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Neuroscience applied

Mind your Ethics!
A Look at Ethical Issues in Clinical Research

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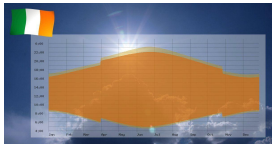
Spring
Summer
Autumn
Winter
THE SEASONS OF IRELAND.

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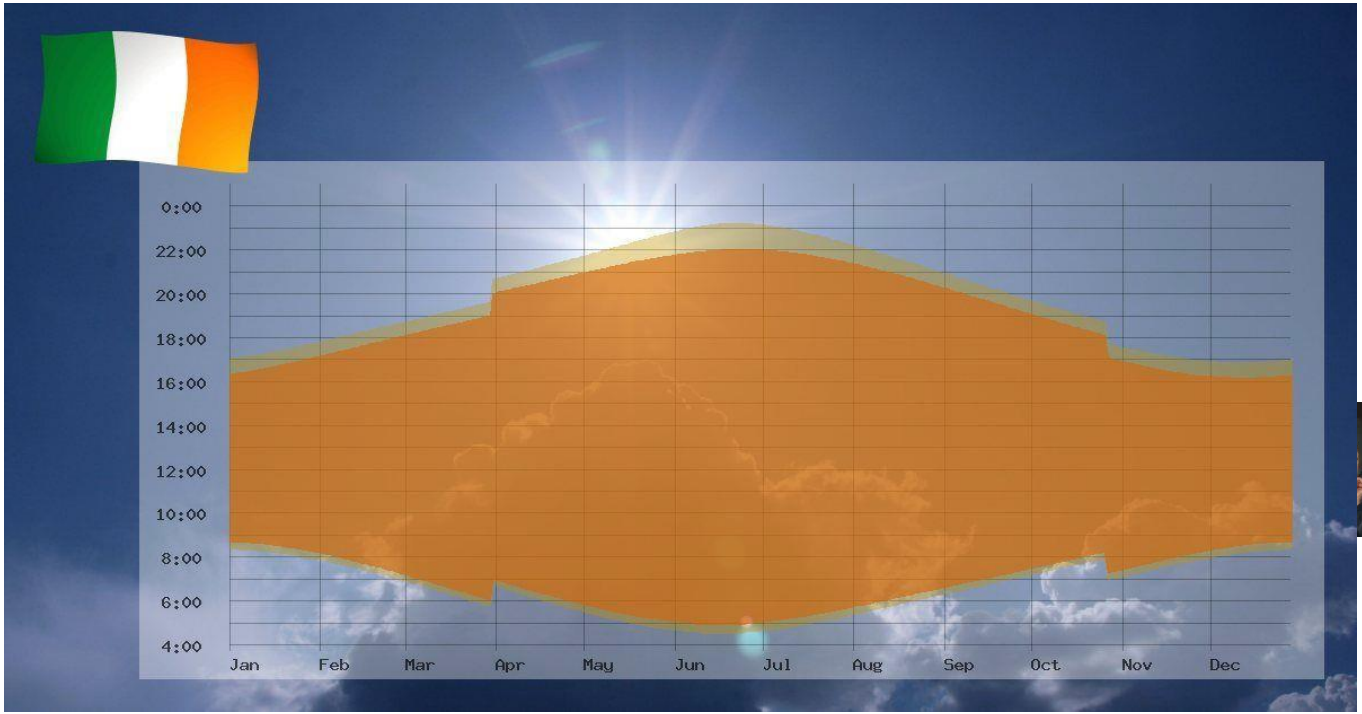
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THE SEASONS OF IRELAND


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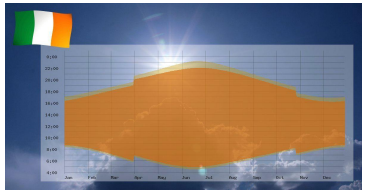



THE SEASONS OF IRELAND.


LIVE Galway
RTÉ News

Shepherd's Pie

- Potatoes
- Lamb (or vegetable alternative!)
- Peas
- Carrots
- Onion
- Butter (and stock!)
- Milk

- Heat onion in pan in butter
- Add veg, then meat…
- Heat oven to 160^{o}
- Boil and mash potatoes
- Layer into dish
- Dish in over 30 mins

Why do we need ethical guidelines?

