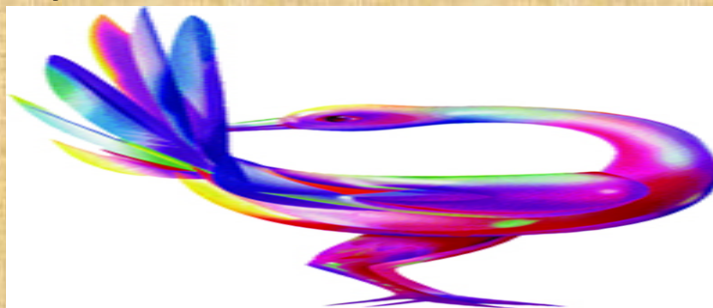




# A “New,” Yet, “Old” Normal For Research



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**iCURE Welcome Ceremony (Virtual)**

**NIH/NCI Center to Reduce Cancer Health Disparities**

**Bethesda, MD 20892**

**Wednesday, November 4, 2020**

**2:00 PM – 4:00 PM EST**



**This presentation is based on “Justice as fairness which has a central place in the VALUE of Community.”**



## National Center for Bioethics In Research And Health Care

- Justice, is according to John Rawls, “Each person possess: An inviolability founded on justice, that even the welfare of society as a whole cannot override. Therefore, in a just society the rights secured by justice are not subject to political bargaining or to the calculus of social interest.”



# Introduction:

- It is an undeniable fact that research involving human subjects can occasionally result in a dilemma for investigators.
- Invariably, when the goals of the research are designed to make major contributions to a field, such as maximizing (improving) the understanding of disease ( e.g. the United States Public Health Service Study of Untreated Syphilis in the Negro Male in Macon County, Alabama) or determining the efficacy of an intervention, investigators can perceive the outcomes of their studies to be more important than providing protections for individual human participants in the research/studies



# Introduction Continued:

While in general it is understandable to focus on research goals, the American society places great value on the rights and general welfare of individuals.

➤ Eminent philosopher John Rawls - in a scholarly work, "A Theory of Justice" (1971), asserted that

*"Each person possesses an inviolability founded on justice that even the welfare of society as a whole cannot override. Therefore, in a just society the rights secured by justice are not subject to political bargaining or to the calculus of social interests."*



# Introduction Continued:

- Inferentially, yet **ethical behavior, therefore is morally unacceptable, to use individuals solely** emphatically stated, in the U.S. society **it is not considered as means to an end.**
- This ethical prohibition is traceable to the German philosopher, Immanuel Kant, whose formulation of the second version of the Categorical Imperative states: “Act so that you treat humanity, whether in your own person or in that of another, always as an end and never as means only”.
- This Categorical Imperative of “respect for persons” is the universally accepted philosophical foundation of principles for the conduct of modern scientific research.
- The importance of unequivocally showing respect for research human participants is demonstrably reflected in the principles used to define ethical research and the various regulations, policies, and guidelines that describe the implementation of those principles.



# Objectives:

The objectives are designed to better inform investigators, physicians and other public health professionals involved in the design and/or conduct of research involving human subjects/participants and thereby enhancing their understanding of the obligations to protect the rights and welfare of subjects involved in research. Hence, upon completion of the presentation, the potential investigators should be able to:

- Demonstrate knowledge of the history and importance of human subjects' protections.
- Identify the risks a research project might pose to participants.
- Comprehend how to minimize the risks posed by a research project.
- Identify and describe additional protections needed for vulnerable populations.
- Overview of the U.S. Public Health Service Syphilis Study at Tuskegee



# Objectives Continued:

- Understand and describe appropriate procedures for recruiting human research participants and obtaining informed consent.
- Identify the different committees that monitor human subjects' protections.
- Identify research activities that involve human subjects.
- Demonstrate knowledge of historically important cases in the field of research ethics e.g., the notorious U.S. Public Health Service Study of Untreated Syphilis in the Negro Male in Macon County, Alabama.





# Brief History:

In order to understand and appreciate the system for the protection of human subjects in research as it currently exists, it is important to offer a short historical review of the events that have shaped or influenced current ethical guidelines and HHS regulations. Few will object to the claim that human subjects are essential to the conduct of research that has as one of its fundamental goals the improvement of human health.

Given this goal, it certainly seems reasonable to accept the suggestion that the relationship between researchers/investigators and human subjects should be predicated on:

- Honesty
- Trust
- Respect



# Brief History Continued:

## Nazi Medical War Crimes (1939-1945)

The Nuremburg Code was drawn up in 1946 as part of the judgment against physicians who conducted medical experiments on humans in Nazi concentration camps. The experiments conducted by Nazi physicians during World War II were, by all measure, unprecedented in their scope and the degree of harm and human suffering.

