ACT AEC Accelerating Clinical Trials Accélérer les Essais Cliniques

Accelerating Clinical Trials (ACT) Consortium: Need for, structure, goals, and progress

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Disclosures

- Based on study questions I originated and grants I wrote
  - I have received grants from
    - Abbott Diagnostics, AOP, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Cloud DX, Covidien, Octapharma, Philips Healthcare, Roche Diagnostics, Roche, Siemens, Smith and Nephew, Stryker, Trimedic
- I have participated in
  - advisory boarding meeting GlaxoSmithKline, Bayer, Quidel Canada, Trimedic
  - expert panel meeting AstraZeneca, BI, Roche
  - International meetings AOP

Goals of presentation

- Background and need for
  - Pan-Canadian Clinical Trials Consortium
- ACT Consortium
  - central guiding principle of
  - structure
  - high-level goals
  - progress

Background

- Main funder of health research is federal government
  - Canadian Institutes of Health Research
    - annual budget $1 billion
- Recent federal government investment
  - Canada’s biomanufacturing and life sciences strategy

Canadian trial landscape

- Canadian should take pride in impact Canadian trials have had on improving health globally
  - however,
  - we have to also acknowledge that COVID-19 pandemic uncovered serious issues related to conducting RCTs in Canada

Canadian trial landscape

- Successful Canadian trials have primarily occurred due to researchers having mindset of long-distance runner
  - trialists have succeeded because of perseverance not because of system
- COVID-19 required trialists to function as sprinters; however
  - barriers and operational bottlenecks to conducting trials in Canada prevented this from happening
  - as a result, Canada was dependent on other countries like UK which
    - conducted trials efficiently and established treatments that reduced mortality

Challenges to conducting trials in Canada

- Many areas of health lack research networks
  - while existing networks are hindered by lack of core funding
- Compared to other developed nations
  - sparse government investment in funding clinical trial units
- Too few RCTs funded by government or charitable organizations
  - large trials – which change care – are underfunded
- Unnecessary bureaucracy deters potential investigators

Challenges to conducting trials in Canada

- Trials take far too long to launch and complete
  - preventing us from rapidly addressing acute and chronic health issues
- Canadian citizens have unequal opportunities to participate in or benefit from clinical trials
- Money is wasted during trial implementation
  - due to delays caused by operational bottlenecks (e.g., contracts)
- Except for most academic hospitals
  - many potential investigators at Canadian hospitals do not have access to study personnel to conduct trials

Challenges to conducting trials in Canada

- Approach of advocating that Indigenous populations participate in RCTs that were not designed to address their health priorities
  - is not optimally addressing their needs
- Insurance costs preclude many Canadian investigators from expanding their trials internationally
- Many Canadians are unaware of importance and benefits of RCTs
  - many develop negative impressions of research participation through television, movies, and social media

Challenges to conducting trials in Canada

- Canadian biotechnology and RCT communities rarely intersect
  - consequently few Canadian researchers undertake RCTs evaluating Canadian biotechnologies
- Few, if any, Canadian small- medium-size biotech companies
  - have capital to fund clinical trials required to obtain regulatory approval
- Few major pharmaceutical or biotechnology companies have their headquarters in Canada
  - funding decisions for large trials are made by global headquarters
    - this limits opportunities for Canadians to lead clinical trials

Need

- Need for Pan-Canadian Clinical Trials Consortium
  - to address these issues
  - need to put personal interests aside and
    - advocate and work for what is in interest of Canadians
  - need to put regional politics aside
- CIHR open competition

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Accelerating Clinical Trials (ACT) Consortium

