Ottawa Hospital Research Institute
Institut de recherche de l'Hôpital d'Ottawa

Conducting patient-oriented pragmatic trials in Ontario: opportunities and challenges

CTO 2015
Clinical Trials Conference
Toronto, Ontario
March 5th

Dean Fergusson
Senior Scientist & Director, Clinical Epidemiology Program, Ottawa Hospital Research Institute
Full Professor, Departments of Medicine, Surgery, and of Epidemiology and Community Medicine, University of Ottawa

Pragmatic Trials

- In the 1960s Schwarz and Llellouch coined the phrase ‘pragmatic trial’ and “explanatory trial”
  - Journal of Chronic Disease, 1967

- In a **pragmatic trial** the design mimics as closely as possible **ROUTINE** clinical practice, with the exception that patients are randomly allocated to treatment

Patient-Oriented Trials

- Pragmatic trials that compare **standard of care/usual care** interventions (drugs, diagnostics, strategies, policies)
  - about ensuring that the right patient receives the right intervention at the right time
- Interventions assigned by randomization
  - ⇧ Internal validity
- Due to randomization… some patients may receive a standard of care different from what they would have outside the trial
  - **All** patients do receive a standard of care/usual care
  - Risks are **no different** inside or outside trial

Components of Pragmatic Patient-Oriented Trials

- Simple protocol
- “Effective” patient-oriented interventions – usual/standard care
- Simple consent - conditions for individual, waived, charted
- Streamlined REB approval
- Easy and simple data collection (ideally admin data)
- Patient important outcomes
- Adequate follow-up time
- Ideally patient engagement

Ottawa Hospital
Research Institute
Institut de recherche
de l'Hôpital d'Ottawa

Facing the major challenges

Major challenges facing academic trials

Institute Level

- Trial “start-up” times are too long
- Costs of doing trials are increasing
- Investigators pulling out of clinical research
- Trial infrastructure (experience & expertise)
- Training of Investigators and Staff (e.g. ethics/GCP)
- Lack of internal review processes

Major challenges facing academic trials

Investigator Level

- Asking the right questions
- The need for a multidisciplinary team
- Need for disease-oriented networks/groups
- Enrolment targets, expectations, and reality
- Funding opportunities
- Trial budgeting
- Identifying efficient design approaches
- Identifying efficient consent approaches

Major challenges facing academic trials

Government Level

- Funding
  - CIHR RCT committee (national treasure) will be terminated in 2015

- Regulation/Conduct
  - Academic trials face the same scrutiny as industry trials?
    - Tremendous effort and investment
  - GCP ≠ good, or clinically relevant, or practical
  - Where's the evidence?
    - Monitoring for data quality/integrity
    - Safety (SAE) reporting

Addressing the challenges

Today's climate and environment stifles our ability to design & conduct academic trials

- especially patient-oriented pragmatic trials

“Systems Problem” (Dr. Robert Califf)

- All stakeholders in the clinical research enterprise share some of the blame

- Fixing requires a collaborative effort
  - Regulators
  - Government
  - Industry
  - Academia: Institutes/Investigators/Methodologists
  - Funders: CIHR/FRQS/HSFC
  - Patients