The Nuremburg Military Tribunal found the defendants to have:

- Corrupted the ethics of the medical and scientific professions.
- Repeatedly and deliberately violated the rights of the subjects.

Significantly, the actions of these criminal defendants were condemned as crimes against humanity.



# Brief History Continued:

## Declaration of Helsinki

In 1964, the World Medical Association (WMA) adopted the Declaration of Helsinki, which added three important points to the Nuremberg Code:

- Distinction between therapeutic research and non-therapeutic research. The aim of therapeutic research is to benefit patients; the aim of non-therapeutic research is not to benefit patients but to generate scientific knowledge.
- An institutional mechanism should be in place to ensure that the main ethical principles were faithfully followed.
- The provision for proxy consent by family members when human subjects such as children could not consent on their own.



# Brief History Continued:

## 2. Radiation Experiments (1944-1974)

- ❖ The federal government funded a series of radiation experiments including the injection of plutonium into unsuspecting hospital patients as well as the intentional release of radiation into the environment for research purposes.
- ❖ Some were conducted to advance biomedical science, while others related to national interest in defense or space exploration. Most of the human experiments involved radioactive tracers administered in amounts similar to those used in research today.
- ❖ Moreover, in several studies, patients died shortly after receiving external radiation or radioisotope doses in the therapeutic range that were associated with acute radiation affects.
- ❖ During this period, physicians typically used patients as subjects in radiation experiments without the patients' informed consent. Scant to no attention, was paid to concerns regarding fairness in selection of subjects. Furthermore, information about the radiation experiments was intentionally kept secret.



# Brief History Continued:

## 3. Jewish Chronic Disease Hospital (1963)

- ❖ This study, partially funded by the Public Health Service/NIH and Sloan-Kettering Cancer Research Institute, involved injection of live cancer cells into indigent, chronically ill, and deliberately elderly patients at the Brooklyn Jewish Chronic Disease Hospital in New York.

## 4. Willowbrook (1956 – 1971)

- ❖ This study was led by Dr. Krugman, and infectious disease researcher at the Willowbrook State School, a New York State institution for “mentally defective persons.”
- ❖ The purpose of the study was to better understand the natural history of hepatitis and the effects of gamma globulin in preventing or moderating its effects. The subjects were deliberately infected with the virus.

In early studies they were fed extracts of stools from infected children, while later subjects received injections or more purified virus preparations.

- ❖ As a result, Krugman’s research established the distinctive features of Hepatitis A and B.



# Brief History Continued:

## Belmont Report

Given these abuses in experiments/studies involving human subjects, the United States Congress established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission issued the Belmont Report in 1979; the Report identified respect for persons as autonomous agents, beneficence, and justice as absolutely essential and necessary principles for any research to be ethically justified.

The principle of respect for persons led to the requirement of informed consent. It is diagrammatically represented thusly:

- Respect for Persons (RP)                      Informed Consent (IC)



# Brief History Continued:

## Belmont Report Continued:

The principle of beneficence led to the requirement of a favorable risk-benefit ratio. This is diagrammatically represented as:

Principle of Beneficence (PB)

Favorable risk-benefit ratio (FRBR)

The principle of justice led to the requirements of an equitable selection of research subjects and a fair distribution of risk among them. This development

may be diagrammatically represented as follows:

PJ

ESRS & FDR

Thus, to be ethical, all medical research on humans must conform to the requirements enunciated above.



# Brief History Continued:

## Design of Clinical Trials

Generally, five conditions must be met for clinical trials to be ethically acceptable:

1. Voluntary informed consent must be obtained from subjects
  2. The research must involved a favorable benefit-risk ratio
  3. There must be an equitable selection of subjects that eliminates any exploitation and adequately represents both sexes and all social groups
  4. The privacy of the subjects must be protected
  5. The confidentiality of the data yielded by the research must be protected.
- Independent review boards (IRB) have the authority and responsibility to monitor research protocols to ensure that these conditions are met.





# Brief History Continued:

## Respect for Persons

The principle of respect for persons can be divided into two basic ideas:

- 1) individuals should be treated as autonomous agents (Kant's position); and
- 2) persons with diminished autonomy are entitled to additional protections.

Challenges in the application of the Belmont principle of respect for persons are

in:

- ensuring that potential participants comprehend the risks and potential benefits of participating in research.
- avoiding influencing potential human participants' decisions either through explicit or implied threats (coercion) or through excessive compensation (undue influence).



