Ethical Considerations in Research

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Clinical Research Community Meeting

Baystate Health | ADVANCING CARE. ENHANCING LIVES.

What word do you associate with ethical conduct of research?

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Defining Ethics

- Ethics (or morals)

  - Standards of conduct (or behavior) that distinguish between right/wrong, good/bad, etc.

- Ethics, applied:

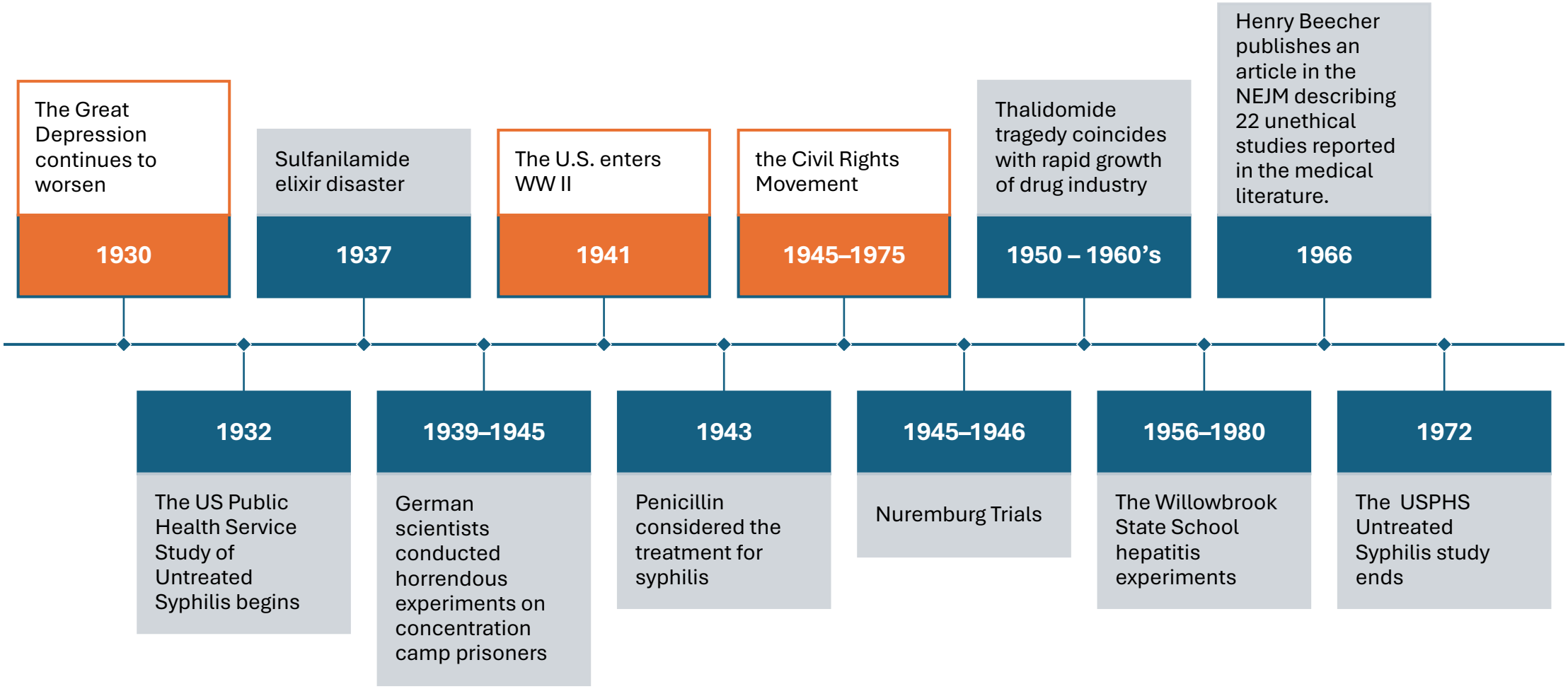
  - The study of ethics in specific situations, professions, or institutions, e.g. medical ethics, research ethics, etc.

Source: Based on Shamoo AE and Resnik DB, Responsible Conduct of Research, 3rd ed. (New York: Oxford University Press, 2015)

What does history tell us?

