

Call for Proposals: Advances in the Conduct of Randomized Controlled Trials

Application Instructions

- To apply your application must be endorsed by one of the [28 ACT Networks](#) (details below)
- Please combine the following application components into a **single PDF** (maximum 7 pages in English or 8 pages in French):
 - Written proposal: Maximum of 5 pages if written in English or 6 pages if written in French (details of the formatting requirements are below); page count includes a 1-page trial summary
 - Budget and justifications (required, up to 1 page)
 - References, figures, or tables (optional, up to 1 page)
- Submit the full application PDF to act-aec@phri.ca by **noon EST on June 8th, 2023**
- Once submitted, written confirmation of receipt will be provided within 24 hours of submission. If you do not hear back within 24 hours, please follow up to ensure successful delivery.

Description and Objectives

We designed this ACT request for 2 separate streams of proposals.

Stream 1: Encourage randomized trials that use non-traditional and efficient designs and approaches. The trial methods should still be robust (i.e., minimize the risk of bias).

Randomized controlled trials (RCTs) are our best tool for generating unbiased intervention effect estimates. Traditionally this is a large, two-group, individual patient, parallel arm, randomized controlled trial, with a trial process optimized for detecting an effect under ideal conditions, and where research staff at participating sites recruit patients into the trial, support intervention delivery, and collect patient data on case report forms. Often robust, the conduct of these trials is expensive, and many interventions are not tested.

For some interventions and settings, alternative approaches to trial design and conduct may be of benefit. These techniques can improve logistical or statistical efficiency, reducing the cost of conducting an RCT and the time needed to answer a research question reliably. Different approaches include, but are not limited to, statistically efficient platform and cross-over designs, Bayesian methods, adaptive trials, cluster trials, factorial designs, innovations that enable rapid patient recruitment, streamlining an ethically justifiable consent process, or more efficient methods to meet the trial data needs (which may use electronic medical records or healthcare administrative data if the information is of sufficient quality). We want to promote more practical experience with these trial designs and elements in Canada.

Any RCT proposed in this stream should still be designed to generate robust results with a minimal risk of bias.

For Stream 1, we are looking for proposals to fund pilot trials and the vanguard phase of larger trials that use alternate designs and approaches.

Stream 2: Generate high-quality evidence on methods to improve the conduct of trials.

We need RCTs testing interventions to improve the conduct of trials. These interventions aim to improve trial efficiency and quality (which may include, but is not limited to, better informed consent, recruitment, retention, adherence to the randomly allocated intervention, inclusivity, efficient data collection, or reduced participant burden). Sometimes this type of research is conducted as a study within a trial (SWAT), and the following describes such efforts.

<https://www.york.ac.uk/healthsciences/research/trials/swats/>

<https://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/SWATSWARInformation/Repositories/SWATStore/>

For Stream 2, we are looking for proposals that test interventions to improve the conduct of trials. If proposing a SWAT nested within a parent RCT, please provide details confirming the parent trial is active, funded and registered.

Notes for Stream 1 and Stream 2.

- The focus is Canadian-led innovation in the conduct of RCTs (e.g., innovative features of trial design, methods, and execution).
- The trials will be Canadian led, referring to trials in which the principal trial investigator is a Canadian citizen/permanent resident, and the location of the central coordinating centre is in Canada.
- Best estimates of intervention effects (including interventions to improve the conduct of RCTs) come from RCTs. Thus, only RCTs will be eligible for this competition (Stream 1 and Stream 2). All types of randomizations are suitable (e.g., single patient, parallel-group, cluster/stepped wedge/cluster cross-over, factorial, platform).
- Projects are up to 2 years in duration. ACT provides half the requested budget at the beginning of year 1 and the remaining half at the beginning of year 2 [if the project is 2 years in duration]. Each team must submit a 1-page annual progress report to ACT, according to a template (to be provided in the future). For Stream 2 proposals using a SWAT format, this means at least one randomization into the SWAT (beyond any randomization performed for the parent trial).
- Proposals that address patient-related aspects of trial conduct (e.g., recruitment [and the informed consent process], retention, adherence) are welcomed. We recommend that such proposals include patient perspectives and partners in the proposed activities.
- SWATs that improve Indigenous people's participation in trials are welcomed. Such proposals should be Indigenous-led or demonstrate authentic partnerships with Indigenous peoples.
- SWATs that test interventions to improve equity, diversity, inclusion, and accessibility in trial participation are welcomed.

Funds Available

A total of \$1.9 million is available for this RFA. Assuming enough meritorious applications, at least \$400,000 is dedicated to applications focused on stream 2. The maximum requested budget for any application in Stream 1 is \$200,000, and the maximum requested budget for any application in Stream 2 is \$100,000.

