The Belmont Report & Human Subjects Research

2023-12-01

Learning Objectives

1. Name and understand the three basic ethical principles in the Belmont Report
2. Apply the principles of the Belmont Report to case studies

Historical Context (20th c. Research Ethics)

- Tuskegee Syphilis Study (1932-1972)
- Nuremberg Code (1948)
- Declaration of Helsinki (1964)
- USA National Research Act (1974)

Tuskegee Syphilis Study [1]

- United States Public Health Service (USPHS) & the Tuskegee Institute
- Aimed to study natural history of syphilis
- Started in 1932
- Enrolled 600 Black men (399 with syphilis, 201 without)
- No informed consent
- Researchers told men that they were being treated for "bad blood" (a term that included syphilis, anemia, and fatigue)
- Men received free medical exams, meals, and burial insurance

[1] https://www.cdc.gov/tuskegee/timeline.htm

Tuskegee Syphilis Study [2]

- By 1943, penicillin was the standard treatment for syphilis & was becoming widely available
- Study participants were not offered treatment
- 1972 Associated Press story broke the news
- Ad Hoc Advisory Panel reviewed the study:
  - ethically unjustified
  - "results were disproportionately meager compared to known risks to human subjects involved"
- Study ended in late 1972

[2] https://www.cdc.gov/tuskegee/timeline.htm

Tuskegee Syphilis Study [4]

- 1973: Panel advised that study survivors be given all necessary medical care
- Tuskegee Health Benefit Program established
- 1975: participants' wives, widows, and children added
- 1995: program expanded to include health as well as medical benefits
- 1997: President Clinton apologized on behalf of the nation [3]
- 2004: last study participant died
- 2009: last widow reveiving THBP benefits died
- Participants' children continue to receive medicacl and health benefits

[3] https://clintonwhitehouse4.archives.gov/textonly/New/Remarks/Fri/19970516-898.html

[4] https://www.cdc.gov/tuskegee/timeline.htm

Tuskegee Syphilis Study [5]

- 128 participants died of syphilis or related complications
- 40 wives were infected
- 19 children were born with congenital syphilis

[5] https://eji.org/news/history-racial-injustice-tuskegee-syphilis-experiment/#:~:text=The%20money%20funded%20medical%20care,also%20suffered%

Tuskegee Syphilis Study [6]

[6] https://en.wikipedia.org/wiki/Tuskegee_Syphilis_Study

Tuskegee Syphilis Study [7]

- Blood draw, circa 1953

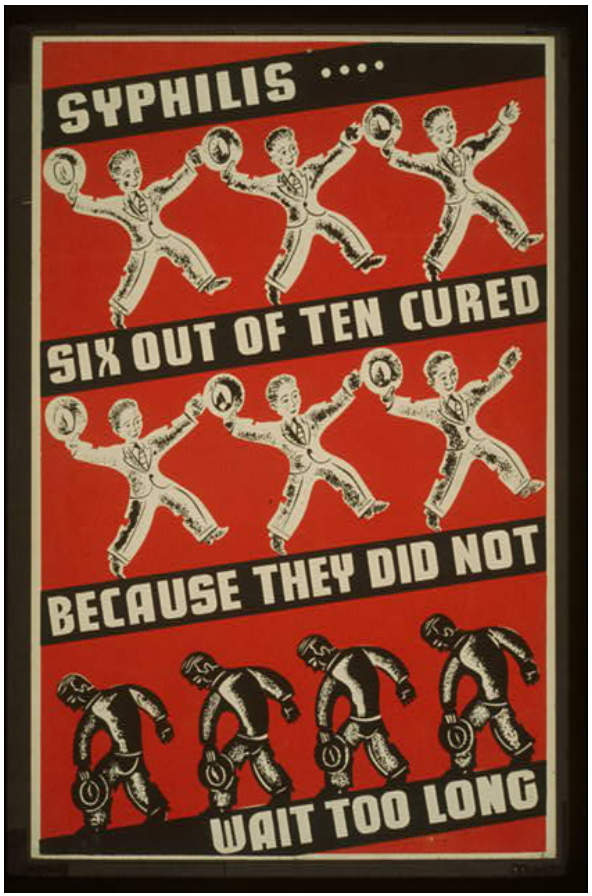
[7] https://en.wikipedia.org/wiki/Tuskegee_Syphilis_Study