Clinical research:
Develop generalisable knowledge

Clinical research may
exploit volunteers

People make research possible

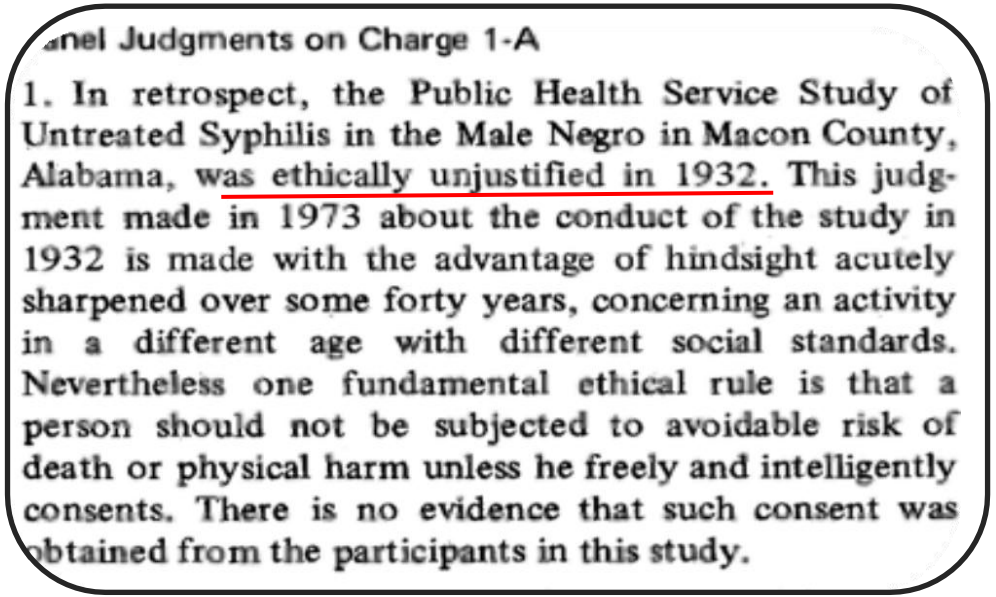
Ethical guidelines:
Protect patients
Preserve integrity of science

Tuskegee Syphilis Study, 1932

Tuskegee Syphilis Study, 1932

- Record the natural history of syphilis: 600 Black men
- **Informed consent not collected**
- 1943: Penicillin was treatment of choice
- 1972: Assistant Secretary for Health and Scientific affairs appointed Ad Hoc Advisory Panel to review the study

Tuskegee Syphilis Study, 1932



anel Judgments on Charge 1-A

1. In retrospect, the Public Health Service Study of Untreated Syphilis in the Male Negro in Macon County, Alabama, was ethically unjustified in 1932. This judgment made in 1973 about the conduct of the study in 1932 is made with the advantage of hindsight acutely sharpened over some forty years, concerning an activity in a different age with different social standards. Nevertheless one fundamental ethical rule is that a person should not be subjected to avoidable risk of death or physical harm unless he freely and intelligently consents. There is no evidence that such consent was obtained from the participants in this study.

"Results were disproportionately meager compared with known risks to human subjects involved."

Tuskegee Syphilis Study, 1932

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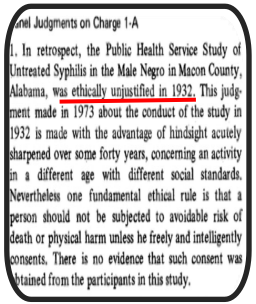

Panel Judgments on Charge 1-A

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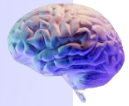
Seven main principles of ethical research

- Social and clinical value
- Favorable risk-benefit ratio
- Scientific validity
- Independent review
- Fair subject selection
- Informed consent
- Respect for potential and enrolled subjects

Grady et al., 2018

What about in psychiatry?

No code of ethics until the 70s



Code of Ethics for Psychiatry (2020)

Galderisi et al., 2024

Code of Ethics for Psychiatry (2020)

Beneficence

Non-maleficence

Respect for users' autonomy

Applying expertise to the service of society

Improving standards in practice

Galderisi et al., 2024

Case 1: Identifying principles of ethical research

Imagine you are a group of researchers, working in a hospital in Europe for people with schizophrenia. Most patients have been in the facility for many years with no hope of being discharged. A large majority also do not have any relatives who visit them regularly or at all.

What ethical issues around fair-subject selection concern you?

A pharmaceutical company contacts you interested in developing a new medication for schizophrenia. They explain that the drug has been tested in America but that more tests are required before approval can be provided and they are eager to advance as it could earn the company a substantial profit. As a researcher you will identify which patients are suitable for recruitment alongside the medical team.

How does this impact the social and clinical value of the study?

The informed consent that you offer patients states that the drug *"has been tested in thousands of patients"* and *"appeared to slightly affect the electrical activity of the heart in some people".* The company insists that this should not hinder recruitment and that it is safe to go ahead.

Would you make any changes to the informed consent?

Informed Consent Process Summary

“Informed consent is the process in which a health care professional educates a patient about the risks, benefits, and alternatives of a given procedure or intervention.”

