Accelerating Clinical Trials (ACT) update: Impact and horizons

funded by CIHR to improve ecosystem for conducting RCTs in Canada

P.J. Devereaux, MD, PhD

Co-Chair of ACT Operations Committee

CEO and Scientific Director of the World Health Research Trust

Deputy Director of the Population Health Research Institute

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Since last CTO meeting…

- CanReview was selected to lead single national REB review and approvals process with strict timelines
- ACT contracts working group has implemented Master Clinical Trials Agreement for CIHR-funded trials
- CTU committee selected RAN Bio Links as preferred eTMF vendor
- Publication and impact of several trials funded by ACT
  - 5 NEJM
  - 2 Lancet

Since last CTO meeting…

- Contributed to international efforts
  - Promotion of WHO guidance for best practices for clinical trials
  - Selected as member of WHO's Global Clinical Trials Forum
- Held 3 funding opportunities
  - Knowledge Mobilization RFA
  - RFA 5 – bring high-impact RCTs to Canada
  - RFA 6 – Canadian Biotech
- Initiation of Indigenous demonstration projects

RFA 5 – To bring high-impact RCTs to Canada

- Call to encourage new collaborations between Canadian researchers and international, high-impact RCTs
- Total $2 million in funding available
  - 10 applications x $200,000 CAD each
- Successful applications announced November 22, 2024
  - Includes collaborations across 5 countries - Australia, Finland, Germany, United Kingdom, United States

RFA 6 – Canadian Biotech Trials II

- Call to fund trials evaluating biotechnologies from Canadian-controlled private corporations (CCPCs) in partnership with Canadian clinical trialists from ACT Networks
- Total $2 million in funding available
  - 5 applications funded x $400,000 each

Why should we focus on Canadian biotech

Global pharmaceutical industry

- 20 pharmaceutical companies make the Fortune 500 annually
- Global pharmaceutical market $1.6 trillion in 2023
- Overwhelmingly these companies are American or European
- Although Canadian scientists have made many life-saving discoveries that have impacted millions of individuals worldwide
    - billions in revenue generated annually by these discoveries have exclusively gone to foreign companies
- Canada does not own a single large brand pharmaceutical or medical device company

Canadian discovery, foreign profit

- Early 1900s with starvation diet
  - 2/3rds of children died within 1 yr of being diagnosed with diabetes
- 1921 Banting and Best discover insulin in Macleod's laboratory at University of Toronto
- 1922 U of T gives
  - Eli Lilly rights to produce and distribute insulin in North America

August and Marie Krogh

- August Krogh (Danish scientist) receives Nobel prize in 1920
  - same year his wife Dr. Marie Krogh diagnosed with diabetes
- 1922 August and Marie travel to US so August can give lectures
  - at Harvard meet with Eliot Joslin (starvation diet)
    - tells them about insulin and puts them in touch with Macleod at U of T
  - August visits Macleod's lab and they become friends

Production rights and Nobel prize

- Macleod presents August Krogh to U of T insulin committee
  - U of T gives August rights to produce insulin for Scandinavia
- August Krogh nominates Banting and Macleod for Nobel prize
  - which they win in 1923

Novo Nordisk

- August and Marie Krogh and Hans Hagedorn with insulin production founded company that would become Novo Nordisk
- 2024 Novo Nordisk market value was $570 billion
  - larger than the rest of the Danish economy
    - Denmark population just under 6 million
    - Canadian population 41 million
- In 2023 Novo Nordisk paid >$3 billion in income tax in Denmark

Recent Canadian SMEs

Canadian SME acquisitions by pharma have dominated pharma M&As in the past few years four notable deals:

- Novo Nordisk acquired Inversago for up to $1.07 billion;
- GSK acquired Bellus Health for $2.0 billion;
- Astra Zeneca acquired Fusion Pharmaceuticals for $2 billion; and
- Novartis acquired Chinook therapeutics for $3.2 billion

Leaving limited footprint or advanced stage trials being in Canada

The missing piece: Clinical trial investment

- Canadian researchers have developed many important innovations, often government funded, and sold the innovation to EU or US companies who then undertook required regulatory clinical trials to bring products to market
- The issue is not a lack of Canadian medical innovation or support of basic research
  - Canada's Biomanufacturing and Life Sciences Strategy
  - Ontario's Life Sciences Strategy
- The missing piece is funding to undertake required clinical trials to obtain regulatory approval

Canada should learn from EU

- EU endowed Research and Innovation budget of EUR 75.6 billion between 2014-2020 (EU Horizon 2020), corresponding to EUR 12.6 billion per year
- EU provides grants with 5-10 X the funding CIHR provides for individual RCTs
  - EU requires trials to incorporate small/medium size EU biotech companies
  - EU not only wants to improve health,
    - they want to grow their economy and
    - recognize that economy is major determinant of health

EU Horizon 2020 - Return on investment

- Each euro of Horizon 2020 funding resulted in
  - private for-profit sector investment of EUR 0.57 and
  - researchers brought in EUR 0.23 of their own resources
- Overall impact of program
  - annual average increase of EUR 15.9 billion to EU GDP
  - net gain in employment levels, 220,000 employees
  - resulted in 4000 intellectual property rights (2/3rds were patents)
  - for every euro invested in Horizon 2020
    - yield 5 euro of benefits for EU citizens by 2040
  - preparedness
    - investments in mRNA research were key to pandemic vaccines

Success has led to further funding

- Horizon 2020 has proven so successful
  - EU is currently investing EUR 95.5 billion in research and innovation funding between 2021 and 2027