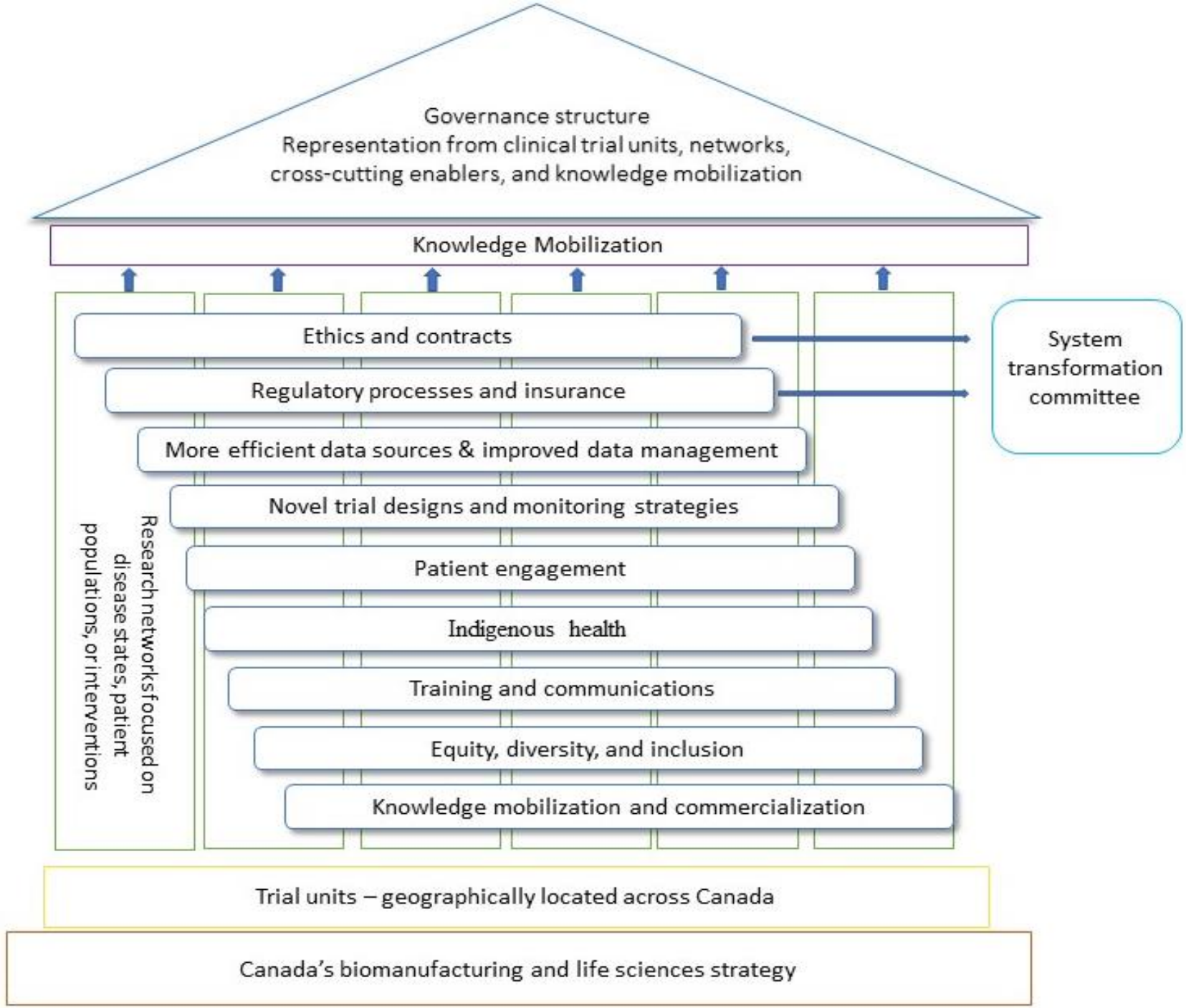
Central guiding principle

- Our activities will accelerate, optimize, and facilitate
  - conduct, implementation, and results translation
  - from high-quality, high-impact RCTs
  - to improve health in Canada and globally

