Introduction to Clinical Research

GCP Lecture II

Dr. Laila Tutunji

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GCP Certification

This is an introduction to our medial students on the **WHO** designed global principles and regulations governing research on human subjects

GCP Certification is part of the Graduation Research Project Requirements

GCP Certification

Session 1:

Introduction/ Ethics/

Session 2:

Global Regulatory Framework

Session 3:

GCP Training/ IRBs.

Session 4:

GCP Training/ Research Protocol Basics.

Link to the Course

- Link to the course:
- https://gcp.nidatraining.org/
- Create an account to sign in:
- https://gcp.nidatraining.org/register
- Under organization kindly write:
  The University of Jordan

GCP Course Information

Enter your Name

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Our IRB requires 80% of answers correct

What Went Wrong in Medical Research ?

Germany The Nuremberg Trials

- Starting in the mid-1920s, German physicians, usually proponents of racial hygiene, were accused by the public and the medical society of unethical medical practices.
- In response to the criticism of unethical human experimentation, the Reich government issued "Guidelines for New Therapy and Human Experimentation" in Weimar, Germany.
- The guidelines were based on beneficence and non-maleficence, but also stressed the legal doctrine of informed consent

Germany The Nuremberg Trials

- The guidelines from Weimar were negated by Adolf Hitler.
- By 1942, the Nazi party included more than 38,000 German physicians, who helped carry out medical programs such as the Sterilization Law, as well as trials conducted in concentration camps.
- German physicians responsible for conducting unethical medical procedures on humans during the war were tried.

Germany The Nuremberg Trials

- After World War II, a series of trials were held to hold members of the Nazi party responsible for a multitude of war crimes. The trials were approved by President Harry Truman in January 1946 and were led exclusively by the United States.

- They began on December 9, 1946 in Nuremberg, Germany, in what became known as the Nuremberg trials.

- The 10 points constituted the "Nuremberg Code", which includes such principles as informed consent and absence of coercion; properly formulated scientific experimentation; and beneficence towards experiment participants. It is thought to have been mainly based on the Hippocratic Oath and the basic ethics governing Medicine.

Milestones in Clinical Trial Regulations
1947
The Nuremberg Code

1947 **Nuremberg Code**

Thalidomide Tragedy

- Thalidomide was one of the greatest cases in history of a drug disaster tragedy
- Thalidomide had been tested on animals extensively prior to its marketing
- The first drug recognized to cause birth defect in humans.
- Around 20,000 children were born with physical disability

Thalidomide Tragedy *(cont…)*

- Thalidomide was first marketed in 1957 in West Germany under the trade name **Contergan**.
- The German drug company Chemie Grünenthal developed and sold the drug. Primarily prescribed as a sedative or hypnotic, thalidomide also claimed to cure "anxiety, insomnia, gastritis, and tension". Afterwards, it was used against nausea and to alleviate morning sickness in pregnant women.
- Thalidomide became an over-the-counter drug in West Germany on October 1, 1957.
- Shortly after the drug was sold in West Germany, between 5,000 and 7,000 infants were born with phocomelia (malformation of the limbs). Only 40% of these children survived