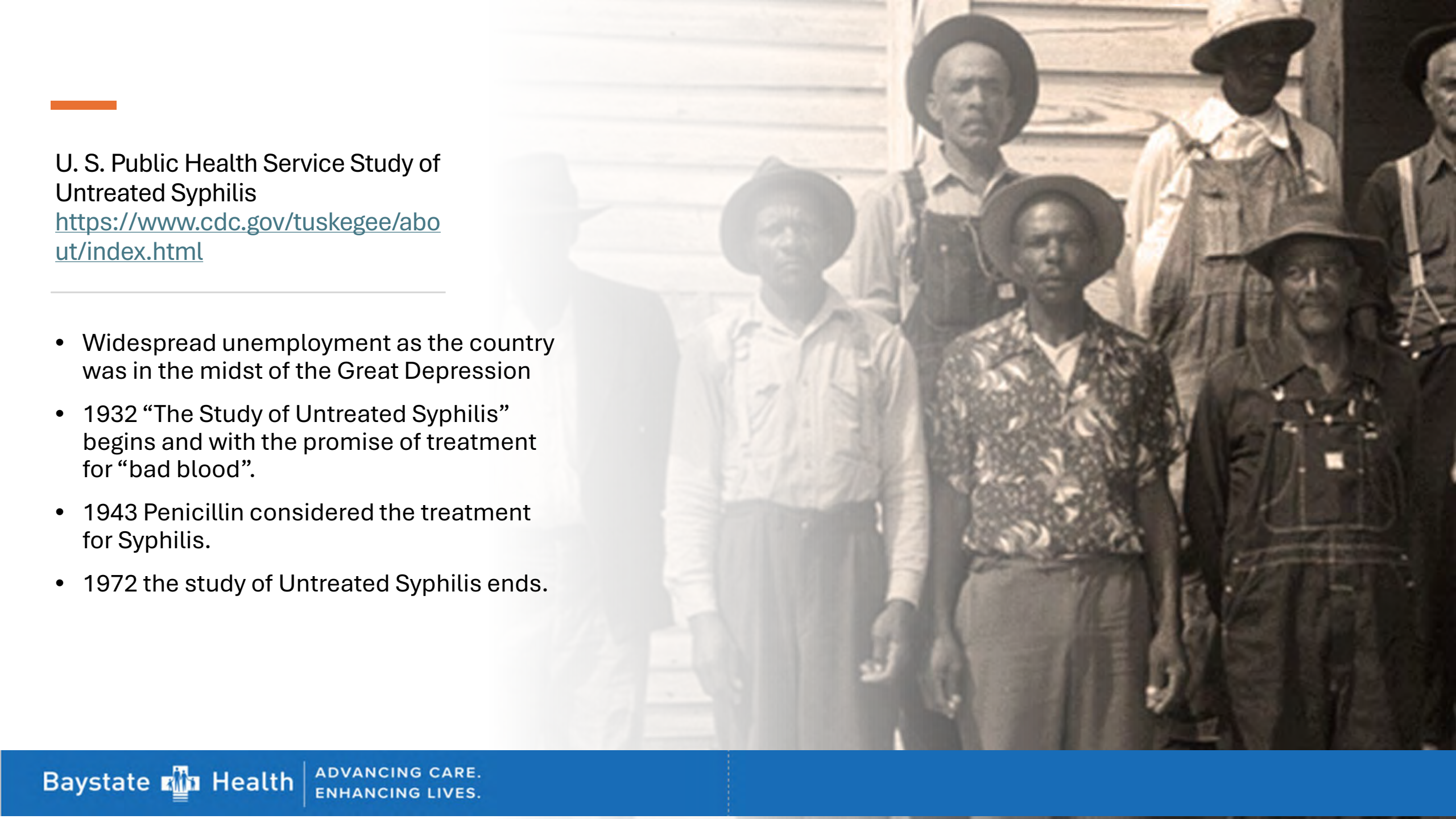


The 1930's through the 1970's



U. S. Public Health Service Study of Untreated Syphilis
https://www.cdc.gov/tuskegee/about/index.html

- Widespread unemployment as the country was in the midst of the Great Depression
- 1932 “The Study of Untreated Syphilis” begins and with the promise of treatment for “bad blood”.
- 1943 Penicillin considered the treatment for Syphilis.
- 1972 the study of Untreated Syphilis ends.