ACT structure

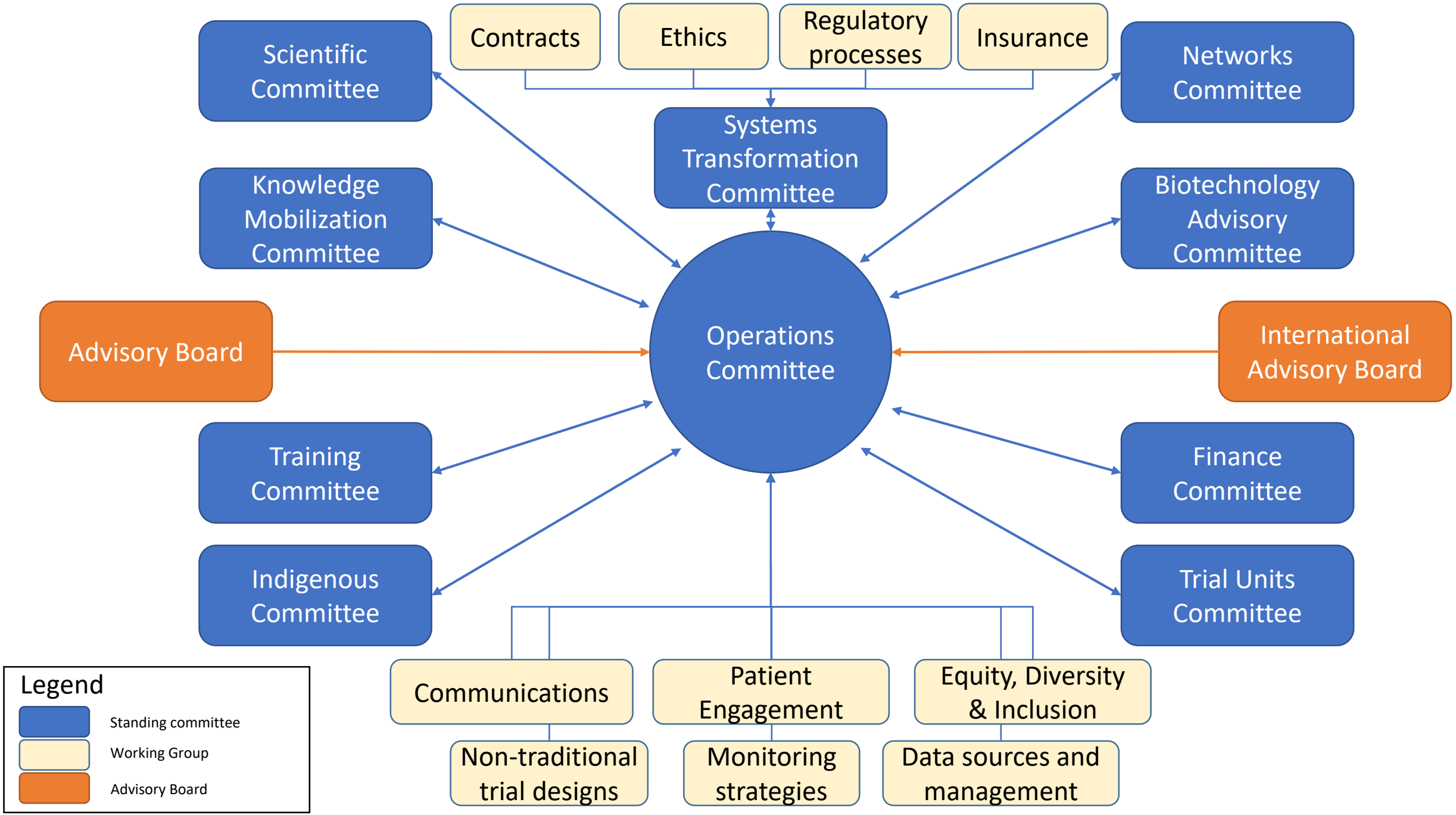
Accelerating Clinical Trials

Accélérer les Essais Cliniques



ACT

- >300 investigators
- >800 HQP
- 23 Canadian Universities and all medical schools
- Spans from NS to BC and Nunavut


Scientific Committee
Contracts
Ethics
Regulatory processes
Insurance
Networks Committee
Systems Transformation Committee
Knowledge Mobilization Committee
Biotechnology Advisory Committee
Advisory Board
Operations Committee
International Advisory Board
Training Committee
Finance Committee
Indigenous Committee
Trial Units Committee
Communications
Patient Engagement
Equity, Diversity & Inclusion
Non-traditional trial designs
Monitoring strategies
Data sources and management
Legend
Standing committee
Working Group
Advisory Board

High level ACT goals

Networks and trial units

- Expand and support existing clinical trial networks and develop new networks in areas of need
- Adopt successful international approaches to trial conduct
  - portfolio program
- Ensure trial units have resources and expertise to conduct high-quality, high-impact trials

Accelerate conduct and efficiency of RCTs

- We need systems that are in best interest of Canadians
  - single national ethic approval process with strict timelines
  - simplify contract process
    - master clinical trial agreements
  - efficient data sources
    - participant identification and outcome data
  - increase expertise in non-traditional trial designs

