

PHIL 543 / EPID 679: Medical Ethics

Topic for 2014: Human Experimentation Ethics

Professor: Jonathan Kimmelman, Biomedical Ethics Unit

Time: Monday, 10:35 a.m.–1:25 p.m.

Room: 3647 Peel, Room 102

Reading Materials for 2014:***Week 1 (January 6)****Introduction to Human Experimentation Ethics**

Themes: Why do we worry about experimenting in human beings? What is research ethics, and how did it arise? How has medical research evolved? How have human protections evolved? Do policies protect all that is ethically at stake in medical research?

- Moreno JD. Goodbye to All That: The End of Moderate Protectionism in Human Subjects Research. *Hastings Cent Rep* 2001; 31: 9-17
- Jonas H. Philosophical Reflections on Experimenting with Human Subjects. In: *Philosophical Essay: From Ancient Creed to Technological Man*. Chicago: University of Chicago Press: 105-31.
- London, AJ, Kimmelman J, Emborg ME. Beyond Access vs. Protection. *Science* 2010; 328: 829-30.
- Belmont Report (see: <http://ohsr.od.nih.gov/guidelines/belmont.html>)
- Declaration of Helsinki (see: <http://www.wma.net/e/policy/b3.htm>)

Week 2 (Jan 13)**What is Research?**

Themes: What is the difference between research and medical care? Why is research “special?” How do we demarcate? Why is this distinction important for establishing ethical policies? How important is it that human subjects understand this difference?

- Cyranoski D. Texas Prepares to Fight for Stem Cells. *Nature* 2011 378: 476-7.
- Appelbaum PS et al. False hopes and best data: Consent to research and the therapeutic misconception. *Hastings Cent Rep* 1987; 17(2): 20-24.
- Kimmelman J. Therapeutic Misconception at 25. *Hastings Cent Rep* 2007; 37:36-42.
- Casarett D, Karlawish JT, Sugarman J. Determining When Quality Improvement Initiatives Should Be Considered Research. *JAMA* 2000; 283: 2275-80.

Week 3 (Jan 20)**Informed Consent**

Themes: What vision of autonomy does informed consent support? How is informed consent obtained in different circumstances? Is it always necessary? Are current practices too restrictive, or are they too limited?

- Anderson A. Ethicists Balk at New Emergency Trials that Skip Informed Consent. *Nat Med* 2007; 13: 765.
- Berg JW, Appelbaum PS, Lidz CW, Parker LS. The Concept and Ethical Justification of Informed Consent. In: *Informed Consent: Legal Theory and Practice*, 2d edition. New York: Oxford University Press (2001).
- Flory J, Emanuel E. Interventions to improve research participants' understanding in informed consent for research: a systematic review. *JAMA*. 2004; 292: 1593-601.
- Kukla R. How Do Patients Know? *Hastings Cent Rep* 2007; 37: 27-35.

Week 4 (Jan 27)**Equipoise**

Themes: when is it ethical for physicians—or the state—to allow invitation to research? How do we establish norms of risk and benefit, and what are the proper goals of research?

- Freedman B. Equipoise and the Ethics of Clinical Research. *NEJM* 1987; 317: 141-5.
- Miller FG, Brody H. Critique of Clinical Equipoise: Therapeutic Misconception in the Ethics of Clinical Trials. *Hastings Cent Rep* 2003; 33: 19-29.
- London AJ. Clinical Equipoise: Foundational Requirement or Fundamental Error? From: *Oxford Handbook of Bioethics*; Steinbock B, ed. New York: Oxford University Press (2007).
- Djulbegovic B, Kumar A, Glasziou P et al. Trial Unpredictability Yields Predictable Therapy Gains. *Nature* 2013; 500: 395-6.

Week 5 (Feb 3)**Risk:**

Themes: How should investigators analyze risk? What counts as acceptable risk? How should risk be disclosed? How do we resolve tensions between paternalism and autonomy in risk?