The Thalidomide Tragedy

- 1957 to 1962 the Thalidomide Tragedy
- Utilized Europe, Australia and Canada as well as the US.
- Over 10,000 births and unknown numbers of miscarriages attributed to the use of the drug.
- 1962- The drug was Drug banned in the US by President John F. Kennedy that's to the work of Dr. Frances Kelsey.



The Willowbrook School

- 1956 to 1980
- Families desperate for their child to be admitted to the Willowbrook School were informed that the child could receive better care if they were part of the Hepatitis Unit.



The National Research Service Award Act July 12, 1974

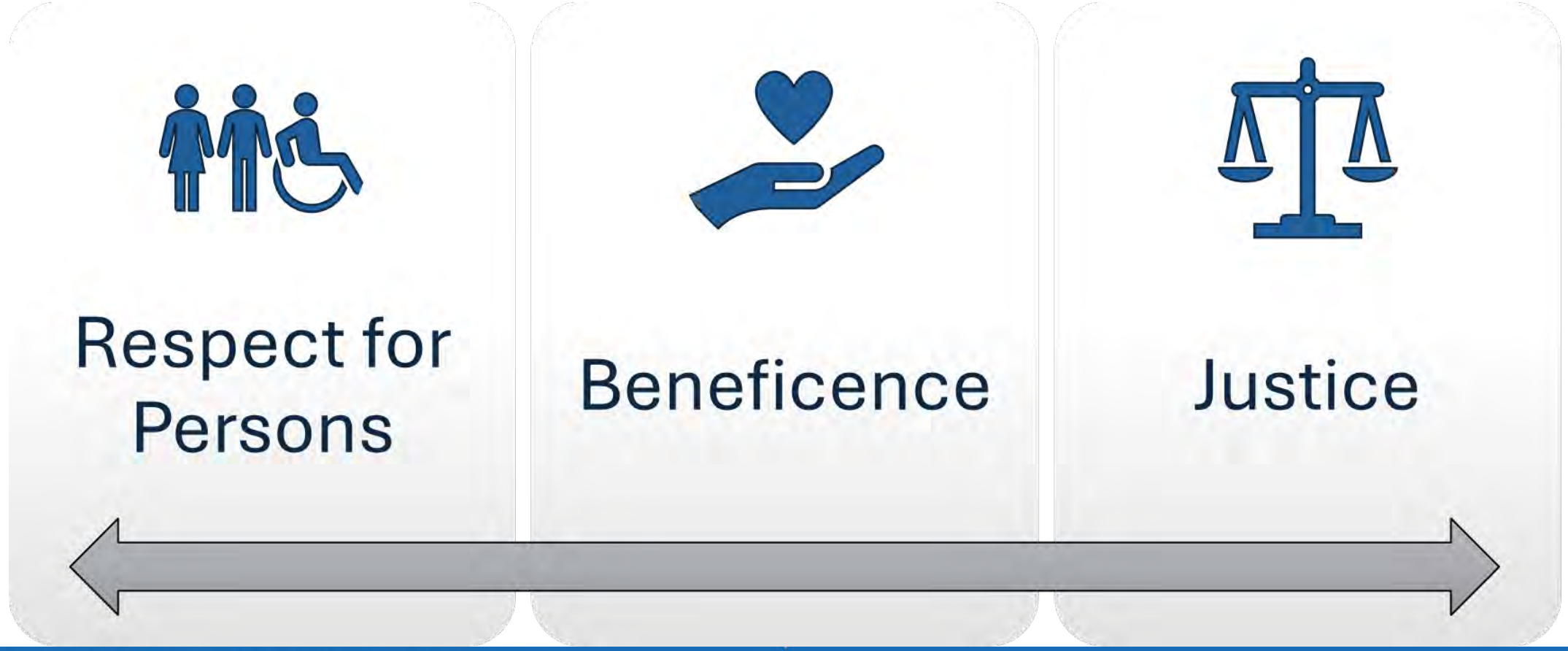


Title I – Biomedical and Behavioral Health Training



Title II - Protection of Human Subjects of Biomedical and Behavioral Research

The Belmont Report



Who is Responsible for Protecting Research Participants? It takes a village.