Informed Consent Process Summary

- Description of the study
- Description of inclusion and exclusion criteria
- Number of subjects and their rights
- Anticipated risks and benefits
- Information about the study sponsor
- Contact information
- Confidentiality
- Financial information
- Provide participants with copy of informed consent form

Investigator Responsibilities

- Judge whether proposed research is ethically sound
- Manage personal conflict of interests
- Ensure adequate protection of research participants (including coercion and truly informed consent)
- Ensure research staff conducts honest, thorough research
- Handle and report adverse events promptly, completely, and accurately

Publishing

Publishing

- ➔ Highly competitive
- ➔ Rigorous peer review – added stress!!
- ➔ Time!
- ➔ Maintaining high quality
- ➔ Tight deadlines

Publishing

- **The Ingelfinger rule (1969):**
  - *"a manuscript could only be considered for publication if its content had not been previously published"*

- Criteria for **redundant** publication:
  - Similar hypothesis
  - Similar sample size
  - Similar methods
  - At least one of the authors is present at both papers
  - No relevant new information is provided

Publishing

- **We often take ideas and forget to attribute them to their original source**
- Always aim to paraphrase
- If you copy, you must follow appropriate citation guidelines
- Always reference
- Discuss authorship with PI
- Maintain detailed record of all steps taken

How Many Scientists Fabricate and Falsify Research? A Systematic Review and Meta-Analysis of Survey Data

Daniele Fanelli*

INNOGEN and ISSTI-Institute for the Study of Science, Technology & Innovation, The University of Edinburgh, Edinburgh, United Kingdom

- ➔ 18 surveys
- ➔ A pooled weighted average of **1.97%** of scientists admitted to having **fabricated**, **falsified** or **modified data or results at least once**

Fanelli, 2009

Case 2: Recordkeeping and authorship

After three years, a PhD fellow wrote a manuscript about the discovery of a biomarker for depression to submit to a high-visibility journal (PhD first author; PI and group members as co-authors. Suddenly, the PhD student had to suspend their studies leaving the draft manuscript with the PI to submit. The PI appointed another student to continue the project and submit for publication, asking them to reproduce an experiment from the draft.

Was it fair of the PI to ask a new lab member to take over this work?

A lack of notes made it difficult for the student to understand the initial experiments. The student, new to research, asked the PI what to do. The PI emailed the PhD student to ask for any possible additional information, but they replied that everything necessary was readily available.

Why is it important to keep highly detailed notes of research data and analyses?

The PI asked the student to prepare the data and experiment again. The student found similar results, but some key differences were observed. The PI, concerned about reproducibility, asked the student to repeat all analyses. The student then helped to edit the manuscript, rewriting some sections. The PhD student emailed the PI to ask if it was going to be submitted soon. The PI no longer felt sure if the PhD student should be first author (or co-author), and told the PhD student that edits were ongoing so as not to upset them.

Should the PhD student be first author or a co-author on the new version?

Contemporary Publishing – Artificial Intelligence

- Publishing increasingly influenced by AI
- Opportunities and challenges in ensuring integrity and quality of scientific publishing
- We are facing new ethical challenges that must be carefully managed

Case 3: Using AI to write a manuscript

Dr. A is a PI who specialises in the role of genetics in mood disorders. A prestigious review journal has requested Dr. A to write an article reviewing the current state of the field. Dr. A is busy with various responsabilities so asks B, a PhD student working in the lab to write the review. Unbeknown to Dr A, B uses artificial intelligence (AI) to summarise the current literature and generate references. Dr. A is very happy with the work and they submit the work to the journal.

Should they retract the article?

During the submission process, both authors do not acknowledge the use of AI in preparing the article. Three months post-publication, an anonymous critique claims that two of the references in the article are fake. The editors advise Dr. A and ask for a correction to be submitted. Dr. A meets with B to discuss the issue and B admits to having used AI. Dr. A is extremely angry at B for using Ai without prior consultation.

Upon resubmission should they address inaccurate references and acknowledge use of AI?

They review the article and discover that both references are indeed fake, as well as finding more reference errors, as well as text cited from other articles without attribution.

Based on Dr. A's contribution, should they be included as an author?

National Institite of Health, 2024

Responsibilities of Authors using AI

- → Pay close attention to search prompts
- → Carefully review the results
- → Check references for accuracy and relevance
- → Check the text for plagiarism
- → Review if important facts or references have not been included
- → Disclose and describe the use of AI

National Institite of Health, 2024

Addressing Ethical Challenges in Publishing with AI

- AI Content and Authorship: who should be credited as an author?
- AI in Data Integrity?
- AI in Peer Review: initial screening?
- Promote adherence to Committee on Publication Ethics (COPE) guidelines
- Collaboration: editors, editorial boards, publishers and researchers must ensure responsible use of AI

Take home messages

- ➔ Ethical challenges are ongoing in clinical research
- ➔ Seven principles of ethical research can inform us and help us to maintain the scientific integrity of our research
- ➔ AI can improve efficiency in research but must be used responsibly and improved usage guidelines are required
- ➔ We will continue to face ethical challenges: don’t be afraid to ask for help and admit we don’t know everything!

ETHICS IS
KNOWING
THE DIFFERENCE
BETWEEN WHAT YOU
HAVE A RIGHT TO DO
AND
WHAT IS RIGHT TO DO

Potter Stewart
(1915 - 1985)
American lawyer and judge who served as an Associate Justice of the US Supreme Court

Some useful links

- Ethics in Clinical Research – National Institute of Health
- NIH Guidelines for the Conduct of Research
- International Committee of Medical Journal Editors

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Thank you!
Go raibh míle maith agaibh!

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