# Brief History Continued:

## Beneficence

The term beneficence is, understood according to the Belmont Report, to cover acts of kindness or charity that go beyond strict obligation. An act qualifies as a beneficent act when one makes every effort to secure the well-being of others.

Two general rules have been articulated as complimentary expressions of beneficent actions:

1. do no harm (*Non nocere*); and
2. maximize possible benefits and minimize possible harms.

Risk is an essential element in the analysis of the principle of beneficence under the Belmont Report/Principle. The Belmont definition of risk is the “probability that a certain harm will occur.” Every research involving human participants is fraught with some level of risk.

Most risks encountered by participants in research can be categorized into the following types:

- Physical
- Psychological
- Social
- Legal
- Economic



# Brief History Continued:

## Privacy and Confidentiality

Investigators are responsible for

- Protecting privacy of individuals
- Confidentiality of data

Definitions:

- ✓ Privacy means being “free from unsanctioned intrusion.”
- ✓ Confidentiality can be defined as holding secret all information relating to an individual, unless the individual gives consent permitting disclosure.



# Brief History Continued:

## Institutional Review Boards (IRB)

IRBs are specialized committees required by HHS regulations that safeguard the rights and welfare of human subjects.

IRBs determine “the acceptability of proposed research in terms of institutional

commitments and regulations, applicable law, and standards of professional conduct and practice (45CFR 469.107).”



# Brief History Continued:

The major roles of IRBs in the oversight of research are:

- Initial review and approval or disapproval of proposed research activity
- Ensuring that the proposed informed consent process meets all of the requirements of 45 CFR 46.116
- Providing continuing oversight for progress reports and protocols for ongoing research studies.

IRBs and investigators have a shared responsibility to ensure that research participant protections are appropriate.

For certain types of research involving no more than minimal risk for minor changes to existing research an IRB may choose to use an expedited review procedure.



# Brief History Continued:

## Additional Protections

Under the Belmont principle of respect for persons, individuals with diminished autonomy may need additional protections.

- ✓ Additional Protections are extended to Pregnant Women, Human Fetuses, and Neonates involved in Research.
- ✓ Prisoners, as human subjects, are also given additional protections.
- ✓ Children involved in research are equally given additional protections.

The above named subjects may be considered vulnerable populations.

The fundamental challenge one encounters in applying the Belmont principle of beneficence is how to determine when potential benefits outweigh considerations of risks and vice versa.



# Brief History Continued:

## Justice

The Belmont Report states:

“Just as the principle of respect for persons finds expression in the requirement for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects.”

- Justice requires that individuals and groups be treated fairly and equitably in terms of bearing burdens and receiving the benefits of research.
- The issue of the principle of justice may emanate from decisions about the criteria for inclusion and exclusion relative to participation in research involving humans.
- Under the rubric of justice, the challenge of applying the Belmont principle of justice is how investigators should decide which criteria should be employed to ensure that harms and benefits of research are fairly and equitably distributed to individuals and populations.
  - 45CFR46 codifies these basic principles.



# Brief History Continued:

## Important Well-Known Cases

### 1. The United States Public Health Service Study of Untreated Syphilis in the Negro Male in Macon County, Alabama

- ❖ In 1932, the United States Public Health Service (USPHS) initiated the Tuskegee Syphilis Study to document the natural history of syphilis.
- ❖ The federal government physicians conducting the Study engaged in willful deception by telling the men that they were being treated for “bad blood” and that the “spinal tap procedures” were “treatment” for it.
- ❖ The men were recruited without the all-important ethical requirement of informed consent; they deliberately denied treatment to the syphilis; and extreme measures were taken to ensure that they would not receive therapy or treatment from any other sources.
- ❖ This infamous Study has come to symbolize racism in medicine, ethical misconduct in research involving humans, paternalism by physicians and government abuse of vulnerable populations.



# “U.S. Public Health Service Syphilis Study at Tuskegee” 1932-1972

• Characterized by:

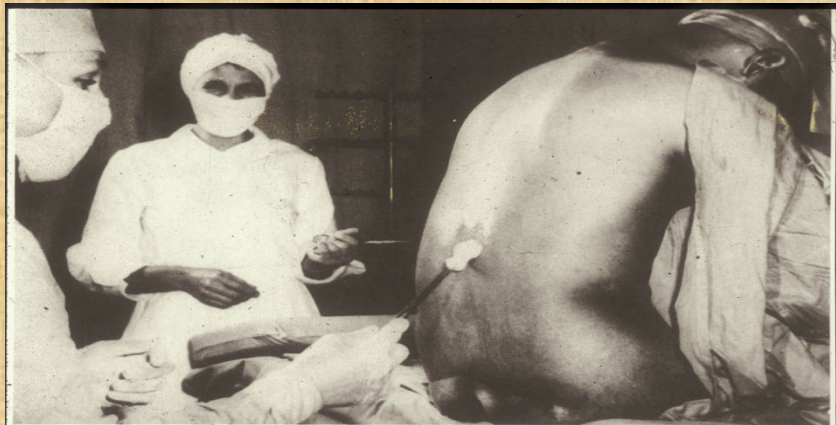
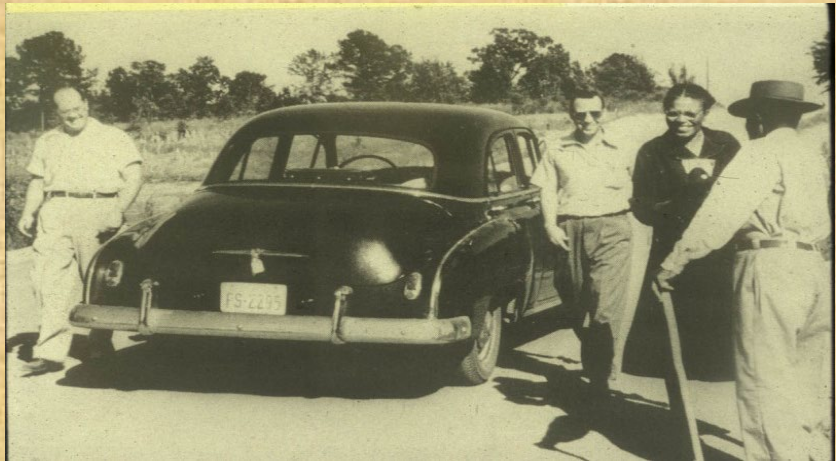
1. Withholding of therapy

2. Cultural sensitivity

3. Deception

4. Exploitation

5. Apology



Spinal tap, 1933. From left: Jesse J. Peters, Nurse Rivers, and unidentified subject. (Center for Disease Control, Atlanta, Ga.)

# The Presidential Apology



In the 1997 Presidential Apology for the U.S. Public Health Service Syphilis Study at Tuskegee, William Jefferson Clinton said, “The United States government did something that was wrong – deeply, profoundly, morally wrong.”



# Salient Language To Discuss Ethical Discourse



# Ethics

- What is ethics?
  - A set of rules, principles, values, and ideals of a particular group of people. The systematic study of morals, concepts, and theories, typically in departments of philosophy.



# Bioethics

- Applied ethics focusing on doctor-patient relationships and how changes in the health care system affect it.



# Public Health Ethics

- Public health strives to improve the quality functioning and longevity of populations. Because public health is viewed, by some very broadly, public health ethics assumes an equally broad conceptual base. Public health ethics places emphasis on the ethical problematic related to interests and health of groups, the social justice of the distribution of social resources, and the positive or social rights of individual. The study of public health ethics requires the practitioner to effectively conceptualize and operate between the tension of individual rights and collective interest. As with public health, it also seeks to resolve the ethical problematic most efficaciously.

Bayer R & Beauchamp, DE. *Public Health Ethics: Theory, policy and practice*. New York: Oxford University Press. 2007.

Bayer R & Beauchamp, DE. *Public Health Ethics: Theory, policy and practice*. New York: Oxford University Press. 2007.

Callahan, D & Jennings, B. Ethics and Public Health: Forging a Strong Relationship. *American Journal of Public Health* 92: 2002, 169-176



# Health Disparities (Inequalities)

- Systematic, potentially avoidable differences in health—or in the major socially determined influences on health—between groups of people who have different relative positions in social hierarchies according to wealth, power, or prestige.



# Health Equity

- Ideally, everyone should have a fair opportunity to attain their full health potential and more pragmatically that no one should be disadvantaged from achieving this full potential if it can be avoided.





# Optimal Health

- The best possible emotional, intellectual, physical, spiritual, and socio-economic aliveness that we can attain.