Tuskegee Syphilis Study [8]

- circa 1970

[8] https://en.wikipedia.org/wiki/Tuskegee_Syphilis_Study

Tuskegee Syphilis Study [9]



- WPA poster promoting syphilis testing and treatment
- WPA ended in 1943

[9] https://en.wikipedia.org/wiki/Tuskegee_Syphilis_Study

Tuskegee Syphilis Study [10]

- Peter Buxtun, PHS venereal disease investigator, whistleblower

[10] https://en.wikipedia.org/wiki/Tuskegee_Syphilis_Study

Tuskegee Syphilis Study [11]

- Charlie Pollard, study survivor

[11] https://en.wikipedia.org/wiki/Tuskegee_Syphilis_Study

Tuskegee Syphilis Study [12]

- Herman Shaw was one of the last surviving participants in the study.

[12] https://en.wikipedia.org/wiki/Tuskegee_Syphilis_Study

Tuskegee Syphilis Study [13]

6—THE ARGUS-PRESS, Owosso, Mich., Tues., July 25, 1972

Public Health Service Study

Human Guinea Pigs Allowed to Die of Syphilis

WASHINGTON (AP) — For 40 years the U S. Public Health Service has conducted a study in which human guinea pigs, denied proper medical treatment, have died of syphilis and its side effects.

The study was conducted to determine from autopsies what the disease does to the human body.

PHS officials responsible for initiating the experiment have long since retired. Current PHS officials, who say they have serious doubts about the morality of the study, also say it's too late to treat syphilis in any of the study's surviving participants.

But PHS doctors say they are rendering whatever other medical services they now can give to the survivors while the study of the disease's effects continues.

The experiment, called the Tuskegee Study, began in 1932 with about 600 Black men, mostly poor and uneducated, from Tuskegee, Ala., an area which had the highest syphilis rate in the nation at the time.

One-third of the group was free of syphilis; two-thirds showed evidence of the disease. In the syphilitic group, half were given the best treatment known at the time, but the other half, about 200 men, received no treatment at all for syphilis, PHS officials say.

As incentives to enter the program, the men were promised free transportation to and from hospitals, free hot lunches, free medicine for any disease other than syphilis and free burial after autopsies were performed.

The Tuskegee Study began 10 years before penicillin was discovered to be a cure for syphilis and 15 years before the drug became widely available. Yet even after penicillin became common, and while its use probably could have helped or saved a number of the experiment subjects, the drug was denied them, according to Dr. J.D. Millar.

He is chief of the venereal disease branch of the PHS' Center for Disease Control in Atlanta and is now in charge of what remains of the Tuskegee Study. Dr. Millar said in an interview he has serious doubts about the program.

"I think a definite moral problem existed when the study was undertaken, a more serious moral problem was overlooked in the post-war years when penicillin became available but was not given to these men, and a moral problem still exists," Dr. Millar said.

"But the study began when attitudes were much different on treatment and experimentation. At this point in time, with our current knowledge of treatment and the disease and the revolutionary change in approach to human experimentation, I don't believe the program would be undertaken," he said.

Syphilis, a highly contagious infection spread by sexual contact, can cause, if untreated, bone and dental deformations, deafness, blindness, heart disease and central nervous system deterioration.

No figures were available on when the last death occurred in the program. And one official said that apparently no conscious effort to halt the program was made after it got under way.

