Research Ethics
Stop sign or Signpost?

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CLINICAL TRIALS ONTARIO

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Issues Arising from Presentations

- Use of existing clinical/admin datasets in RCTs
  - outcome measures
    - long-term follow-up, retrospectively (WOSCOPS)
    - during clinical trial
    - as part of research platform (EHR4CR, Learning health system)
  - sampling frame
- Pragmatic trials, Standard-of-care RCTs
- Common questions:
  - When may consent requirements be altered or exempted?
  - Is there an obligation to participate in research or permit use of data for research?
- How to better involve the patient / public in research
  - notification, participation
  - learning from their perspective, priorities

USE OF EXISTING CLINICAL/ ADMINISTRATIVE DATASETS FOR RCTs

Use in Observational Studies

- Considerations:
  - TCPS2 provisions (Article 5.5A)
    - Identifiable information is essential
    - Use w/o consent unlikely to affect welfare of data subjects
    - Privacy protections / security safeguards
    - Comply with known preferences
    - Impossible or impracticable to obtain consent
    - Necessary permissions obtained
  - Relevant laws of jurisdiction
    - … not using for re-contacting individuals

Use in RCTs

- Outcome measures
  - treat equivalent to observational studies
    - Long-term follow up (retrospectively): – e.g. WOSCOPS
      - Easy to justify – impracticability
      - Adequate security and governance
    - When designed into clinical trial prospectively:
      - More difficult to argue impracticable
        - » Build into the consent to participate in study
      - When unit of intervention is care provider or the system?
- As a sampling frame
  - Who screens? Who makes first contact?
    - reasonable expectation of access to data
    - opt-in vs. opt-out

USE OF ROUTINELY COLLECTED DATA AS PART OF RESEARCH PLATFORM

Integrating Research and Practice: Health system leaders working towards high-value care

[Institute of Medicine (2014)]

- Evidence base decision-making involves both use and generation of "research" evidence.

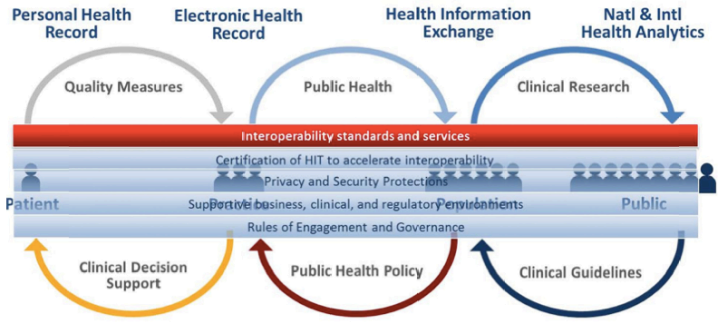

FIGURE 2-2 The Office of the National Coordinator's vision of a learning health system.
SOURCE: Reprinted with permission from Douglas Fridsma.

Ethics framework for the Learning Health System

[Faden et al (Hastings Center Report 2013)]

Obligations
1. Respect the rights and dignity of patients/families.
2. Respect the judgment of clinicians.
3. Provide each patient optimal clinical care.
4. Avoid imposing non-clinical risks and burdens.
5. Address unjust health inequalities.
6. Clinicians and health care institutions should conduct continuous learning activities
7. Patients and families should contribute to the common purpose of improving the quality and value of clinical care.

Limitations to Obligation #7

1. Patients are not obliged to participate in all learning activities, regardless of additional risk or burden they may impose.
   - Different learning activities will have differential effects on the rights and interests of patients
     → different implications for obligations to participate

Limitations to Obligation #7 (cont.)

2. Healthcare institutions must inform patients about:
   - their commitment to learning
   - the specific learning activities that are underway
   - how they are being conducted
   - how care has been improved as a result
   - that consent will be sought when a learning activity may (a) have a negative impact on quality of care or (b) impose burdens above and beyond what they would otherwise experience

3 Categories of Research (Kass / IOM 2014)

Category 1	Category 2	Category 3
No additional risk or burden to patient	Low-level risk or burden to patient	More risk and/or burden to patient
Chart reviews, Some systems level interventions, Prospective observational studies that do not change care	Study comparing efficacy of two very similar blood pressure medications	Traditional intervention research
	No reason to think that patients would object or prefer one approach over another	The different approaches being studied present meaningful differences to patients.
No prospective oversight (but retrospective audit)	Prospective oversight	Prospective oversight
No consent required	Streamlined consent	Prospective consent

Criticism of no-consent model for comparative effectiveness trials

[Kim & Miller (NEJM 2014)]

- Transparency is assumed in the clinician-patient relationship
  - Exemption from consent requires the treating MD to conceal (or obfuscate) inclusion in study
  - Even if no medical reason for choosing A over B, people have a right to exercise choice in participation in RCT
  - Arguments of no non-clinical burdens and minimal non-clinical risks do not justify this loss of agency
- If patients came to understand that intentional concealment of randomization occasionally occurs, this uncertainty could erode trust.

Integrated consent model

[(Kim & Miller (2014)]

- Consent to randomization is integrated into "usual clinical discussion about treatment"
  - verbal
  - brief description
  - documentation in clinical record
- Limitation:
  - assumes there is a thorough discussion about treatment options, risks, etc.

Sample script

- "As we've talked about, you have high blood pressure. . . . We've already tried exercise and diet, and unfortunately they have not worked. . . . I can treat you with drug A or drug B. They're both approved by the Food and Drug Administration, and I commonly use either one of them in patients to control high blood pressure; they are both taken once a day and they have similar side effects, which are . . .

- … But honestly, we doctors really don't know if one is better than the other. So our hospital is doing a study by randomly (like a flip of a coin, so that we can obtain an unbiased answer) giving patients one or the other drug and then comparing results over a period of 1 year.
- You might remember that ours is a learning health care system and this means that we do the study as part of providing care, so there won't be any special procedures or visits. And if at any point you or I think it would be good to try another medication instead, we can do that.

- … So unless you have a preference for drug A or B, I'd like to include you in the study.
- [Do you have any questions?]"

CAN WE PROVIDE GENERAL ETHICAL GUIDANCE FOR STANDARD-OF-CARE TREATMENT RCTs?

Varieties of Standard-of-Care Treatment RCTs

[Kim & Miller (JAMA 2015)]

- 7 examples of "standard-of-care RCTs"
- Not a homogeneous class of studies. Differ on:
  - level of risk and level of burden
    - Research-specific procedures / data collection
  - what should be communicated to the patient
  - vulnerability of participants
  - need for consent
  - focus: cost, efficacy, safety
  - implications of "no difference" findings
- Must consider on a case-by-case basis

HOW TO BETTER INVOLVE THE PATIENT / PUBLIC IN RESEARCH

Increasing awareness / Participation

- Notices, videos, posters from conferences in waiting areas
- Website for further information about opportunities
- Portray research as a regular part of doing business
- Routinely approach (at appropriate time) for permission to contact about relevant research
  - registry of potential research participants

Learning from Perspective of the Patient

- Process:
  - When is exemption from consent acceptable?
  - How / what should patients be told about the study?
  - Methods of accrual
  - Burden / risks of participation
- Outcomes:
  - Priority outcome measures
  - Potential (+/-) impact of the study on their interests