a study and who do end up becoming eligible, their date of consent would be considered the date they become eligible as their consent is contingent on meeting eligibility criteria for the trial. This process could potentially reduce the door to randomisation times and increase rates of enrolment, but it would also give people at risk of stroke a better opportunity to express their wishes about research participation, whether that is to participate or not.

METHODS

Overall study design

This study aims to examine the feasibility of implementing a system of advance consent. We will conduct our five-part study at The Ottawa Hospital, a quaternary care stroke centre in Ottawa, Ontario, Canada (figure 1). Our study includes (1) inviting patients attending an initial consultation in the Ottawa Hospital Stroke Prevention Clinic (SPC) to complete a questionnaire that will examine patients' perspectives on research participation and advance consent; (2) inviting them to consent in advance to two currently enrolling acute stroke trials; (3) tracking patient enrolment into these trials over 1 year; (4) administering a follow-up participant questionnaire at 1 year and (5) administering a questionnaire to participating hospital staff in order to interrogate their experiences with advance consent.

Part 1

All patients assessed for new consultations in the stroke prevention clinic will be screened by the clinic nurse for eligibility. If they meet the eligibility criteria, they will be invited to speak to the research coordinator. The research coordinator will invite them to complete a close-ended questionnaire (online supplemental appendix 1) in which they are asked about research participation and consent, including whether they think it is appropriate to approach people who are at risk of stroke about future participation in acute stroke research. The questionnaire takes approximately 5 min to administer. It has been pilot tested with clinical staff and with people with lived experience. It is available in English and French.

Part 2

Those who respond positively to the idea of advance consent will then be invited to review and provide consent in the clinic (or at their convenience) to either or all of our two partner trials—EASi-TOC[12] (Endovascular Acute Stroke Intervention—Tandem OCclusion Trial) and FASTEST (Recombinant Factor VIIa (rFVIIa) for Haemorrhagic Stroke Trial).[13] Both studies have been approved by our research ethics board and are live at our site. The principal investigators for both trials, locally and centrally, have endorsed their partnership with this feasibility study. The research coordinator will guide patients and their families to review the full informed consent document. Participants who opt to provide advance consent

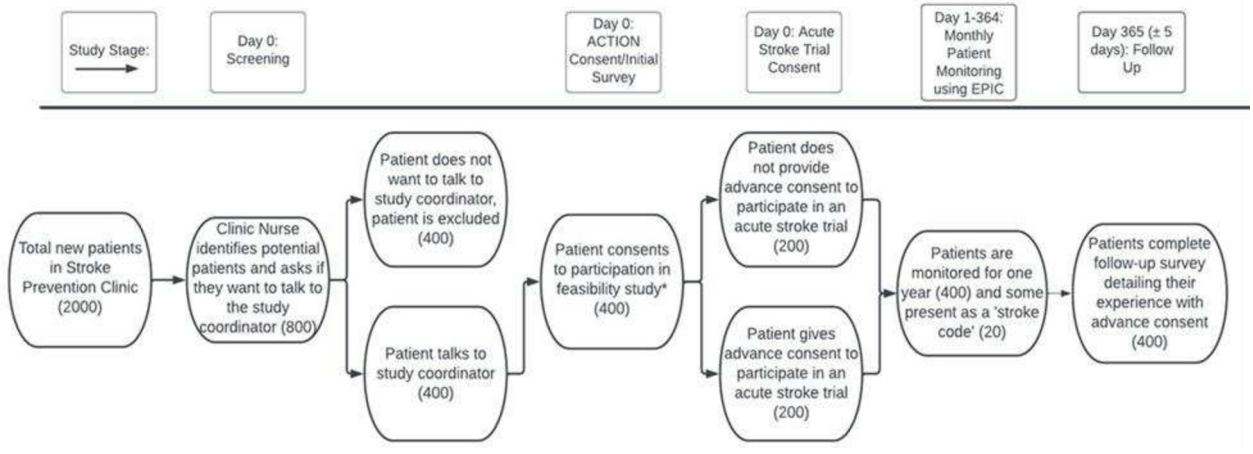

Figure 1 A diagram of the planned workflow of participants for this study. *If patient responds neutrally or positively to advance consent, they are asked if they want to actually provide consent.

will receive a copy of the informed consent document to keep, and research staff will ensure that their families are aware of their decision to participate in one or all of the trials. Any consent signed in the clinic will only serve as informed consent if three conditions are met:

1. The patient presents to hospital within 1 year with an acute stroke (as there is an increased risk of stroke within the first year following the diagnoses described below).
2. The patient is eligible for enrolment into the trial(s) to which she or he has consented.
3. The patient is unable to consent for herself or himself at that time. Participants' wishes to participate or not to participate will be documented in their electronic medical records and in the documentation pertaining to the trials they have considered.