- Research Institutions
- IRB's
- Researchers
- OHRP
- OCR – Privacy Rule
- FDA
- Funding Organizations
- Individuals

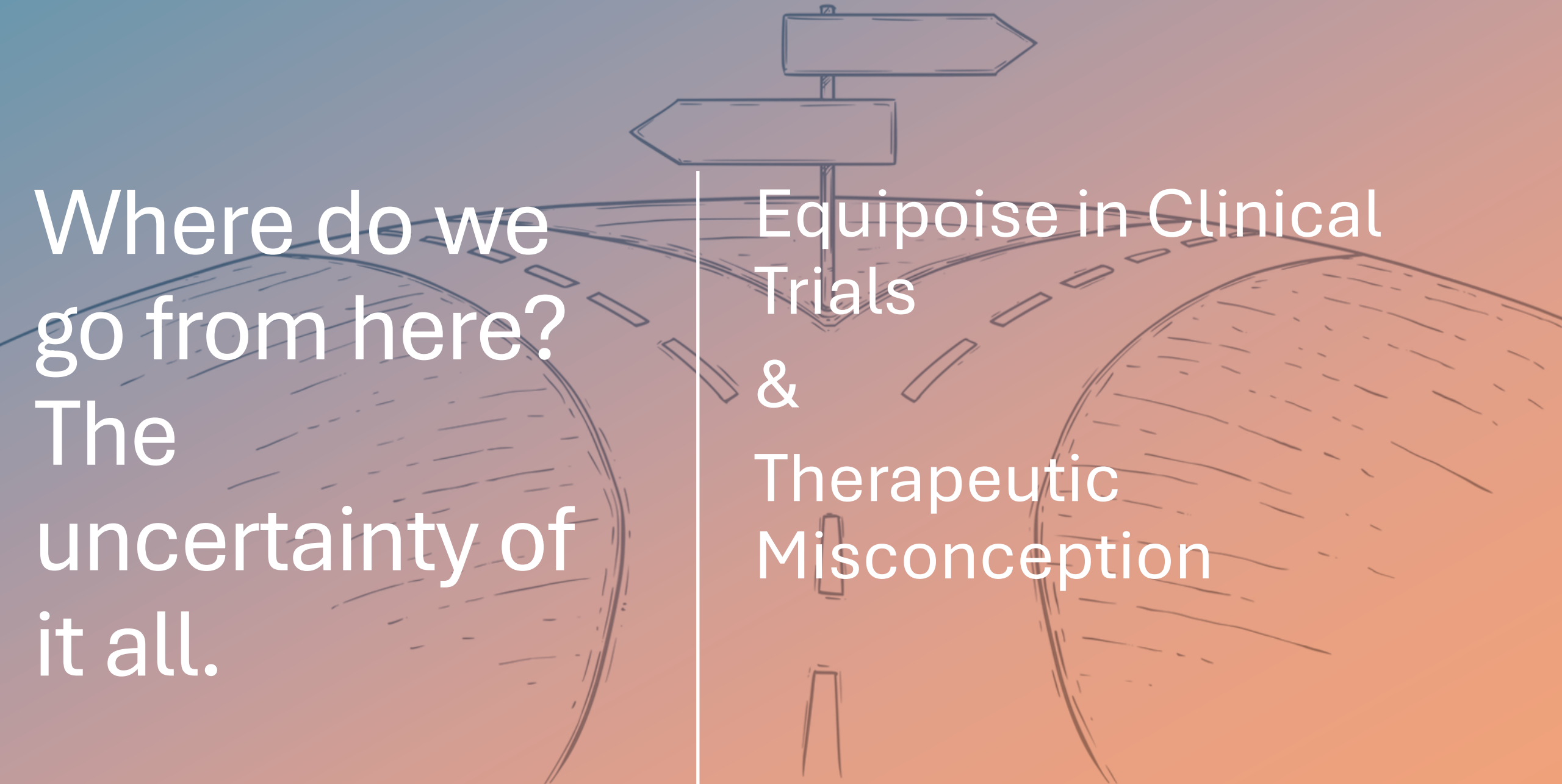
FDA and NIH Requirements



Continuing education of investigators, IRB members and staff as well as research staff.



Basic Biomedical and GCP training



Where do we go from here? The uncertainty of it all.

Equipoise in Clinical Trials

&

Therapeutic Misconception



Equipoise in Clinical Trials

Clinical equipoise is the state of genuine uncertainty by the investigator about the superiority of one treatment arm over the other, meaning that the participant is experiencing a fair distribution over the study's treatment arms. In case the investigator discovered that one treatment arm is superior to the other, an ethical obligation for providing the superior emerges.