- Wadman M. London's Disastrous Drug Trial has Serious Side Effects for Research. *Nature* 2006; 440: 388-9.
- Weijer C, Miller PB. When are research risks reasonable in relation to anticipated benefits? *Nat Med* 2004; 10: 570-3.
- Slovic P, Peters E, Finucane ML, MacGregor DG. Affect, Risk, and Decision Making. *Health Psychol* 2005; 24: 535-40.

- London AJ. Reasonable risks in clinical research: a critique and a proposal for the Integrative Approach. *Stat Med* 2006 Sep 15; 25:2869-85

Week 6 (Feb 10)

Value and Validity

Themes: what do we mean by value and validity? How do we prospectively evaluate it? How are is value attained in research? How should policy-makers establish a research agenda?

- Sox H, Rennie D. Seeding Trials: Just Say ‘No.’ *Ann Int Med* 2008; 149: 279-80.
- Claxton K, Cohen JT, Neumann PJ. When is Evidence Sufficient? *Health Affairs* 2005; 24: 93-101.
- Shadish, WR, Cook TD, Campbell DT. Chapter 3: Construct Validity and External Validity. *Experimental and Quasi-Experimental Designs for Generalized Inference*. New York: Houghton Mifflin (2002). pp64-96
- Tunis SR, Stryer DB, and Clancy CM. Practical Clinical Trials: Increasing the Value of Clinical Research for Decision Making in Clinical and Health Policy. *JAMA* 2003; 290: 1624-32.
- Glasziou P, Chalmers I, Rawlins M. When Are Randomized Trials Unnecessary? Picking Signal from Noise. *BMJ* 2007; 334: 349-51.

Week 7 (Feb 17)

Inducement and Financial Interest Conflicts

Themes: Do incentives jeopardize important ethical values, like voluntariness or value, in research? What are appropriate inducement measures?

- McHugh J. Drug Test Cowboys: The Secret World of Pharmaceutical Trial Subjects. *Wired* 2007; April 24.
- Emanuel EJ. Undue Inducement: Nonsense on Stilts? *AJOB* 2005; 5: 9-13.
- Grant RW, Sugarman J. Ethics in Human Subjects Research: Do Incentives Matter? *J Med Phil* 2004; 29: 717-738.
- Loewenstein G, Sah S, Cain DM. The Unintended Consequences of Conflict of Interest Disclosure. *JAMA* 2012; 307: 669-70.
- Chambers T. Participation as Commodity, Participation as Gift. . *AJOB* 2001; 1: 48.

Week 8 (Feb 24)

Placebos and Sham Procedures

Themes: What is a placebo, and what is a placebo effect? Why are they used in research, and why do major controversies persist around placebo use? Is use of active placebo—sham—ethical?

- Marcus A. Fighting Cancer With a Sugar Pill—Move to Give Some Patients Instead of Drugs Causes Rift. *Wall Street Journal* 8 June 2004: D1
- Freedman B, Weijer C, Glass KC. Placebo orthodoxy in clinical research. I: Empirical and methodological myths. *J Law Med Ethics*. 1996 Fall;24(3):243-51.
- Flum DR. Interpreting Surgical Trials Involving Subjective Outcomes: Avoiding UnSPORTSman Conduct. *JAMA* 296: 2483-5.
- Kaptchuk TJ, Placebo Effect: Illness and Personal Healing. *Perspect Biol Med* 2009; 52: 518-39.

----- Reading Week -----

Week 9 (Mar 10)

Midterm Exam (1 hr)

Deception

Themes: What is deception, lying, and manipulation? What are the effects and consequences of deception? When is deception and manipulation acceptable? Are single blind run-in phases deceptive? Is use of sham control deceptive?

- Hunt M. Research Through Deception. *New York Times*. September 12, 1982.
- APA Ethical Principles of Psychologists. 2003. 8.07: Deception in Research.
- Ortmann A, Hertwig R. The Costs of Deception: Evidence from Psychology. *Experimental Economics* 2002; 5: 111-31.
- Benham B. The Ubiquity of Deception and the Ethics of Deceptive Research. *Bioethics* 2008; 22: 147-56.

