ETHICS OF CLINICAL RESEARCH

Indicative Syllabus

Credits: 15
Module Convenor: Dr Silvia Camporesi & Dr Annette Rid
Office: D6, 3rd floor, East Wing, King's Building
Consultation time: TBD
Semester: Second
Lecture time and venue: TBD

MODULE DESCRIPTION

This module aims to offer students an introduction to the foundations of clinical research ethics, through the discussion of paradigmatic cases of research misconduct from the post WWII up-to-now, the analysis of national and international guidelines for clinical research, and a critical discussion of fundamental concepts, such as autonomy, risk, benefit, clinical equipoise, and exploitation.Where appropriate case studies will be used to enhance the analysis of these concepts.

The course will run over 10 weeks for 2 hours weekly: 1 hour of lecture and 1 hour of presentation and discussion of an illustrative case study.

Assessment methods and deadlines

Written summative assessment: one x 3,000-word essay (100 % total grade)

OUTLINE OF CONTENTS AND READINGS

Week 1: The Ethics of Clinical Research: A critical analysis of the origins and establishment of international guidelines

Where we will critically discuss the origina of research ethics through a historical lens, discussing paradigmatic cases of research misconduct from the post WWII to the present.

Readings:

Required:

Beecher, H. K. (2001). Ethics and clinical research. *Bulletin of the World Health Organization*, *79*(4), 367-372.

Harkness, J, S E Lederer, and D Wikler. 2001. Laying ethical foundations for clinical research. Bulletin of the World Health Organization 79, no. 4: 365-366.

Lederer, Susan. 1997. Subjected to science : human experimentation in America before the Second World War. Johns Hopkins Paperbacks ed. Baltimore: Johns Hopkins University Press.

Rid, Annette, and Harald Schmidt. 2010. The 2008 Declaration of Helsinki - first among equals in research ethics? The Journal of Law, Medicine & Ethics: A Journal of the American Society of Law, Medicine & Ethics 38, no. 1 (March): 143-148. doi:10.1111/j.1748-720X.2010.00474.x.

Recommended:

Goodyear, M. D E, L. A Eckenwiler, and C. Ells. 2008. Fresh thinking about the Declaration of Helsinki. BMJ 337, no. oct17 2 (10): a2128-a2128. doi:10.1136/bmj.a2128.

Goodyear, M. D E, T. Lemmens, D. Sprumont, and G. Tangwa. 2009. Does the FDA have the authority to trump the Declaration of Helsinki? BMJ 338, no. apr21 1 (4): b1559-b1559.

doi:10.1136/bmj.b1559.

Kimmelman, Jonathan, Charles Weijer, and Eric M Meslin. 2009. Helsinki discords: FDA, ethics, and international drug trials. Lancet 373, no. 9657 (January 3): 13-14. doi:10.1016/S0140-6736(08)61936-4.

Week 2: A critical analysis of the ethical justification(s) of clinical research

Where we will critically discuss the criteria for the ethical justification of both clinical research and research oversight.

Readings:

Emanuel, E. J., Wendler, D., & Grady, C. (2000). What makes clinical research ethical?. *JAMA: the journal of the American Medical Association*, *283*(20), 2701-2711.

Miller, F. G., & Wertheimer, A. (2007). Facing up to paternalism in research ethics. *Hastings Center Report*, *37*(3), 24-34.

Wertheimer, Alan (2010). *Rethinking the Ethics of Clinical Research: Widening the Lens: Widening the Lens*. Oxford University Press (Chapters 1-2. Pp 1-44)

Brody, B. A., McCullough, L. B., & Sharp, R. R. (2005). Consensus and controversy in clinical research ethics. *JAMA: the journal of the American Medical Association*, *294*(11), 1411-1414.

Rhodes R. Rethinking research ethics. *American Journal of Bioethics* 2005, 5(1):7-28.

Week 3: Fundamental concepts 1) Informed Consent and Therapeutic Misconception

Where we will critically discuss the fundamental concepts of respect for autonomy, informed consent, and the criteria for valid consent.

Readings:

Required:

Faden, R and Beauchamp T (1986), A History and Theory of Informed Consent, New York: Oxford University Press. (Chapter 7, pp 235-273).

Appelbaum, P S, L H Roth, C W Lidz, P Benson, and W Winslade. 1987. False hopes and best data: consent to research and the therapeutic misconception. The Hastings Center Report 17, no. 2 (April): 20-24.

Beecher, H K. 1966. Ethics and clinical research. The New England Journal of Medicine 274, no.24 (June 16): 1354-1360. doi:10.1056/NEJM196606162742405.