Pimple KD, Research ethics. Routledge 2017

Community and Individual Equipoise

Community equipoise evaluates the uncertainty at the level of patients and advocacy groups. This definition relies on the notion by Freedman, that competent medical practice is social rather than individual in nature.

Karlawish JH, LantosJ. Community equipoise and the architecture of clinical research. Camb Q Health Ethics Volume 6, Issue 4, Fall 1997 pp. 385-396.

Djulbegovic B. The paradox of equipoise: the principle that drives and limits therapeutic discoveries in clinical research Cancer Control 2009, 16(4)





Managing Therapeutic Misconception in Clinical Research



Participants' Recent Comments

- "I had just been given my diagnosis. I was devastated. I was asked to participate [in the trial] very shortly thereafter. I just signed the forms; I signed everything in front of me - without thinking much about it."

- "It was an easy decision, a no-brainer: we would be receiving better care."

- "When you are given a chance to improve your odds, you say yes. You just agree. When you are fighting for your life, you do whatever it takes."

Defining Therapeutic Misconception

- TM occurs when a research subject fails to appreciate the distinction between the imperatives of clinical research and of ordinary treatment, and therefore inaccurately attributes therapeutic intent to research procedures.

- In other words, TM exists when individuals do not understand that the defining purpose of clinical research is to produce generalizable knowledge, regardless of whether the subjects enrolled in the trial may potentially benefit from the intervention under study or from other aspects of the clinical trial.

CW Lidz and PS Appelbaum, "The therapeutic misconception: problems and solutions," Medical Care 40, no. 9 (2002): V55-63.

GE Henderson et al., "Clinical trials and medical care: Defining the therapeutic misconception," PLoS Medicine 4, no. 11 (2007): 1735-38.

The Ethical Significance and Importance of Limiting Therapeutic Misconception

- Recognition that TM is potentially at play in the research context serves as a warning that informed consent, designed to protect human participants in research, may not fulfill its intended object when it is in place merely as a bureaucratic measure.

- Studies report that participants in clinical trials that included randomization, non-treatment control groups and placebos, and double-blind procedures were unaware of study design implications, especially random assignment to a control group, often believing that they were assigned a medication based on what was best for them personally.

PA Appelbaum et al., "Therapeutic misconception in research subjects: Development and validation of a measure," Clinical Trials 9, no. 6 (2012): 748-61.
GE Henderson et al., "Clinical trials and medical care: Defining the therapeutic misconception," PLoS Medicine 4, no. 11 (2007): 1735-38.
CW Lidz and PS Appelbaum, "The therapeutic misconception: problems and solutions," Medical Care 40, no. 9 (2002): V55-63.

Hope and Misconception in the Context of Clinical Research

- Hope is a complex topic, but there is a consensus that hope has a role in helping individuals to cope with existential challenges, including the ability of a research participant to cope with his or her life limiting disease.
- Hope seems problematic when it takes the form of self-deception.
- Where (unexamined or unarticulated) hope becomes the sole motive for entering into a study, it has the potential to feed into a serious misconception.
- This sort of “blind optimism” ought to be distinguished from a form of hope that results in a disposition not to despair and thus acts as a means of coping