Eligibility

For a trial to be eligible, it must fulfill each of the following points:

1. Be led by a Canadian researcher who is a member of an [ACT Network](#).
 - The nominated principal investigator(s) can only submit 1 application to this competition.
2. Endorsed by 1 of the [28 ACT Networks](#).
 - Each Network can endorse a maximum of 3 applications to this competition.
 - For this criterion, applicants only list one principal Network.
 - Networks endorse proposals most relevant to their constituents, especially their patients.
3. Is an RCT
4. Applicant agrees to transfer funds to an organization eligible to hold CIHR funding; this organization will report the use of funds according to CIHR-eligible expenses.
5. Applicant will acknowledge ACT Consortium partnership and funding in all related presentations and publications.
6. If funded, the applicant must be accountable for their progress, which will be summarized in annual ACT reports. A summary of their project will also be shared within ACT to raise awareness and foster new collaborations. Applicants also commit to making their trial results publicly available (open-access publication).

Proposal Sections and Adjudication Criteria

Applicants submit their maximum 7-page pdf proposal in English, or maximum 8-page pdf proposal French.

- Written proposal: Please use 12-point font size, black type; a minimum of single line spacing; a minimum margin of 2 cm (3/4 inch) around the page; letter size [21.25 X 27.5 cm / 8.5" X 11"]; Maximum of 5 pages if written in English or 6 pages if written in French, this page limit includes the 1-page trial summary.
- Maximum of 1 page can be used for the trial budget and justification (required).
- Optional - Can have a maximum of 1 additional page to include any references, figures, or tables.

Each proposal that meets eligibility for review will receive a mark out of 100 (we will not grade ineligible applications).

Sections [with the adjudication value]

- 1st page

- Proposal Title
- Indicate proposal should be considered in Stream 1 or Stream 2
- Confirm ACT Eligibility (4 bullet points)
 - Canadian Led Trial: <list nominated NPI(s); confirm Canadian citizenship or permanent residency>, <list location of trial data coordinating centre>.
 - Indicate which of the 28 ACT Networks endorses the proposal.
 - Confirm proposal is an RCT.
 - Institution paid (if proposal successful).
 - Add statement: If funded: “I agree to acknowledge partnership and funding with the ACT Consortium in all related presentations and publications. I agree to be accountable for my progress, which ACT will summarize in annual reports. I agree that a summary of my proposal will be shared within ACT to raise awareness and foster collaborations. Finally, I commit to making my results publicly available (open access).”
- Provide a summary of the trial proposal (i.e., structured abstract) listing key trial elements (e.g., rationale, question, participants, intervention, outcomes, anticipated impact).
- Remaining 5 pages (or 6 pages if written in French), including budget:
 - Further details about the trial methods (expanding on the 1-page trial summary) [adjudicated with trial summary; adjudication value of 50%; in addition to trial concept adjudication considers improvements to trial efficiency and novel methods]
 - For stream 1, we encourage applicants to stress how conducting an RCT with the chosen design or approach to answer the specific research question will be more efficient than traditional method.
 - We encourage applicants to stress how their trial will generate estimates of the intervention effect that are at low risk of bias.
 - Anticipated impact and knowledge translation plan of the trial findings [20%]
 - Describe the team/partnerships [15%]
 - We encourage teams with multiple perspectives (healthcare providers, researchers, patients, private sector partners, or healthcare organizations).
 - Describe how the project will be completed within 2 years [15%]
 - Budget required (up to 1 page).

Adjudication Process

ACT personnel will review each application for eligibility. ACT will not further consider any ineligible application based on the information provided.

As possible, reviewers for Stream 1 will be persons who have completed trials using alternative designs. Similarly, reviewers for Stream 2 will be persons who have conducted trials on interventions to improve the conduct of trials. If this is not possible, reviewers will be experienced in the conduct of RCTs. For transparency, the names and locations of reviewers who participated in the review process will be disclosed at the end of the review process (but not the applications they reviewed).

We recognize that a modest amount of funding is available to applicants through this RFA to conduct an RCT. Additional partnership funding to conduct the RCT is acceptable and welcomed.

Applications will be circulated to reviewers (after they confirm they have no conflict with the application) to:

- Confirm that the application is eligible for the competition.
- (if eligible) provide a score out of 100.
- In the instructions, reviewers will be asked to avoid scores that are exactly divisible by 10 (e.g., 60, 70, 80, 90) to reduce the chance of different applications having tied scores.

Reviewers are asked to flag whether additional, internal budget review is recommended.

Each application will receive an average score out of 100.

Applications with an average score <60 are ineligible for funding.

We will fund applications with a score of 60 or more based on rank until we reach the maximum budget for this RFA. If trials have tied scores for the remaining funds, we will recirculate to reviewers for a rank order.

Feedback to Applicants

We will give the principal applicant of each eligible application information on the number of eligible applications submitted to this RFA, the number awarded, and whether they were successful.

We will provide brief written comments from reviewers back to applicants, along with each reviewer's score.

Timelines

- Announcements through the ACT networks: Tues **April 11th, 2023**
- Opportunity shared at ACT conference April 16/17/18
- Deadline for Proposals: Thursday, **June 8th, 2023**
- Awardees Announced: by Thursday **August 3rd, 2023**