Manson, N. C., & O'Neill, O. (2007). *Rethinking informed consent in bioethics* (Vol. 1). Cambridge: Cambridge University Press. (Chapter 7: 154-171)

Horng, Sam, and Christine Grady. 2003. Misunderstanding in clinical research: distinguishing therapeutic misconception, therapeutic misestimation, and therapeutic optimism. Irb 25, no. 1 (February): 11-16.

Recommended:

de Melo-Martín, I, and A Ho. 2008. Beyond informed consent: the therapeutic misconception and trust. Journal of Medical Ethics 34, no. 3 (March): 202-205. doi:10.1136/jme.2006.019406.

Week 4: Fundamental concepts 5) Benefit, Risk and Clinical Equipoise

Where we will critically discuss the concepts of benefit, risk, and clinical equipoise in clinical research, and the different frameworks that have been proposed to evaluate them.

Readings:

Required:

King, N M. 2000. Defining and describing benefit appropriately in clinical trials. The Journal of Law, Medicine & Ethics: A Journal of the American Society of Law, Medicine & Ethics 28, no. 4: 332-343.

Rid, A., Emanuel, E. J., & Wendler, D. (2010). Evaluating the risks of clinical research. *JAMA: the journal of the American Medical Association*, *304*(13), 1472-1479.

Rid, A., & Wendler, D. (2011). A framework for risk-benefit evaluations in biomedical research. *Kennedy Institute of Ethics Journal*, *21*(2), 141-179.

Anderson, James A. 2009. Contextualizing clinical research: the epistemological role of clinical equipoise. Theoretical Medicine and Bioethics 30, no. 4: 269-288. doi:10.1007/s11017-0099104-6.

Miller, Franklin G, and Howard Brody. 2003. A critique of clinical equipoise. Therapeutic misconception in the ethics of clinical trials. The Hastings Center Report 33, no. 3 (June): 19-28.

Miller, Franklin G. 2006. Equipoise and the ethics of clinical research revisited. The American Journal of Bioethics: AJOB 6, no. 4 (August): 59-61; discussion W42-45. doi:10.1080/15265160600755672.

Recommended:

Miller, Franklin G. 2007. Clinical equipoise and the incoherence of research ethics. The Journal of Medicine and Philosophy 32, no. 2 (April): 151-165. doi:10.1080/03605310701255750.

Anderson, J. A., & Kimmelman, J. (2010). Extending clinical equipoise to phase 1 trials involving patients: unresolved problems. *Kennedy Institute of Ethics Journal*, *20*(1), 75-98.

Kimmelman, J. (2012). The social function of clinical equipoise. *Clinical Trials*,*9*(5), 630-631.

Case study tbc.

Week 5: Fundamental concepts 3) Vulnerability

Where we will critically discuss the concept of 'vulnerability' in clinical research, and its implications for the protection of specific subjects in research.

Readings:

Required:

Eckenwiler, L. A, C. Ells, D. Feinholz, and T. Schonfeld. 2008. Hopes for Helsinki: reconsidering "vulnerability". Journal of Medical Ethics 34, no. 10 (10): 765-766. doi:10.1136/jme.2007.023481.

Levine, C., Faden, R., Grady, C., Hammerschmidt, D., Eckenwiler, L., & Sugarman, J. (2004). The limitations of "vulnerability" as a protection for human research participants. *The American Journal of Bioethics*, *4*(3), 44-49.

Reverby, S. M. (2011). " Normal exposure" and inoculation syphilis: A PHS" Tuskegee" doctor in Guatemala, 1946-1948. *Journal of Policy History*, *23*(1), 6-28.

Presidential Commission for the Study of Bioethical Issues President's Bioethics Commission Releases Report on Human Subjects Protection http://bioethics.gov/node/559

Recommended:

Zenilman, J. M. (2013). Ethics gone awry: the US Public Health Service studies in Guatemala; 1946–1948. *Sexually transmitted infections*, *89*(4), 295-300.

The White House Office for the Press Secretary, Presidential Memorandum--Review of Human Subjects Protection, November 24, 2010 http://www.whitehouse.gov/the-press-office/2010/11/24/presidential-memorandum-review-human-subjects-protection

Tanne, J. H. (2010). President Obama apologises to Guatemala over 1940s syphilis study. *BMJ*, *341*.

Susan M. Reverby (2012) Reflections on Apologies and the Studies

Week 6: Fundamental concepts 4) Exploitation

Where we will critically discuss the concept of 'exploitation' applied to the context of clinical research, especially in relation to research being conducted in low and middle income countries.

Readings:

Benatar, S. R. (2000). Avoiding exploitation in clinical research. *Cambridge Quarterly of Healthcare Ethics*, *9*(4), 562-565.

Hawkins, Jennifer S, and Ezekiel J Emanuel. 2005. Clarifying confusions about coercion. The Hastings Center Report 35, no. 5 (October): 16-19.