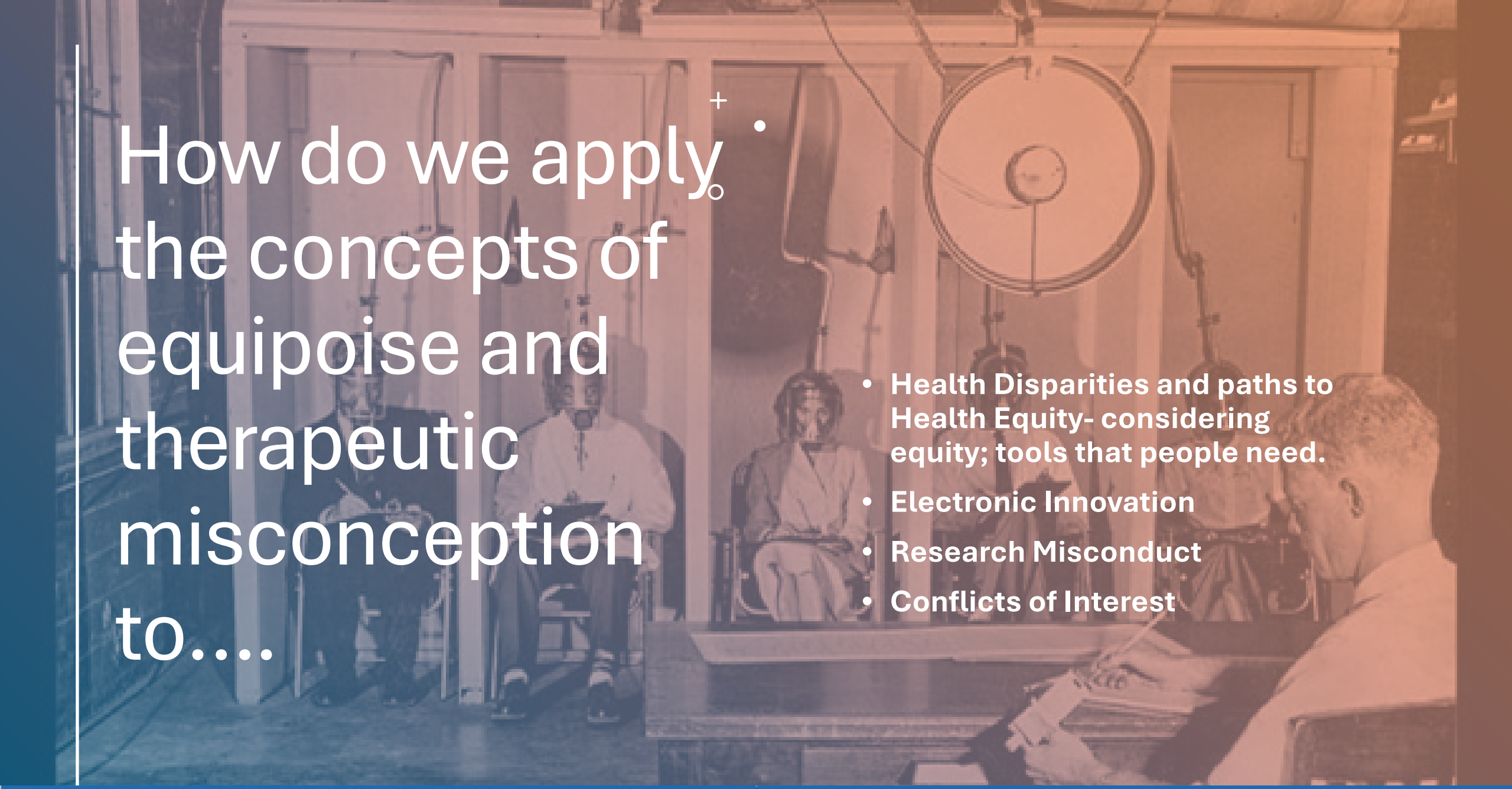


S Woods, LE Hagger, and P McCormack, “Therapeutic Misconception: Hope, Trust, and Misconception in Paediatric Research,” Health Care Annals 22 (2014): 3-21.

Strategies to Limit Therapeutic Misconception

Prior to Informed Consent:

- Subjects must understand not only how treatment and research differ, but also why.
  - Unless subjects understand in general terms the reasoning behind these design features, they are unlikely to be able to use the information to comprehend the research to which they are consenting.
- The role distinction between a treating physician and a research investigator must be explained in full.
  - In particular, it should be explained that these studies are done so that researchers (and medical science as a whole) can learn what works and what doesn't work, not for therapeutic reasons.
- The participant must be allowed personal time to reflect on the decision to enroll.
  - "Choices need time, the fullness of time, time being the horizontal axis of morality – you make a decision and then you wait and see, wait and see." – Z. Smith
  - "Time is what prevents everything from happening at once." – J. Wheeler



How do we apply the concepts of equipoise and therapeutic misconception to….