What Canada needs to do

- Establish $2.5 billion endowment that would facilitate $100 million in annual investment in RCTs evaluating Canadian biotechnology
- Create tax incentives for
  - Canadian biotechnology companies that remain in Canada and run clinical trials in Canada
  - venture capitalists to invest in Canadian biotechnology companies
  - Canadian citizens through tax free investments when they invest in Canadian biotechnology companies

What Canada needs to do

- Ensure competition for money would favour trials that
  - undertake the biomanufacturing in Canada
  - use Canadian clinical trial unit to coordinate the trial
  - engage Canadian clinical trials network group
- Create platforms that bring
  - Canadian biotechnology companies, trialists, clinical trial units, venture capitalists, and governments together

What would Canada get for $100 million annual investment into clinical trials

- Facilitate 4 regulatory phase-3 trials ($20 million/trial)
- Facilitate 10 phase-2 trials ($2 million/trial)
- Biotech companies and venture capitalists will provide additional funding for these trials
  - doubling or tripling funding for each trial

What would Canada get for $100 million annual investment into clinical trials

- Expect at least 1 in 5 phase-3 trials to lead to regulatory approval with potential to create biotech anchor company
- Expect at least 2 in 5 phase-2 trials to go on to phase-3 trials
- Each phase-3 trial takes an average of 3 years and each phase-2 trial takes an average of 2 years

Direct new jobs in Canada – at steady state

- 12 active regulatory phase-3 trials that will seek Canadian, EU, and US regulatory approval and need to be conducted in all 3 regions
- 20 active phase-2 trials that can be restricted to Canada
- Phase-3 trials will include 100-150 sites per trial, of which there will be 75 Canadian, 25 EU, and 25 US sites
- Phase-2 trials will include 10 sites per trial that will be restricted to Canada
  - sites will hire 1 new full time equivalent (FTE) research position for each 2 trials
    - in Canada: steady state of
      - 12 phase-3 trials will result in 6 FTEs per site, and with 75 Canadian sites recruiting participants, there will be 450 FTEs
      - 20 phase-2 trials will result in 10 FTEs per site, and with 10 Canadian sites recruiting participants, there will be 100 FTEs
      - therefore, 32 active trials will result in 550 FTEs (i.e., 450 + 100) across Canadian sites

Direct new jobs in Canada – at steady state

- Canada has world leading clinical trial units (CTUs) and trialists with knowledge and expertise to design, run, and lead these clinical trials
- At steady state of 32 trials can expect
  - CTUs will hire 8 FTEs per trial, therefore 256 FTEs in Canadian CTUs
  - Canadian biotech companies will hire 2 new FTEs per trial (i.e., 64 new FTEs)
  - for every new direct FTE hired through this funding (i.e., 550 + 256 + 64 = 870), Canada can expect 0.65 additional support FTE positions in Canada (i.e., 870 X 0.65 = 566 FTEs)
- This investment will therefore result in 1436 new FTE jobs in Canada
  - 550 site FTEs, 256 CTU FTEs, 64 biotechnology FTEs, and 566 support spin-off FTEs

Additional return on investment

- Based on EU experience can expect private for-profit sector investment of at least $0.8 per government invested dollar, hence $80 million annually
- Expect at least 1 in every 5 phase-3 trials to result in regulatory approval that can then result in ≥$100 million in annual sales
  - creating large tax base for Canada
  - create Canadian anchor pharmaceutical or device company
- Beyond these financial benefits
  - Canadians will gain health opportunities

Reflections on ACT

- A lot has been **achieved** in first 2.5 yrs
- **Issue** is whether roots of system change are deep enough to be sustained with only 3 years of program funding

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ACT-2.0 goals

- Seek additional **3 years of funding** to solidify system changes
  - Ensure success of pan-Canadian, distributive, single REB review and approval process with strict timelines
    - provides platform that would allow CIHR to require single review process for CIHR funded trials, consistent with government goal of avoid duplication of approvals
  - Sustain and expand portfolio funding embedding study personnel in community hospitals across Canada creating
    - greater democratization of access to trials for more Canadians and
    - facilitating pandemic preparedness

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ACT-2.0 goals

- Seek additional **3 years of funding** to solidify system changes
  - Ensure successful implementation of master clinical trial contracts
    - improve clinical trial timelines and bring more trials to Canada
  - Continue to help grow Canadian biotech though granting opportunities for trials evaluating Canadian biotech
    - help keep Canadian biotechnology Canadian and grow Canadian economy
  - Ensure implementation of WHO regulatory guidance for conduct of clinical trials
    - enhance efficiency of trials

ACT-2.0 goals

- New **Initiatives**
  - Creating change to ensure study personnel can **inform** all eligible patients about trials relevant to their health
  - Create network **contact process** to facilitate rapid determination of interested sites for pharma and investigator-initiated trials
  - Create **concierge service** to help direct investigators and companies regarding Canadian processes and services for conducting trials (e.g., regulatory, ethics, CTUs, networks)
  - Create more equitable system to ensure women of childbearing potential or **pregnant/lactating** women are not automatically excluded from trials
- Request additional $40 million in funding for next 3 years

Conclusions

- RCTs provide **health opportunities** for Canadians and have **positive impacts** on our economy
- ACT-1 has been successful
- There is a need for ACT-2
  - to solidify the implementation of several ACT-1 initiatives and
  - create further system change to make Canada the most efficient country in the world for doing trials
  - so investigators and companies will bring their trials to Canada
  - we will create more health opportunities for Canadians and
  - we will grow the economy in the process

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