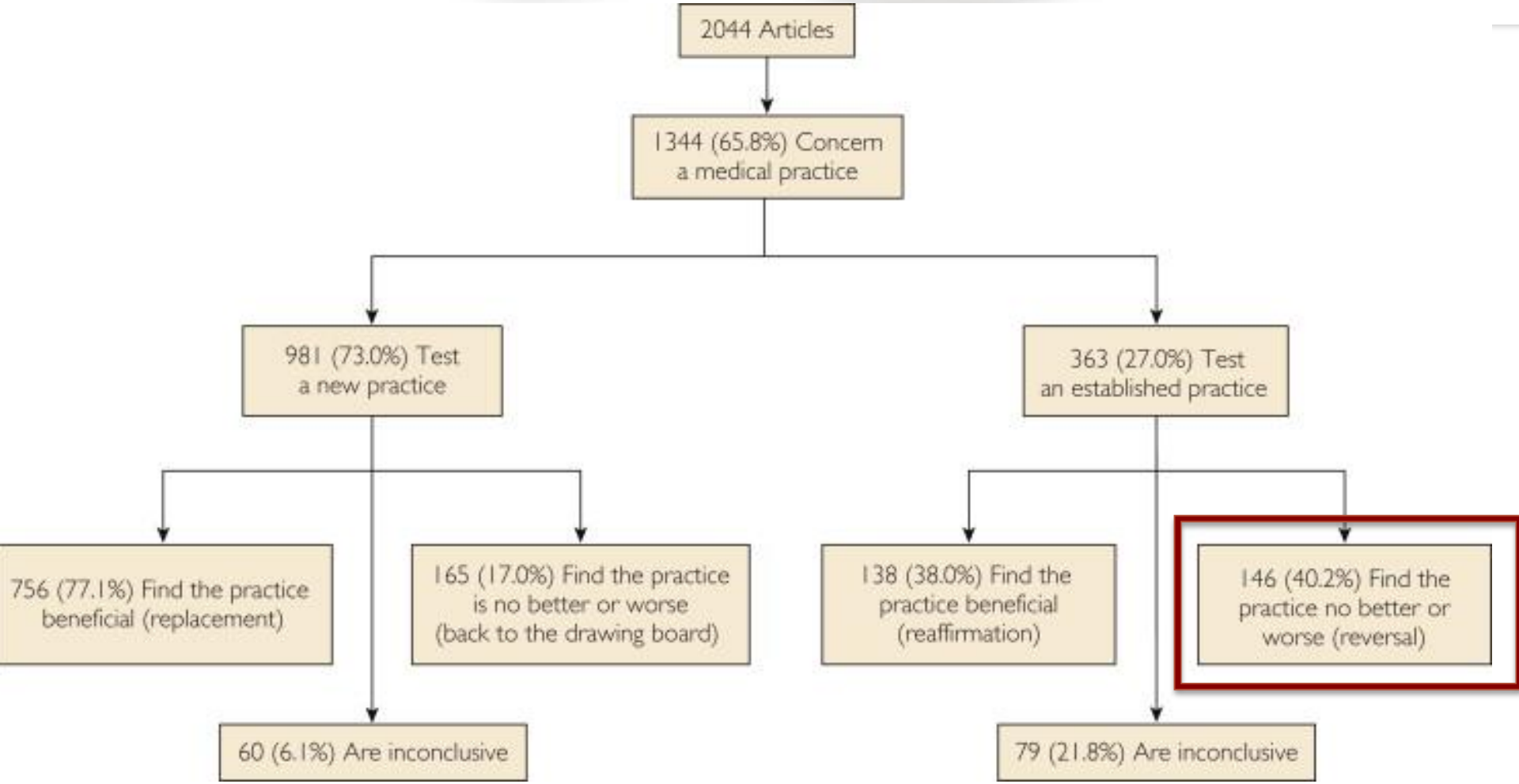
Why we need patient-oriented pragmatic trials?

- Ontario spends about $54 billion annually on health care
- Studies suggest that
  - 25% of patients receive care that is not needed or could be potentially harmful
  - Less than 60% of bedside decisions on general medical services are backed by an adequate level of evidence

- Gaps need to be addressed with research and proper implementation & evaluation

http://www.cihr-irsc.gc.ca/e/44000.html

Why we need patient-oriented pragmatic trials? (Prasad, 2013: 146 contradicted medical practices)



Mayo Clinic Proceedings 2013 88, 790-798DOI: (10.1016/j.mayocp.2013.05.012)

A new way forward

Given the challenges of the current “system”

Disruptive innovation is needed to create a very different system based on electronic data collection in practice with quality built in through a systematic approach (Clinical Trial Transformation Initiative)

System Solution: The Learning Health System

- Articulated goal of the Institute of Medicine
- By implementing electronic health records, data warehouses and disease registries, **every** patient's data will be used to further knowledge
  - All places of practice will become research sites
- Research must become a normal part of clinical practice, **not** something done separately from clinical practice (except for very special early phase and highly controlled types of studies)

- https://www.nihcollaboratory.org

- Supported by the Common Fund at the National Institutes of Health (NIH), the Health Care Systems (HCS) Research Collaboratory is intended to improve the way clinical trials are conducted by creating a new infrastructure for collaborative research. ***The ultimate goal is to ensure that healthcare providers and patients can make decisions based on the best available clinical evidence***

- The NIH HCS Research Collaboratory also supports the design and rapid execution of several high-impact Pragmatic Clinical Trial Demonstration Projects that will address questions of major public health importance that engage health care delivery systems in research partnership.

