Proposal Class 2: Research Ethics

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What are research ethics?

Research ethics are normative

- Explicitly and implicitly codified values and norms in research that distinguish between acceptable and unacceptable behavior

- Contrast with theoretical/meta ethics

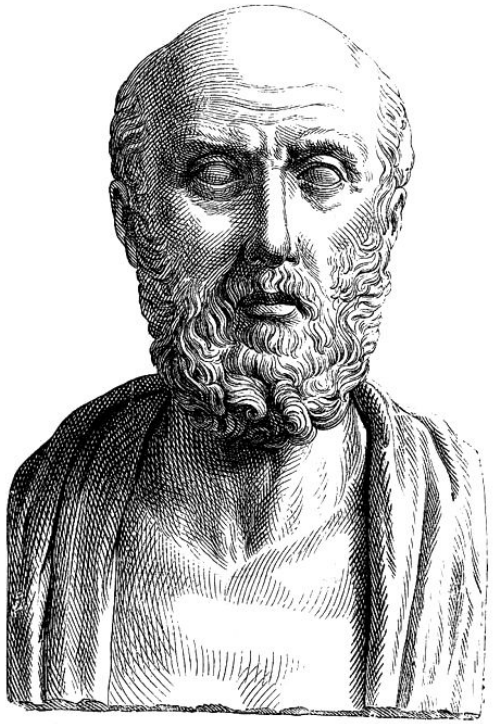
- Laws may also codify norms but ethical != legal

Research ethics blends theoretical frameworks

- Consequentialism
  - Bentham (Utilitarianism)
  - Based on outcomes
- Deontological ethics
  - Kant (categorical imperative)
  - Rawls (contractualism/veil of ignorance)
  - Duties and rights in research
- Virtue ethics
  - Aristotle, Aquinas
  - Related to character of researcher not necessarily actions (not really codified!)

Strongly established in medical/social science research

- "Hippocratic" Oath
  - "Do no harm"
  - But also no abortions or euthanasia (maybe) - medical paternalism
- Nuremberg Code (1947):
  - Trial of 23 Nazi physicians
  - Permissible Medical Experiments
  - Codified: consent, benefit, harm
- Helsinki Declaration (1964):
  - Research Ethics Committees (IRB/REB)
  - Concerns for individual outweigh concerns for society
  - Patient must benefit (or be healthy)
- Tri-Council Policy Statement 2 (2018):
  - Codification of principles for Canadian research involving human subjects



https://en.wikipedia.org/wiki/File:Hippocrates.jpg

Short version:

- **Beneficence**
- **Nonmaleficence**
- **Autonomy**
- **Justice**

Not well established in data science

Many challenges:

- Specific consent difficult to impossible to obtain
- “Public data” and “minimal risk” research e.g., social media data/open deidentified data are historically exempted from REB
- Privacy/Anonymity issues
- Data Misuse (societal not individual benefit)
- Validity/Accuracy/Contextualisation (large datasets can be MORE vulnerable to biases)
- Personal/Group harm
  - Model reinforces biases in dataset
  - Subjectivity in model design
  - Model abuse/misuse

- Existing frameworks often unwieldy/inappropriate: lots of active ethical theory (e.g., duty of easy rescue, social contract)

Why are research ethics important?

Many egregious failures of research ethics

- 1845-1849: James Marion Sims (11 women slaves with vesicovaginal fistula, four years of surgical experiments, morphine addiction)
- 1933: Qu'Appelle SK TB Vaccine (600 indigenous children: ⅕ died due to conditions)
- 1946-1948 Guatemala Experiment (directly infected 1,300 people including prisoners, inmates, orphans, sex workers)
- 1942-1952: First Nationals Nutrition Studies (>1000 children in residential schools)
- 1957-1964 MK-ULTRA - Royal Victoria Hospital in Montreal (>300 patients, ECT, Thorazine, Sensory deprivation attempts at brainwashing)
- 1932-1972 Tuskegee Syphilis Study (399 black men deliberately not treated for syphilis)

So, how do we do propose ethical research in health data science?

Start with big conceptual questions

- What potential good comes from this research cause?
- What potential harm?
- Can we do anything to mitigate the harm?
- Are there any alternatives to the same benefit?

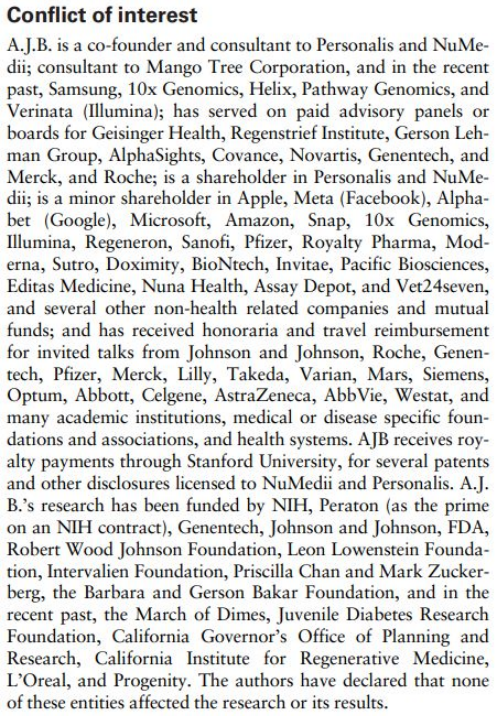
Identify your conflicts of interest

A conflict of interest is a set of conditions in which professional judgment concerning a primary interest (such as a patient's welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain). Conflict-of-interest rules [...] regulate the disclosure and avoidance of these conditions.