Hawkins, J. S., & Emanuel, E. J. (Eds.). (2008). *Exploitation and developing countries: The ethics of clinical research*. Princeton University Press.

Wertheimer, A. (2008). Exploitation in clinical research. *The Oxford textbook of clinical research ethics*, 201-10.

Week 7: Current controversies 1): Focus on the off-shoring of clinical trials to developing countries

Where, following up from the discussion in the previous week, we will critically discuss the increasing trend of pharmaceutical companies to outsource clinical trials to developing countries, and the ethical issues related to this practice.

Readings:

Wilkinson, T. (2010). Assessing the Case for the Regulation of Research. *The American Journal of Bioethics*, *10*(8), 63-65.

Potter, N. N. (2010). Civic trust, scientific objectivity, and the publicity condition. *The American Journal of Bioethics*, *10*(8), 57-58.

Petryna, A. (2009). *When experiments travel: clinical trials and the global search for human subjects*. Princeton University Press.

Petryna, A. (2007). Experimentality: On the global mobility and regulation of human subjects research. *PoLAR: Political and Legal Anthropology Review*,*30*(2), 288-304.

Week 8: Current controversies 2): A 'moral duty' to participate in clinical research?

Where we will critically discuss the arguments for and against a 'moral duty' to participate in clinical research.

Readings:

Required:

Caplan A, Is there a duty to serve as a subject in biomedical research? *IRB*, 1984 (5):1-5.

Harris, John. Scientific research is a moral duty, J Med Ethics 2005, 31(4):242-248.

Brassington, Ian. John Harris' argument for a duty to research, *Bioethics* 2007, 21(3):160-168.

Harris, John & Chan, Sarah. Free riders and pious sons – why research remains obligatory. *Bioethics* 2009, 23(3):161-171.

Brassington, I. (2011). Defending the duty to research?. *Bioethics*, *25*(1), 21-26.

Recommended:
de Melo-Martìn, I. A duty to participate in research: does social context matter? *American Journal of Bioethics* 2008; 8(10):28-36.

Evans, HM. Should patients be allowed to veto their participation in clinical research? *J Med Ethics* 2004;30:198-203.

Week 9: Current controversies 3) Research exceptionalism

Where we will critically discuss the arguments for and against "research exceptionalism" (i.e. treating research participation as a special ethical case), asking, for example, whether repeat participation in Phase 1 trials with healthy volunteers is different from other forms of work.

Readings:

Required:
Wilson, J., & Hunter, D. (2010). Research exceptionalism. *The American Journal of Bioethics*, *10*(8), 45-54.

Hansson, S. O. (2010). Reversing "Research Exceptionalism". *The American Journal of Bioethics*, *10*(8), 66-67.

Hunter, D., & Wilson, J. (2010). Responses to Open Peer Commentaries on "Research Exceptionalism". *The American Journal of Bioethics*, *10*(8), W4-W6.

Elliott, C., & Abadie, R. (2008). Exploiting a research underclass in phase 1 clinical trials. *New England Journal of Medicine*, *358*(22), 2316-2317.

Recommended:
Fisher, J. (2008). *Medical research for hire: the political economy of pharmaceutical clinical trials*. Rutgers University Press.

Abadie, R. (2010). *The professional guinea pig: Big Pharma and the risky world of human subjects*. Durham: Duke University Press.

Glickman, S. W., McHutchison, J. G., Peterson, E. D., Cairns, C. B., Harrington, R. A., Califf, R. M., & Schulman, K. A. (2009). Ethical and scientific implications of the globalization of clinical research. *New England Journal of Medicine*, *360*(8), 816-823.

Week 10: Current controversies 4): Human Genomics Research

Where we will critically discuss the recent developments in human genomics research and the unique challenges that this kind of research raises for the existing ethical and regulatory framework for clinical research.

Readings:

Caulfield, T., McGuire, A. L., Cho, M., Buchanan, J. A., Burgess, M. M., Danilczyk, U., ... & Timmons, M. (2008). Research ethics recommendations for whole-genome research: consensus statement. *PLoS biology*, *6*(3), e73.

McGuire, A. L., Caulfield, T., & Cho, M. K. (2008). Research ethics and the challenge of whole-genome sequencing. *Nature Reviews Genetics*, *9*(2), 152-156.

McGuire, A. L., Caulfield, T., & Cho, M. K. (2008). Research ethics and the challenge of whole-genome sequencing. *Nature Reviews Genetics*, *9*(2), 152-156.

Greely, H. T. (2001). Human genomics research: new challenges for research ethics. *Perspectives in Biology and Medicine*, *44*(2), 221-229.

Knoppers, B. M., Joly, Y., Simard, J., & Durocher, F. (2006). The emergence of an ethical duty to disclose genetic research results: international perspectives. *European Journal of Human Genetics*, *14*(11), 1170-1178.