Week 10 (March 17)

Children

Themes: what is the moral status of children, and how do we protect their interests in medical experimentation? What are the consequences of *not* experimenting on children? How do standards of risk change when minors are involved?

- Couzin J. Diabetes' Brave New World. *Science* 2003; 300: 1862-5.
- Ross LF. Children in Medical Research. *Perspect Biol Med* 2004; 47: 519-36.
- Coffey MJ, Wilfond B, Ross LF. Ethical assessment of Clinical Asthma Trials Including Children Subjects. *Pediatrics* 2004; 1: 87-94.
- Nelson RM. Justice, Lead, and Environmental Research Involving Children. In: *Ethics and Research with Children: A Case-Based Approach*. New York: Oxford University Press (2005). Pp.161-78.

Week 11 (Mar 24)**Disadvantaged Populations**

Themes: To what extent should deprivations of low-income countries drive the research agenda? Can research be considered a type of economic transaction, subject to the same rules and norms of other economic transactions between advantaged and disadvantaged countries? What counts as exploitative research? What counts as unjust research?

- Jayaraman KS. Outsourcing Clinical Trials to India Rash and Risky, Critics Warn. *Nat Med* 2004; 10: 440.
- Participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries. Moral Standards for Research in Developing Countries: From “Reasonable Availability” to “Fair Benefits.” *Hastings Cent Rep* 2004; 3:17-27.
- London AJ. Justice and the human development approach to international research. *Hastings Cent Rep* 2005 Jan-Feb;35(1):24-37.
- Flory JH, Kitcher P. Global Health and the Scientific Research Agenda. *Philos Public Affairs* 2004; 32: 36-65.

Week 12 (Mar 31)**Public Health and Epidemiology**

Themes: in what ways does the moral appraisal of public health activities and research overlap? Do public health studies represent a special category of research- bound by different rules? What about research aimed at assessing the implementation of research findings?

- Kolata G. States and V.A. at Odds on Cancer Data. *New York Times* 2007 (Oct 10).
- Burris S, Buehler J, Lazzarini Z. Applying the Common Rule to Public Health Agencies: Questions and Tentative Answers About a Separate Regulatory Regime. *J Law Med Ethics* 2003; 638-53
- Bayer R, Fairchild AL. Surveillance and Privacy. *Science* 2000; 290: 1898-9.
- Carrel M, Rennie S. Demographic and Health Surveillance: Longitudinal Ethical Considerations. *Bull World Health Assoc* 2008; 86: 612-6
- Weijer CW et al. Ethical Issues posed by cluster randomized trials in health research. *Trials* 2011; 12: 100.

Week 13 (Apr 8)**What is “Human”?**

Themes: So far, this class has viewed the category “human subjects” as fixed and well demarcated. This session takes up the question of whether human protections ought to be extended to categories of “research subjects” that lack full human status, including embryos, animals, and future generations.

- Cohen J. The Endangered Lab Chimp. *Science* 2007; 315: 450-2.

- Dresser R. Designing babies: human research issues. *IRB*. 2004 Sep-Oct;26(5):1-8.
- Klitzman R. The Use of Eggs and Embryos in Stem Cell Research? *Semin Reprod Med* 2010; 336-44.
- Grazia, D. Animals' moral status and the issue of equal consideration. In: *Taking Animals Seriously: Mental Life and Moral Status*. Cambridge University Press (1996): 36-74

* Students are expected to familiarize themselves w/ major policy documents, including:

- Tricouncil Policy: http://www.pre.ethics.gc.ca/english/pdf/TCPS%20June2003_E.pdf
- U.S. Human Protections Regs (45 CFR 46—esp. subparts A and D): <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>
- CIOMS: http://www.cioms.ch/frame_guidelines_nov_2002.htm
- Declaration of Helsinki: <http://www.wma.net/e/policy/b3.htm>

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