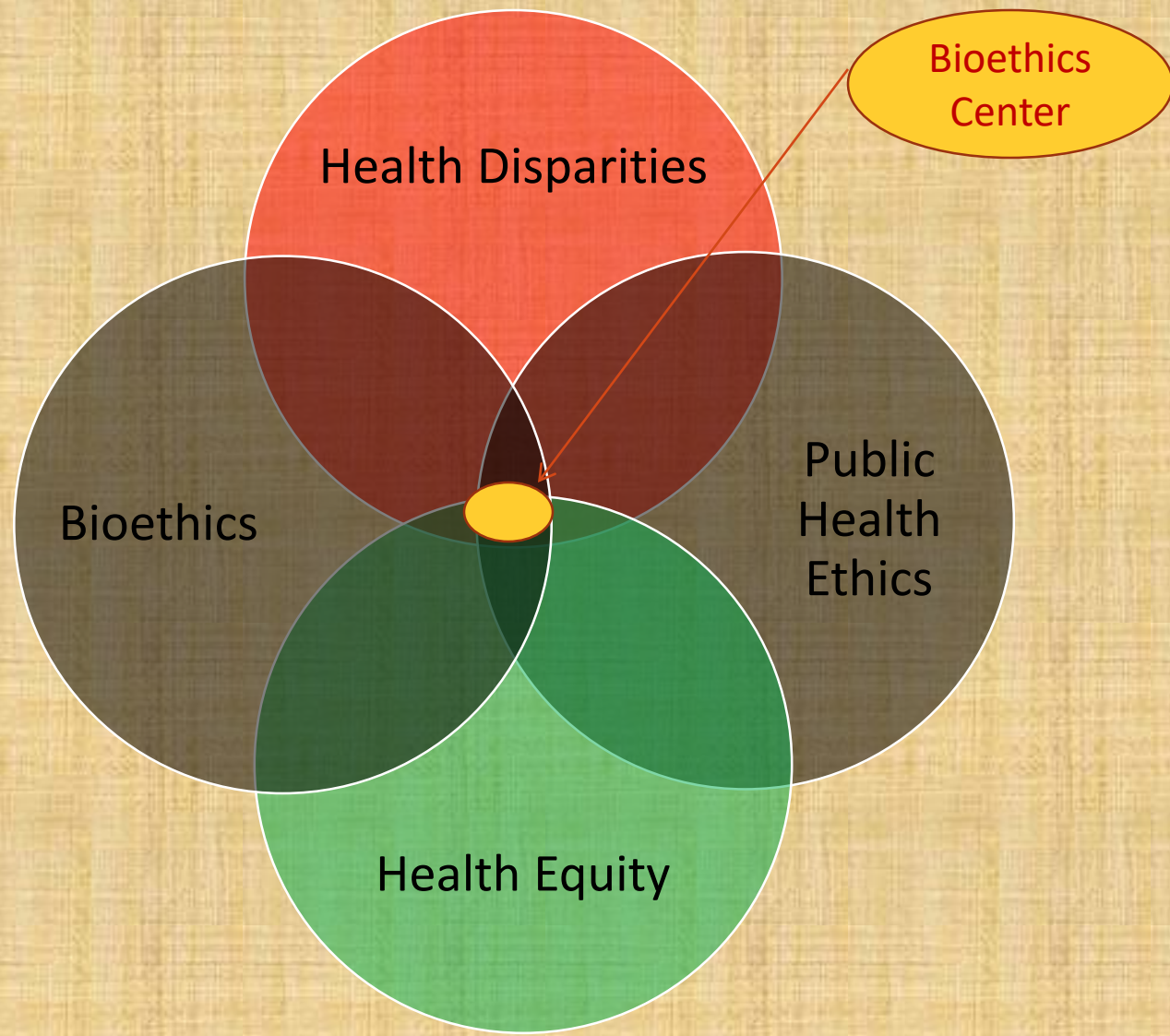


# Domains of Optimal Health

- Optimal Intellectual Health
- Optimal Emotional Health
- Optimal Physical Health
- Optimal Spiritual Health
- Optimal Socio-economic Health



# Venn Diagram





National Center for Bioethics In Research And Health Care



*We must know enough, care  
enough, do enough to make  
a change"*

*..... Dr. David Satcher*

*16<sup>th</sup> US. Surgeon General*



# In Honor of Dr. Maya Angelou

- “History, despite its wrenching pain, cannot be unlived, but if faced with courage need not be lived again”
- .....Dr. Maya Angelou,
- “On the Pulse of Morning”

**Birth Date:** April 4, 1928

**Death Date:** May 28, 2014





# Thank You

San means: *to return*      ko means: *to go*      fa means: *to look, to seek and take*

**NOTICE:** The Sankofa Bird has sought its past trail to take back what was lost, in order to protect its future!

## ***The Meaning of Sankofa***

*Sankofa literally means to go back and get what was taken. After the term made its way to the United States, African-American scholars coin the term to mean “remembering our past, to protect our future” within the African-American culture.*



**SANKOFA  
BIRD**