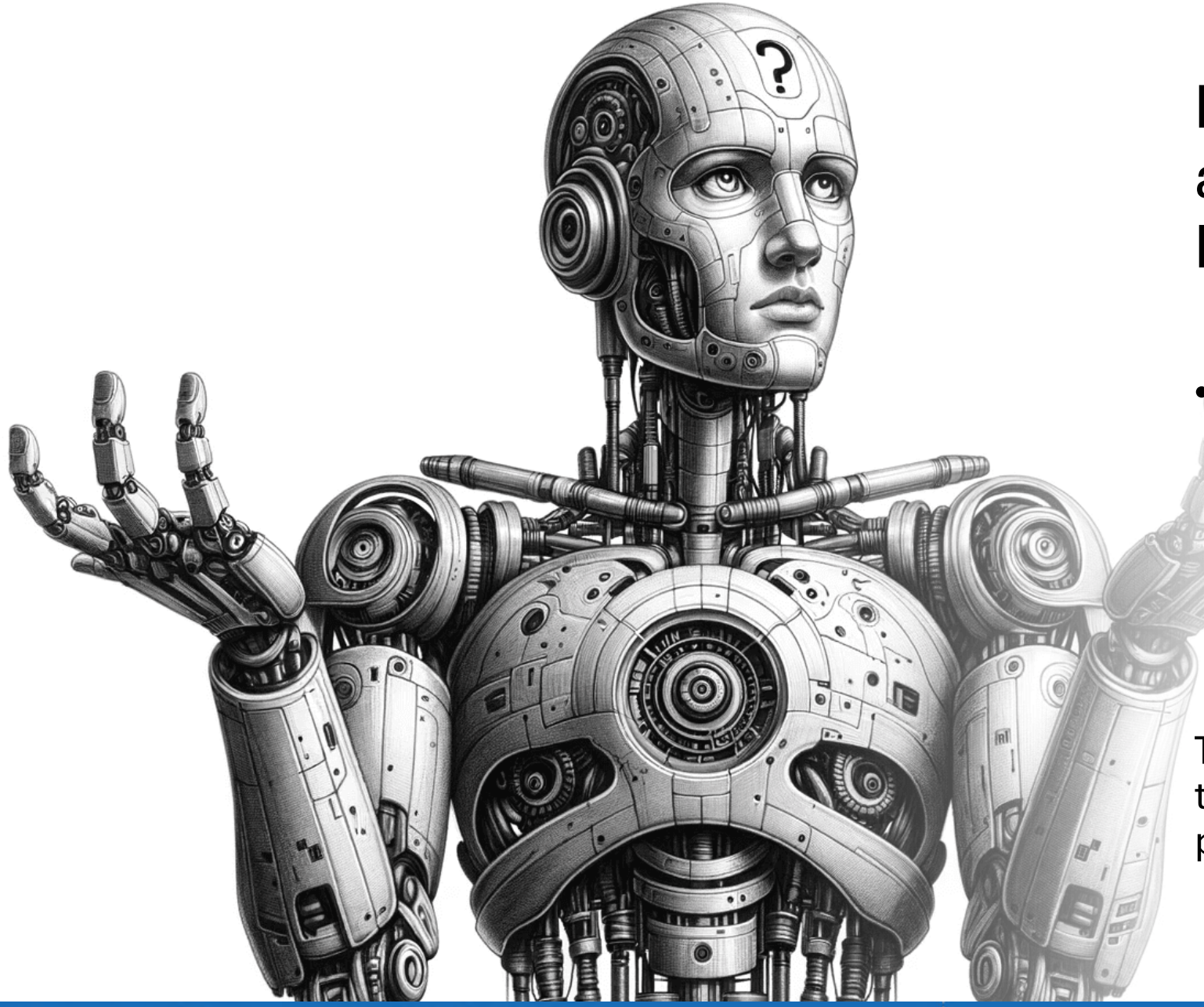
- **Health Disparities and paths to Health Equity- considering equity; tools that people need.**
- **Electronic Innovation**
- **Research Misconduct**
- **Conflicts of Interest**

Health Disparities

A recent analysis by the NIH Office of Disease Prevention found that fewer than 1 in 6 health prevention projects funded by NIH included a randomized intervention. Fewer than 1 in 25 included an intervention focused on minority health or health disparities.

Ashley J. Vargas, PhD, MPH, RDN; Sheri D. Schully, PhD; Jennifer Villani, PhD, MPH; Luis Ganoza Caballero,MD, MPH; David M. Murray, PhD, JAMA Network Open. 2019.2(11);e1914718





Electronic Innovation and Protecting Participant Privacy

- Artificial intelligence is software that learns by example. It is any human-made process or system that makes decisions or solves problems.