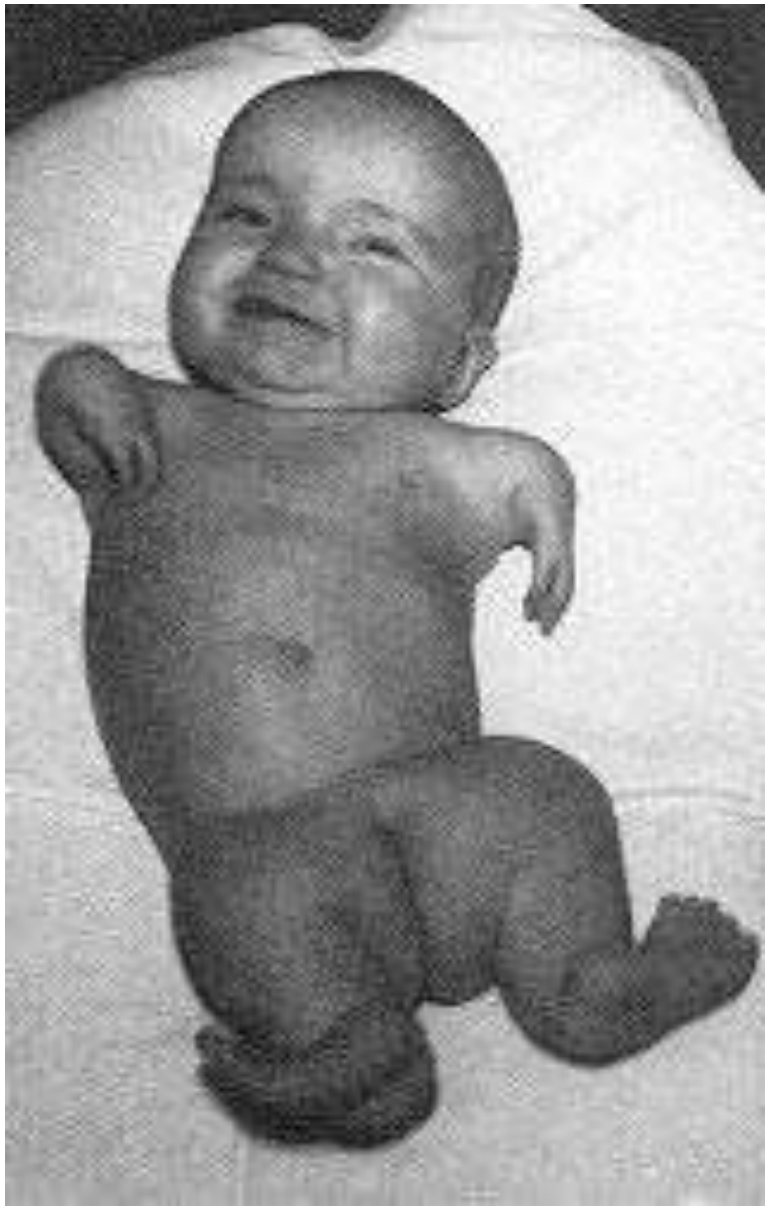
Thalidomide Tragedy *(cont…)*

- Throughout the world, about 10,000 cases were reported of infants with phocomelia due to thalidomide; only 50% of the 10,000 survived.

- Those subjected to thalidomide while in the womb experienced limb deficiencies in a way that the long limbs either were not developed or presented themselves as stumps.
- Other effects included deformed eyes and hearts, deformed alimentary and urinary tracts, blindness and deafness

Thalidomide Tragedy *(cont…)*

- The Medical Research Council maintained that the vast bulk of evidence from laboratory and animal tests is against thalidomide having any genetic effects



- **Researchers tried to reproduce the same effect in dozens of species of lab animals without success.**

Thalidomide Tragedy *(cont…)*

- **The negative effects of thalidomide led to the development of more structured drug regulations and control over drug use and development.**

Milestones in Clinical Trial Regulations
1964 – Declaration of Helsinki

1947 Nuremberg Code

1964 **Declaration of Helsinki**

The Declaration of Helsinki

- **Is a set of ethical principles regarding human experimentation developed for the medical community by the World Medical Association (WMA).[1]**

- **It is widely regarded as the cornerstone document on human research ethics.**

- **The Declaration was originally adopted in June 1964 in Helsinki, Finland, and has since undergone seven revisions (the most recent *by the 75th WMA General Assembly, Helsinki, Finland, October 2024***

The Tuskegee Experiment

- An unethical clinical study conducted between 1932 and 1972 by the U.S. Public Health Service.
- Investigators enrolled in the study a total of 600 impoverished, African-American sharecroppers from Macon County, Alabama.
- Of these men, 399 had previously contracted syphilis before the study began, and 201 did not have the disease and were purposely infected.

The Tuskegee Experiment

- The participants were primarily sharecroppers, and many had never before visited a doctor.

- Doctors from the U.S. Public Health Service (PHS), which was running the study, informed the participants—399 men with latent syphilis and a control group of 201 others who were free of the disease—they were being treated for bad blood, a term commonly used in the area at the time to refer to a variety of ailments

The Tuskegee Experiment

- The men were monitored by health workers but only given placebos such as aspirin and mineral supplements, despite the fact that penicillin became the recommended treatment for syphilis in 1947, some 15 years into the study.
- PHS researchers convinced local physicians in Macon County not to treat the participants, and instead, research was done at the Tuskegee Institute. (Now called Tuskegee University, the school was founded in 1881 with Booker T. Washington as its first teacher.)
- In order to track the disease's full progression, researchers provided no effective care as the men died, went blind or insane or experienced other severe health problems due to their untreated syphilis.

The Tuskegee Experiment

- In the mid-1960s, a PHS venereal disease investigator in San Francisco named Peter Buxton found out about the Tuskegee study and expressed his concerns to his superiors that it was unethical.
- In response, PHS officials formed a committee to review the study but ultimately opted to continue it—with the goal of tracking the participants until all had died, autopsies were performed, and the project data could be analyzed.