It should be noted that, for those who have consented to EASi-TOC and/or FASTEST, if admitted to the hospital within the 1-year time frame, eligibility criteria for both the EASi-TOC and/or FASTEST trial are checked again by an authorised representative before the administration of trial medications or before undergoing trial procedures. Only patients who have had an acute ischaemic anterior circulation stroke and ipsilateral extracranial carotid stenosis or occlusion can participate in EASi-TOC, and only patients who have had an intracerebral haemorrhage will participate in FASTEST.

Part 3

Informed consent forms for participants who have given advance consent to any or all of our two partner trials (EASi-TOC and FASTEST) will be uploaded to the integrated electronic health record EPIC. We will use EPIC to monitor participants' presentations to hospital with stroke, determine whether they are enrolled on one of our acute stroke trials and whether the advance consent was used over 1 year. As the Ottawa Hospital is the only acute stroke centre in our region, all acute stroke patients who are eligible for trial enrolment will necessarily be brought to our emergency department. We are the only centre enrolling patients into these trials and so a review of our electronic records will ensure that we have not missed any enrolments that might occur.

Part 4

All participants will be contacted by telephone at 1 year and invited to complete an exit questionnaire (online supplemental appendix 2). They will be asked the same set of questions about consent, research participation and advance consent that they were asked in the clinic. Participants will be contacted a week before the 1-year mark to remind them of their exit questionnaire and verify their availability. The exit questionnaire will be administered by telephone 1 year (plus/minus 1 week) after completing the intake survey. Patients will be considered lost to follow-up if the study coordinator tries and fails to contact the patient over the phone two times in 2 weeks.

Part 5

Clinic and hospital staff will receive an invitation to complete a 10 min online questionnaire (online supplemental appendix 3) at study conclusion. They will be asked about their experiences administering advance consent and enrolling patients into trials with advance consent.

PATIENT POPULATION

Inclusion criteria

Parts 1–4: Patients who:

1. Are receiving a consultation in the Ottawa Hospital's Stroke Prevention Clinic during the study period.
2. Are diagnosed by the treating physician with a condition that confers a greater than background likelihood of stroke. This is defined as either all ischaemic or haemorrhagic stroke, transient ischaemic attack, carotid artery stenosis (symptomatic or asymptomatic), atrial fibrillation or cerebral amyloid angiopathy.
3. Are able to participate in English or French.
4. Are able to complete the questionnaire independently.
5. Have a life expectancy of at least 1 year.
6. Live within the catchment area of The Ottawa Hospital.

Part 5: Doctors, nurses, residents and coordinators working in the stroke prevention clinic, emergency department or research team who screened participants for enrolment into the feasibility study, administered questionnaires, screened participants for enrolment into participating acute stroke trials.

Exclusion criteria

Parts 1–4: Patients assessed in the stroke prevention clinic who:

1. Have a confirmed wish not to be approached for research participation.
2. Are not diagnosed with a condition that confers an increased likelihood of stroke.
3. Are unable to consent on their own behalf.
4. Have a life expectancy of less than 1 year.

Part 5: Staff members who do not interact with patients in the setting of advance consent recruitment, enrolment or follow-up will not be invited to participate.

Consent procedures

As part of the Ottawa Hospital's institutional policy, patients seen at the hospital can indicate a preference to be contacted or spoken to about research. Clinic patients who indicate 'yes' to being spoken to/contacted about research and who agree to speak to a member of the research team will be approached by the research coordinator who will describe the study to them and seek their consent to be enrolled. Clinic patients who give their consent to participate will then sign the consent form for the feasibility study (intake questionnaire, being tracked through EPIC, follow-up questionnaire). If they are interested, they can then review the informed consent forms for both active trials. These consent forms have been modified to include an additional cover page explaining

that they are written from the point of view of the potential participant at the moment of enrolment, whereas in this setting, participants are being asked to consent in advance. Participants may agree to complete the initial questionnaire and then decline ongoing participation. They may complete the initial questionnaire and decline the advance consent portion but may then complete the 1-year follow-up survey. If participants consent to any particular study but wish to change their minds, they may reach out to the study team at any point and rescind their advance consent. The study team will also contact participants who provide advance consent 6 months after signing the consent form to confirm if their decision has changed. The advance consent will only become active if the participant becomes clinically eligible for one of the two studies within 1 year, and if she or he is unable to consent on her or his own behalf at that time. If a participant has consented in advance to one of the studies but becomes clinically eligible for that study and is capable of providing informed consent at that time, then she or he will be asked to sign a standard informed consent form at that time. If a participant has provided advance consent and is incapable of consenting the documented advance consent will be followed.