Expand Canadian participation in international trials and vice versa

- Share collaborative connections
- Insurance
  - open market too expensive
  - need captive insurance company structure for Canadian RCTs

Strengthen coordination of Canadian clinical trials, facilitate harmonization across trial units and networks

- Shared electronic trial master file across trial units
  - comply with regulatory requirements
- Canadian drug packaging and distribution and biobanking

Democratize clinical trials

- Create equitable access to trial participation
  - portfolio program
  - novel partnerships
    - pharmacies
- Communications strategy

Improve process of involving Indigenous peoples in trials

- Indigenous people should identify their health priorities
- Trials should be funded to address these priorities
- Support, expand, and foster Indigenous clinical trialists

Growing funding pie

- Too much time wasted among Canadian health researchers debating how to divide CIHR funding pie
- Learn from EU
  - Canadian trialists need to help support and grow Canadian biotechnology industry by evaluating their products in RCTs
- Work with Canadian headquarters of major pharmaceutical or device companies to
  - bring more trials to Canada and have more Canadian clinical trial units lead trials funded by these companies

ACT progress to date

The beginning

- January 19, 2023 ACT funding announced
- Established 22 committees and working groups
  - appointed co-chairs, members
  - established terms of reference

First ACT request for applications (RFA)

- RFA announced February 27, 2023
- Support completion of high-impact RCTs
- Submission deadline April 3, 2023
- 43 applicants from 19 ACT networks
- Targeted peer review process
  - each application reviewed and scored by 5 independent individuals
    - who had previously led high-impact clinical trial
    - 24 expert peer reviewers

1st ACT RFA

- 11 successful applicants announced May 18, 2023
- Total of $2 million in funding
- One successful trial
  - completed randomization at end of June, follow-up mid July, paper submission late July, presented at European Society of Cardiology Hotline Session end of August,and simultaneously published in Lancet

PI name	Funded RCT
David Conen	COP-AF: Colchicine For The Prevention Of Perioperative Atrial Fibrillation In Patients Undergoing Thoracic Surgery
Deborah Cook	REVISE: Re-Evaluating the Inhibition of Stress Erosions in the ICU Trial
Derek Exner	Risk Estimation Following Infarction Non-invasive Evaluation - ICD Efficacy (REFINE-ICD)
Amit Garg	EnAKT (Effect of a Multi-Component Quality Improvement Intervention on Patient Access to Kidney Transplantation and Living Kidney Donation: The EnAKT LKD Randomized Clinical Trial
Jeff Healey	ARTESIA: Trial Apixaban for the Reduction of Thrombo-Embolism in Patients with Device-Detected Sub-Clinical Atrial Fibrillation
Sanjit Jolly	CLEAR: A 2x2 factorial placebo-controlled trial of colchicine and spironolactone in patients with acute myocardial infarction (MI)
Michelle Kho	CYCLE: Critical Care Cycling to Improve Lower Extremity Strength
Jessica Spence	B-Free: Benzodiazepine-free cardiac anesthesia for reduction of postoperative delirium
Ian Stiell	RAFF4: A Randomized Trial of Anti-Arrhythmic Agents to Improve Management of Emergency Department Patients with Acute Atrial Fibrillation
Alexis Turgeon	HEMOTION: HEMOglobin transfusion threshold in Traumatic brain Injury OptimizatioN
Michael Walsh	ACHIEVE: Aldosterone bloCkade for Health Improvement EValuation in End-stage renal disease (ACHIEVE) trial

First annual ACT Consortium meeting

- April 17 and 18, 2023 – Hamilton Ontario
- Focus – discuss ACTs goals and structure and bring Canadian biotech and trial community together
- 300+ attendees, 65 biotech companies
- Unanimous support to pursue single national distributive REB approval model

2nd ACT RFA

- RFA announced Apr 11, 2023
- 2 streams of funding
  - Stream 1 – non-traditional trial designs
  - Stream 2 – trials evaluating methods to improve conduct of trials
- Submission deadline June 8, 2023
- Stream 1 - 33 applicants from 18 ACT networks
- Stream 2 – 8 applications from 6 ACT networks
- Each application reviewed and scored by 5 independent reviewers

2nd ACT RFA

- 8 stream 1 and 5 stream 2 successful applicants
- Total of $1.9 million in funding