The Tuskegee Experiment- The Whistleblower

- **Buxton then leaked the story to a reporter friend, who passed it on to a fellow reporter, Jean Heller of the Associated Press.**
- **Heller broke the story in July 1972, prompting public outrage and forcing the study to finally shut down.**

- **By that time, 28 participants had perished from syphilis, 100 more had passed away from related complications, at least 40 spouses had been diagnosed with it and the disease had been passed to 19 children at birth.**

- **In 1973, Congress held hearings on the Tuskegee experiments, and the following year the study's surviving participants, along with the heirs of those who died, received a $10 million out-of-court settlement. Additionally, new guidelines were issued to protect human subjects in U.S. government-funded research projects.**

The Tuskegee Experiment

- The Tuskegee Syphilis Study, cited as "arguably the most infamous biomedical research study in U.S. history",[8] led to the **1979 Belmont Report** and to the establishment of the **Office for Human Research Protection (OHRP).**[9]
- It also led to federal laws and regulations requiring **Institutional Review Boards for the protection of human subjects in studies involving them.**

The Belmont Report 1978/1979

The *Belmont Report* summarizes ethical principles and guidelines for research involving human subjects.

Three core principles are identified: respect for persons, beneficence, and justice.

Three primary areas of application are also stated: informed consent, assessment of risks and benefits, and selection of subjects.

The Tuskegee Experiment

On May 16, 1997, President Bill Clinton formally apologized on behalf of the United States to victims of the experiment.

During his apology, Clinton announced plans for the establishment of Tuskegee University's National Center for Bioethics in Research and Health Care.

The final study participant passed away in 2004.

Hippocrates, Principles of Medical Ethics

1. Non-Maleficence
2. Beneficence
3. Justice
4. Respect for Autonomy
5. Confidentiality

Milestones in Clinical Trial Regulations
1989 – US French and Japanese GCP Laws

1947 Nuremberg Code

1964 Declaration of Helsinki

1989 **US French and Japanese GCP Laws**

Milestones in Clinical Trial Regulations
1991 – European Union – GCP Guidelines

1947 Nuremberg Code

1964 Declaration of Helsinki

1989 US French and Japanese GCP Laws

1991 European Union – GCP Guidelines

Milestones in Clinical Trial Regulations
1994 – WHO – GCP Guidelines

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Milestones in Clinical Trial Regulations
1997 – ICH – GCP Guidelines

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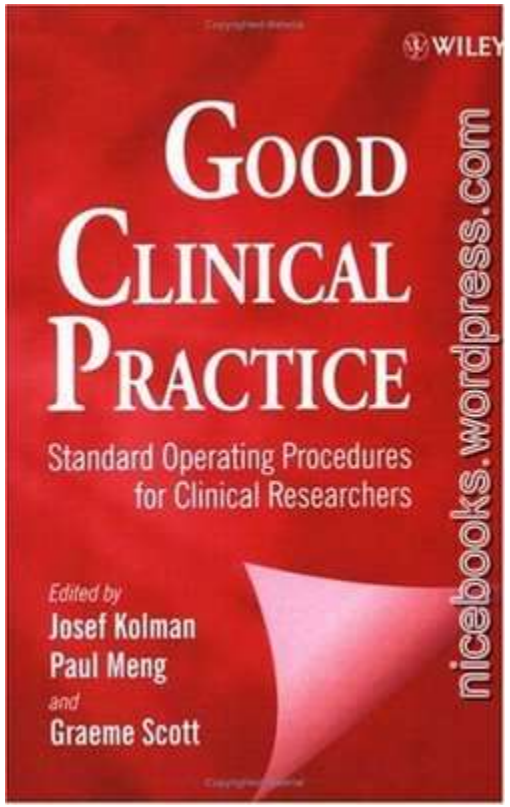
1989 US French and Japanese GCP Laws

1991 European Union – GCP Guidelines

1994 WHO - GCP Guidelines

1997 **International Conference on Harmonisation ICH – GCP Guidelines**

What is GCP



- Good Clinical Practice (GCP):

"Standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of trial subjects are protected"

Ethics
The Soul of Medicine

The First Principle

Non-Maleficence

“Primum, Non Nocere”

First, DO NO HARM

The Second Principle

Beneficence

The Third Principle

Justice

The Forth Principle

Respect for Autonomy

The Fifth Principle

Confidentiality

To see and See Again

- Shoulder of giants
- The spirit of inquiry, our responsibility ?
- Al Rhazi
- Ibn Sena
- Ibn Al Haitham
- Where do We Stand?

To See and See Again

You Can Make A Difference