The question is does this technology protect participant privacy?

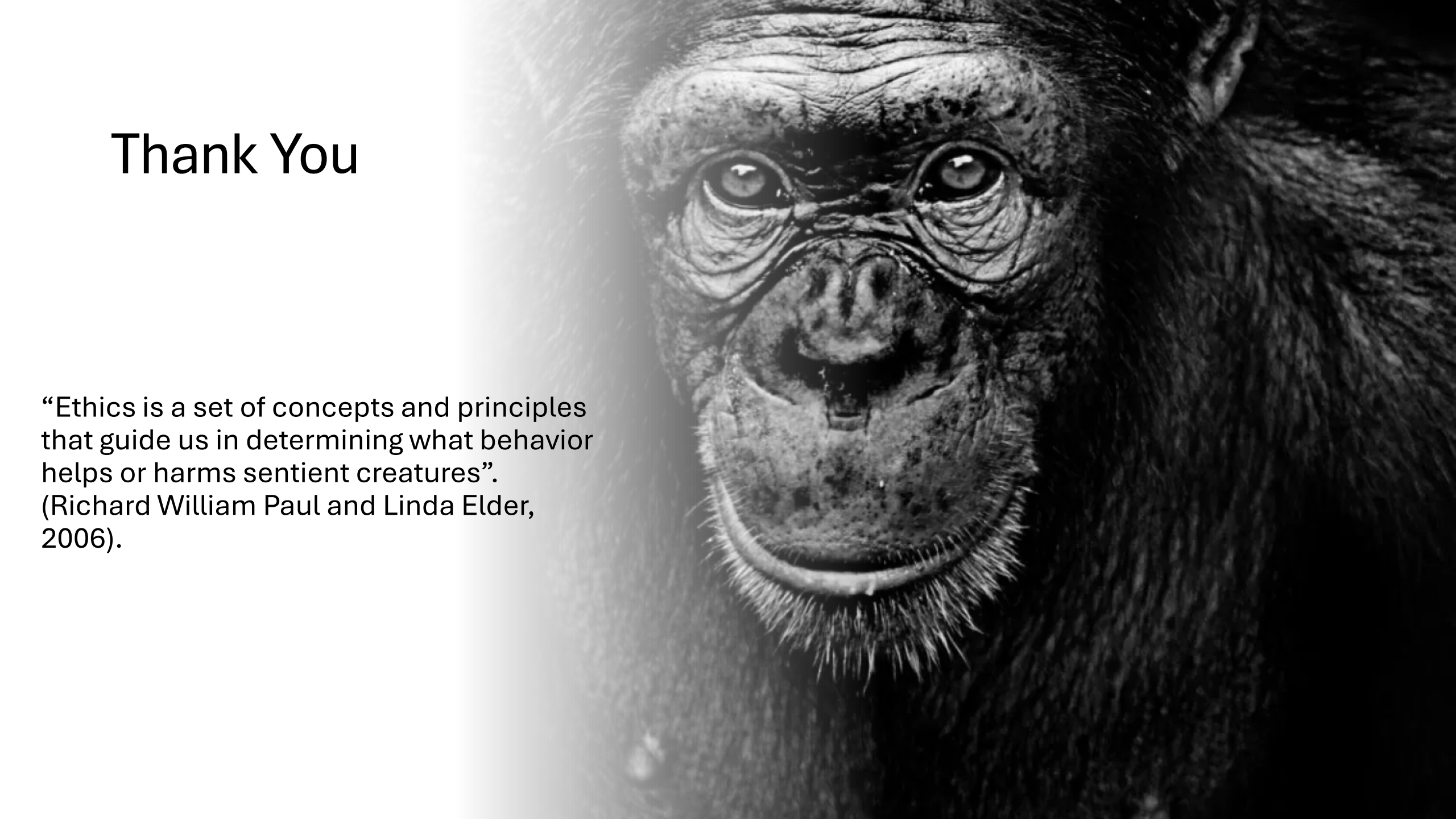


Research Misconduct and Conflicts of Interest

- Research Misconduct
- Conflicts of Interest

Thank You

“Ethics is a set of concepts and principles that guide us in determining what behavior helps or harms sentient creatures”. (Richard William Paul and Linda Elder, 2006).



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