— Dennis F. Thompson, *The New England Journal of Medicine*, 1993

- Requirement to declare COIs during knowledge translation

- All conflicts of interest should be identified and managed, whether they are **real, potential, or perceived**.
- Researchers may be able to avoid conflict of interest issues by foreseeing where they may arise and adjusting their study design accordingly.
- Appropriate disclosure and management of conflicts of interest promotes the integrity of the research, and of the consent process for research participants.



Conflict of interest

A.J.B. is a co-founder and consultant to Personalis and NuMedii; consultant to Mango Tree Corporation, and in the recent past, Samsung, 10x Genomics, Helix, Pathway Genomics, and Verinata (Illumina); has served on paid advisory panels or boards for Geisinger Health, Regenstrief Institute, Gerson Lehman Group, AlphaSights, Covance, Novartis, Genentech, and Merck, and Roche; is a shareholder in Personalis and NuMedii; is a minor shareholder in Apple, Meta (Facebook), Alphabet (Google), Microsoft, Amazon, Snap, 10x Genomics, Illumina, Regeneron, Sanofi, Pfizer, Royalty Pharma, Moderna, Sutro, Doximity, BioNtech, Invitae, Pacific Biosciences, Editas Medicine, Nuna Health, Assay Depot, and Vet24seven, and several other non-health related companies and mutual funds; and has received honoraria and travel reimbursement for invited talks from Johnson and Johnson, Roche, Genentech, Pfizer, Merck, Lilly, Takeda, Varian, Mars, Siemens, Optum, Abbott, Celgene, AstraZeneca, AbbVie, Westat, and many academic institutions, medical or disease specific foundations and associations, and health systems. AJB receives royalty payments through Stanford University, for several patents and other disclosures licensed to NuMedii and Personalis. A.J.B.'s research has been funded by NIH, Peraton (as the prime on an NIH contract), Genentech, Johnson and Johnson, FDA, Robert Wood Johnson Foundation, Leon Lowenstein Foundation, Intervalien Foundation, Priscilla Chan and Mark Zuckerberg, the Barbara and Gerson Bakar Foundation, and in the recent past, the March of Dimes, Juvenile Diabetes Research Foundation, California Governor's Office of Planning and Research, California Institute for Regenerative Medicine, L'Oreal, and Progenity. The authors have declared that none of these entities affected the research or its results.

Evaluate your proposal on TCPS criteria:

1. Respect for autonomy
    a. Respect freedom of thoughts and action
    b. Take special measures to protect vulnerable individuals
2. Beneficence (non-maleficence)
    a. Minimize potential harms
    b. Maximise potential benefits
3. Justice
    a. Ensure fair spread of burdens/benefits (e.g., avoid exclusion of individuals solely on the basis of class, race, gender, disability, age (**TCPS-2**))
    b. Ensure those assuming burdens access benefits
4. Respect for community
    a. Engage community that is subject to the research in the research (patient-involved research)
    b. Open communication/knowledge translation
    c. Explicit requirement for research involving First Nations, Inuit, and Metis people (**TCPS-9**)

Consider consent

- Clinical standard: Informed voluntary opt-in to research (no coercion, care with vulnerable groups)
- How well can you inform someone else when doing inductive/prospective research?
- If the dataset had broad consent (e.g., “we can use data for research purposes”) is your research proposal in keeping with what participants might expect?
- If not, is it actually possible to get more specific consent?
- Can you reduce sensitivity of data to make broad consent more appropriate?

- Again: this is a **mess** in health data science

Ensure compliance with legal privacy requirements

- Privacy legislation
  - **Federal**: Personal Information Protection and Electronics Documents Act
  - **Provincial**:
    - Nova Scotia Personal Information International Disclosure Protect Act
    - Nova Scotia Personal Health Information Act
- Include considerations: data shouldn't leave Canada (thorny with cloud computing), consent is required for recruitment AND participation in research (although waiver of consent can be requested due to "impracticality").

General principles:

- Collect the minimum amount of data required
- Securely handle it/store it/share it with access logs

In pre-collected datasets this will have been considered but need to justify (and additional linkage/analyses may require reconsideration).

Procedural compliance

- REB application is still required (even if exempt) for any research involving humans
- Databases often have specific additional data access applications
- Will formalise the other components but are a **MINIMUM** requirement!