The Future

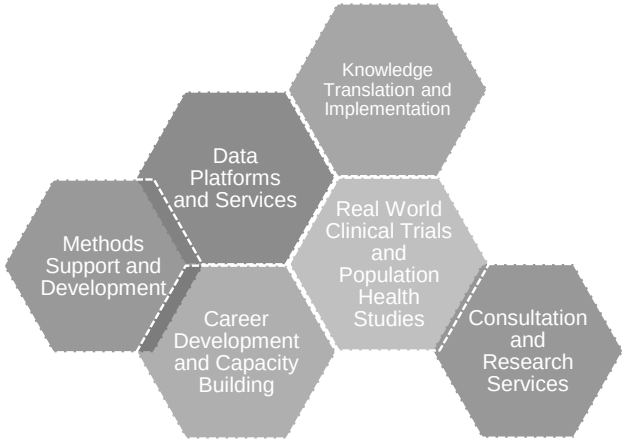
- Obviously, still a place for earlier phase trials (I-II/III)
- But…evidence and practice gaps, funding pressures, and patient-oriented research emphasis demand large pragmatic trials

OSSU represents an unprecedented opportunity

ONTARIO SPOR SUPPORT UNIT

Ontario's Assets (OSSU)

- Track record of conventional "pragmatic trials"
  - International impact & leadership
- Cluster trials expertise (design and ethics)
- Methods and analytical know-how
- ICES
- Hospital level data systems/infrastructure
- CTO (e.g. centralized REB)
- Excellent & engaged collaborative



Demonstration Projects: OSSU IMPACT awards

ONTARIO SPOR SUPPORT UNIT

- Anticipated that IMPACT Award recipient(s) will allow Ontario researchers in partnership with OSSU members to design and conduct pateint-oriented pragmatic trials.
- Offers a valuable and innovative opportunity to test the waters, make a difference, and build capacity/infrastructure

4 areas needing attention

1. Consideration of alternate consent models such as registered consent, charted consent, waived consent
   - Discussion/debate…leading to Ontario guidelines for REBs/trialists/funders
   - e.g. when do pragmatic patient-oriented trials represent minimal risk?

1. Matching consent requirements with intervention:
   - Continuum: from disinfectant soaps to nursing ratios to type of antiemetics to type of surgery
   - Individual versus “group” interventions
     - Impacts type of consent

2. What constitutes amenable POR interventions/justifying standards of care
   - (>XX% utilization? on the formulary? hospital policy? expert opinion?)
   - Need guidance and methods

4 areas needing attention

4. understanding, considering and implementing a “learning health system”

- no easy task

The future is bright

- Ontario is uniquely placed to conduct pragmatic patient-oriented trials to ensure the right patient receive the right treatment at the right time
  - Assets (e.g. OSSU)
  - Health system
  - Expertise
  - Willingness
- But we have some homework to do

Ending with an example: impact of design and consent choices

Two Canadian-led pragmatic trials assessing the impact of **age of stored blood**

INFORM TRIAL (McMaster)

- Interventions: fresh versus oldest blood available
- Enrollment over 2 years
- $1.6 million in peer-reviewed funding
- 4 sites
- Outcome: mortality
- **25,000+** hospitalized adults (aim is 38,000)

Waived Consent

ABLE TRIAL (Ste. Justine/OHRI)

- Interventions: fresh versus usual care
- Enrollment over 6 years
- 70+ sites
- $5+ million in peer-reviewed funding
- Outcome: mortality
- **2,510** adult ICU pts

Patient/proxy consent or deferred consent

Thank you

dafergusson@ohri.ca