A 1969 CDC study of 276 treated and untreated syphilitics who participated in the Tuskegee Study showed that seven had died as a direct result of syphilis. Another 154 died of heart disease. CDC officials says they cannot determine at this late date how many of the heart disease deaths were caused by spyhilis or how many additional deaths could be linked to the disease.

However, several years ago an American Medical Association study determined that untreated syphilis reduces life expectancy by 17 per cent in black men between the ages of 25 and 50, a precise description of the Tuskegee Study subjects.

Don Prince, another official in the venereal disease branch of CDC, said the Tuskegee Study had contributed some knowledge about syphilis, particularly that the morbidity and mortality rate among untreated syphilitics was not as high as previously believed.

Like Dr. Millar, Prince said he believes the study should have been concluded with penicillin treatment after World War II.

"I don't know why the decision was made in 1946 not to stop the program," Prince said. "I was unpleasantly surprised when I first came here and found out about it."

At the beginning of 1972, according to CDC data, 74 of the untreated syphilitics were still living. All of them, Dr. Millar said, were men who did not suffer any potentially fatal side effects from their bouts with the disease.

Some of them received penicillin and antibiotics in past years for other ailments, Prince said, but none has ever received treatment for syphilis. Now, both men agree, it's too late.

Recent reviews of the Tuskegee Study by CDC indicate that treatment now for survivors is medically questionable, Dr. Millar said. Their average age is 74 and massive penicillin therapy, with possible ill side effects, is deemed too great a risk to the individuals, particularly for those whose syphilis is now dormant.

However, Dr. Millar added, there was a point in time when survivors could have been treated with at least some measure of success.

"The most critical moral issue about this experiment arises in the post-war era, the years after the end of World War II when penicillin became widely available.

"I know some were treated with penicillin for other diseases and then dropped from the program because the drug had some positive effect on the primary disease (syphilis). Looking at it now, one cannot see any reason they could not have been treated at that time.

[13] https://bpb-us-e1.wpmucdn.com/sites.lib.jmu.edu/dist/c/332/files/2016/12/human-guinne-pigs.png

Belmont Report (1978)

Three Principles of the Belmont Report

1. Respect for Persons
2. Beneficence
3. Justice

Respect for Persons [14]

- Protecting the autonomy of all people and treating them with courtesy and respect and allowing for informed consent. Researchers must be truthful and conduct no deception (integrity)

[14] https://en.wikipedia.org/wiki/Belmont_Report

Beneficence [15]

- The philosophy of "Do no harm" while maximizing benefits for the research project and minimizing risks to the research subjects

[15] https://en.wikipedia.org/wiki/Belmont_Report

Justice [16]

- Ensuring reasonable, non-exploitative, and well-considered procedures are administered fairly — the fair distribution of costs and benefits to potential research participants — and equally

[16] https://en.wikipedia.org/wiki/Belmont_Report

Case Studies

Case Studies [17]

- For each case study, consider the extent to which the study meets or does not meet the three ethical principles of the Belmont Report

[17] https://www.nwabr.org/sites/default/files/2Belmont_Principles_HinR_1.pdf

Case Study Number 1: Saving Lives in a Heartbeat? [18]

In cardiac arrest (heart attack) cases, it is critical to control and monitor body temperature. To increase the likelihood of survival, hospitals will quickly place the victim in an ice bath to produce hypothermia (a lowering of core body temperature), then gradually raise the body temperature. To ensure that the most accurate temperature is being recorded, researchers would like to perform a study on cardiac arrest patients in the emergency room at the county hospital. Temperatures will be taken using different methods for different patients, comparing results from forehead or fingertip thermometers to those from standard oral thermometers, to see which consistently offers the most accurate temperature reading. Because cardiac arrest patients are often unconscious upon arrival, and because the temperature reading must occur very quickly, the researchers would like to do the following:

1. If possible, speak to the next of kin to gain permission to enroll their family member in the study.
2. If next of kin cannot be located, record the patient's temperature, and then obtain permission to use the data once the next of kin arrive or after the patient regains consciousness (the data can be discarded if consent is not obtained).
3. If the next of kin or patient does not speak English, exclude them from the study (translators are difficult to obtain quickly).