PI name	Stream 1 Funded RCT
Naveen Poonai	ALICE: Anxiolysis for Laceration Repair in Children: Open-Label Multicentre Adaptive Trial
Jason Weatherald and Lisa Mielniczuk	CRAVE: The Canadian Right ventricular AdatiVE (CRAVE) platform
Samuel Silver and Amber Molnar	Dial-Bicarb: The Dial-Bicarb Trial investigates dialysate bicarbonate levels
Ann Young	KidneyCare Outreach: Vanguard phase of a population-based randomized clinical trial to strengthen kidney care delivery for patients at high risk of kidney failure
Corinne Hohl	NAPTEM-C: Developing a National Adaptive Platform Trial in Emergency Medicine to Evaluate COVID-19 Therapies
Emilie Belley-Côté and Richard Whitlock	SAFE-AFIB: Surgical Ablation of Atrial Fibrillation (SAFE) Trial
Jessica Spence and Deborah Siegal	TheRAPy: The effect of retrograde autologous priming on transfusion requirements after cardiac surgery (TheRAPy): A multi-centre, multi-period, vanguard randomized cluster crossover trial
Sylvie Aucoin	Virtual, Innovative, postsurgical Care To Optimize Return home for older people with frailtY: the VICTORY randomized trial

PI name	Stream 2 Funded RCT
Sylvain Lother	CAPTIVATE: A consent trial for Adaptive Platform Trials using patient-centered audiovisual methods
Paul Karanicolas	PROMs: Interventions to Optimize Response Rates for Online, Patient-Reported Outcomes Measures
Nick Daneman	SIMPLY-SNAP: Evaluating the impact of a SIMPlified LaYered consent process versus a conventional informed consent form on recruitment of potential participants to a large platform clinical trial: a pragmatic nested randomized controlled trial
Shrikant Bangdiwala and Susan Jack	SWIFT Recruitment Intervention for BRAVE SWIFT
Balpreet Singh	WHEAT-SWAT: Examining the efficacy of a parent-targeted co-designed digital media intervention to increase recruitment rates across a multi-site randomized clinical trial in Canadian NICU's

National Portfolio Funding Competition

- Funding opportunity announced February 17, 2023
- 41 applicants
- Review panel interviewed and independently scored application
- Results announced mid June
- 20 portfolio hospitals funded from 9 provinces and 1 territory

3rd RFA

- RFA announced May 12, 2023
- Canadian biotechnology trials
- Submission deadline July 7, 2023
- Review process will finish in next couple of weeks and results will be announced

Second Annual ACT Consortium Meeting

- Sept 21, 22, 2023 Charlottetown, PEI
- Focus
  - portfolio hospitals
  - regulatory: review, understand, and comment on draft ICH E6 (R3)
  - single national distributive REB model with clear review timelines
  - recognize and celebrate 1st and 2nd RFA

Reflections

- Substantial activity during first 8 months of ACT
- Gratitude for
  - co-chairs and committee members who have worked diligently towards ACT goals
  - ACT networks and CTUs
  - RFA reviewers and Portfolio review panel
  - partners (CIHR, pharma, device companies, IMC, Canadian biotech, Health Canada)
  - central ACT support team

Immediate upcoming work

- RFA 4 funding for new networks in areas of need
- Planning subsequent RFAs
- Activating portfolio hospitals
- Selecting system for single national distributive REB model

Reality and success

- Our timeline is short
  - <2 years left in ACT grant
  - requires being expeditious but not careless
- Measure of success
  - having structures in place that persist to benefit RCTs
    - e.g., single national distributive REB process
  - convince government to support long-term funding strategies for RCTs
  - grow Canadian biotech

How to achieve our broader goal

- Deliver on what we said we would do
  - e.g., master clinical trial agreements
- Collaborate with key stakeholders
- Think strategically regarding
  - arguments to bring required groups on side
- Focus on bigger picture, move past regional politics
- Need trials community to step up and help with ACT activities (RFA reviews, work on structure changes, national REB)

Need to recognize

- Our bigger competition is
  - world outside our national boarders
- Every CTU, network, or group does not need to benefit from every ACT initiative
  - If ACT is overall successful and
    - permanent efficient systems are implemented, government implements sustained funding for RCTs, Canadian biotech grows, and more big pharma and device company trials come to Canada
      - then Canadian public benefits and we will have achieved our goal