A patient advisory group was involved in the initial design of the Advance Consent for participation in Acute Stroke Trials study. The members of this group contributed to the design of the study and reviewed and provided feedback on the questionnaires. The patient advisory group will meet after 6 months of patient recruitment to discuss study milestones and address potential challenges to patient recruitment and retention. Focus groups involving people with lived experience of stroke were also conducted and these focus groups highlighted various themes that were important to patients around the consenting process, which informed the way we designed this study. All groups agreed that advance consent was a potentially helpful approach to consenting for acute stroke trials.

DATA

Data collection and management

Data for this study will be collected from questionnaire responses and participants' medical records. All participants will receive a unique study identifier and collected data will be deidentified and entered into a password, protected worksheet. Data will be deidentified. Confidentiality will be maintained except as required by law. The research assistant in conjunction with the research manager will carry out monthly checks to see if any participants present to the emergency department as well as data quality checks.

Outcome measures

Primary outcome measures

1. Over 1 year, how many patients seen in the stroke clinic will be eligible to provide advance consent? Based on established data,[14] we conservatively expect this number to be 800 patients.
2. Over 1 year, how many eligible patients will agree to participate in our feasibility study? Based on the fact that 51% of patients seen in the SPC agree to be contacted for research studies, we are estimating that 50% of eligible patients (400/800) will agree to participate in our study.
3. Among participants, how many will agree or strongly agree with this statement: 'I believe it is appropriate to invite people at risk of stroke to provide or decline consent for participation in a clinical research trial in case they have a stroke'? We expect that 50% of participants of the 400 participants above (200) will agree. This expectation is based on studies of emergency department patients in which 45%–70%[15 16] of respondents felt this is acceptable for emergency studies.
4. Among participants, how many will agree to provide advance consent for a specific stroke trial? Our expectation is that 200 (50%) will provide consent to at least one of the current active trials (3).
5. How many participants who provided advance consent for one or several trial(s) will be enrolled on that trial or another trial? Based on analysis of available data, we anticipate this number to be 5%–10% of eligible patients.[17]

Secondary outcome measures

1. Proportion of participating patients that will still report that advance consent is acceptable after 1 year.
2. Proportion of patients who will withdraw their advance consent or withdraw from the feasibility study.
3. The reasons for patients' decisions to provide or not provide advance consent, both at the time of initial assessment and at follow-up.
4. The male–female breakdown among patients agreeing to provide advance consent.
5. Proportion of patients who provide advance consent are enrolled on a trial using the advance consent.
6. Door-to-door randomisation times of patients enrolled on acute stroke trials with advance consent.
7. Given the number of enrolments into trials using advance consent and the cost of an advance consent programme, the cost per enrolment.
8. Feelings of staff in the emergency department and acute stroke team about enrolling via advance consent.
9. Experiences of clinic staff with identifying patients for consideration of advance consent

Sample size estimates

There is no formal power calculation for this feasibility study, though we aim to recruit for 1 year during which time we hope to recruit at least 400 patients. Our clinic sees about 2500 new patients annually and we conservatively estimate that 800 will meet the inclusion criteria. We expected that 50% of eligible patients will agree to participate but will also evaluate this assumption as a feasibility outcome.

Statistical analyses

Feasibility outcomes will be assessed both quantitatively and qualitatively. Quantitative analyses will be descriptive

and outcome data will be presented in descriptive tables and charts that would report means with SD for continuous outcomes or proportions with 95% CI for categorical outcomes as appropriate.

Free-text responses from questionnaires will be analysed qualitatively using an inductive thematic approach to identify and define themes. This approach is data driven, that is, no initial coding template has been created and themes identified are strongly linked to the data.[18] Responses will be coded independently by two researchers who will then discuss between themselves to validate the identified themes and ensure consistency,[19] before presenting their analyses to the broader team for comments and further discussion.

CONCLUSION AND DISSEMINATION STRATEGY

This study will test the feasibility of enrolling patients at risk of stroke into acute stroke trials using advance consent. Findings will be disseminated in oral or poster presentations at conferences or rounds and publication in academic journals. We have identified key stakeholder groups, including the Heart and Stroke Foundation of Canada, the Canadian Stroke Consortium, Clinical Trials Ontario and the Canadian Association of Research Ethics Boards, with whom we will directly engage on study completion.

Contributors All authors made significant contributions to this manuscript. UU wrote the initial draft of the manuscript. UU, BD and MS developed the protocol. All authors reviewed and revised the manuscript.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and ethics approval was granted by the Ottawa Health Science Network Research Ethics Board (OHSN-REB) on 29 June 2023 (Protocol ID: 20230286-01H). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data sharing not applicable as no datasets generated and/or analysed for this study.

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