Can the study proceed, obtaining informed consent as described?

[18] https://www.nwabr.org/sites/default/files/2Belmont_Principles_HinR_1.pdf

Case Study Number 2: A Gamble Worth Making? [19]

Aggressive cancers can take a person's life in as little as three to six months. An experimental procedure called interleukin therapy is currently being studied in a clinical trial. In 7% of cases, the treatment has been highly effective. In one such case, a man with breast, kidney, and lung cancers with very little hope for survival agreed to participate to receive the experimental therapy. The experimental therapy effectively treated the tumors, and he has been cancer-free for five years. Unfortunately, the treatment has no effect for many people, and there is also a large risk involved: in some trials, the patients suffered immediate cardiac failure.

A woman diagnosed with aggressive cancer, who doctors estimate will live another six months, is interested in pursuing this therapy. In an intense informed consent process over a two-week period, she and her husband are given all the scientific background, the pros and cons, the risks and benefits, and more. After the informed consent process, the woman would like to pursue the treatment, but her husband is against it. The couple is from a cultural background in which the man of the family makes all of the important decisions and this couple is faithful to their cultural traditions.

Should researchers enroll this woman in the study to receive the experimental therapy?

[19] https://www.nwabr.org/sites/default/files/2Belmont_Principles_HinR_1.pdf

Case Study Number 3: Better Than Nothing? [20]

Researchers want to test the effectiveness of a new formulation of insulin that will allow patients with diabetes to take a pill with every meal instead of injecting themselves with liquid insulin three times a day. Liquid insulin must be kept refrigerated, the injections can be painful, and sterile syringes have to be purchased regularly. With the insulin pill (which has an estimated future cost of $5.00 a day for people with insurance), diabetics would be free of these burdens. Researchers discover that in a small, isolated, rural community, diabetes affects 45% of the residents (compared to 8.3% of the general population), and decide to run clinical trials of the drug there. Because there is no hospital or clinic nearby, researchers will set up a temporary clinic in the center of town for easy access. In addition to the experimental medication, participants will receive health screenings, check-ups, and basic medical care, plus compensation for lost time at work and transportation. After two years of gathering data, researchers will close the clinic and return to the laboratory to analyze the data and determine the efficacy of the pill.

Should the research proceed as described?

[20] https://www.nwabr.org/sites/default/files/2Belmont_Principles_HinR_1.pdf

Case Study Number 4: Text Me When You're Ready! [21]

In Zambia, one in seven adults is HIV positive (HIV+). Treatment is not readily available to all who need it, and researchers are interested in developing effective, low-cost treatment options for HIV+ patients. The study of a new medication for HIV faces a complication in that many Zambian people are mobile—they move from region to region because of jobs, political hostility, or to seek housing—making consistent contact with participants difficult. Furthermore, researchers worry that participants will send other family members to receive the experimental medication instead of coming in themselves in an effort to share the treatment. (This compromises both the study and the therapeutic value of the medicine, which must be taken consistently.) Researchers propose using technology to solve several issues. They will scan the thumbprints of participants and add them to an electronic database so that participants can prove they are in the research study before receiving treatments. Researchers will also provide participants with cell phones, on which researchers can text reminders to participants about their study visits and reschedule appointments. Enabling the GPS tracking on the phones will also allow researchers to find participants when needed, so they can go to meet them in person.

Should the research proceed as described?

[21] https://www.nwabr.org/sites/default/files/2Belmont_Principles_HinR_1.pdf

Current and Future Issues

- Human genetics research & enrollment of ethnically diverse populations
- Human genetics and privacy

Resources

https://cphs.berkeley.edu/working_humansubjects_presentation.pptx

https://www.nwabr.org/sites/default/files/2Belmont_Principles_HinR_1