Ethics in research: what, why, how

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Objectives and Outcomes

- An awareness through action and in writing of the ethical and legal responsibilities involved in research participant protections, research conduct and reporting, and the research ethics review processes;

- Competency in incorporating ethics into research methodology.

Outline

1. Concepts
2. Research Ethics: The need
3. International Instruments
4. Local Instruments
5. The National Health Act
6. Principles, Processes & Structures
7. Benchmarks

“The benefits of biomedical progress are obvious, clear and powerful. The hazards are much less well appreciated.”

Leon Kass

Introduction

What are the objectives of Ethics?

- *How we ought to act in a given situation*
- *Provide strong reasons for doing so*

involves a critical reflection of morality with its intent to safeguard human dignity and to promote justice, equality, truth, and trust.

Principle-based Ethics

- Autonomy
- Beneficence
- Non-maleficence
- Justice

Prima facie – not absolute; overridden by weightier concerns

- lack hierarchical order rendering ranking arbitrary

Ethics & Law

- Distinct entities
- Ethics constrained by law
- Law: minimal standard
- *Quasi legal* status of guidance documents

Analysis Process

- Determine whether issue at hand is ethical one

- Check facts of the case
- Check which ethical values are involved
- Consult authoritative sources
- Consider alternative solutions in light of values and principles they uphold & their likely consequences
- Discuss proposed solutions with those whom it will effect
- Make decision – act on it with sensitivity to others affected
- Evaluate decision – be prepared to act differently in future

Research Ethics - Components

- Regulatory
- Ethical

HEALTH RESEARCH - CHALLENGES

CAN THE DEMANDS AND GOALS OF SCIENCE AND HEALTH RESEARCH BE PURSUED WITH FULL PROTECTIONS OF THE RIGHTS AND DIGNITY OF THE RESEARCH PARTICIPANT AND COMMUNITY?

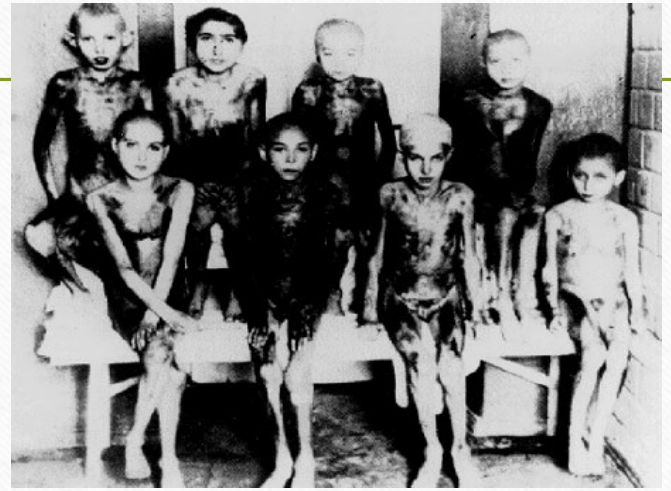
Early Gains of Health Research

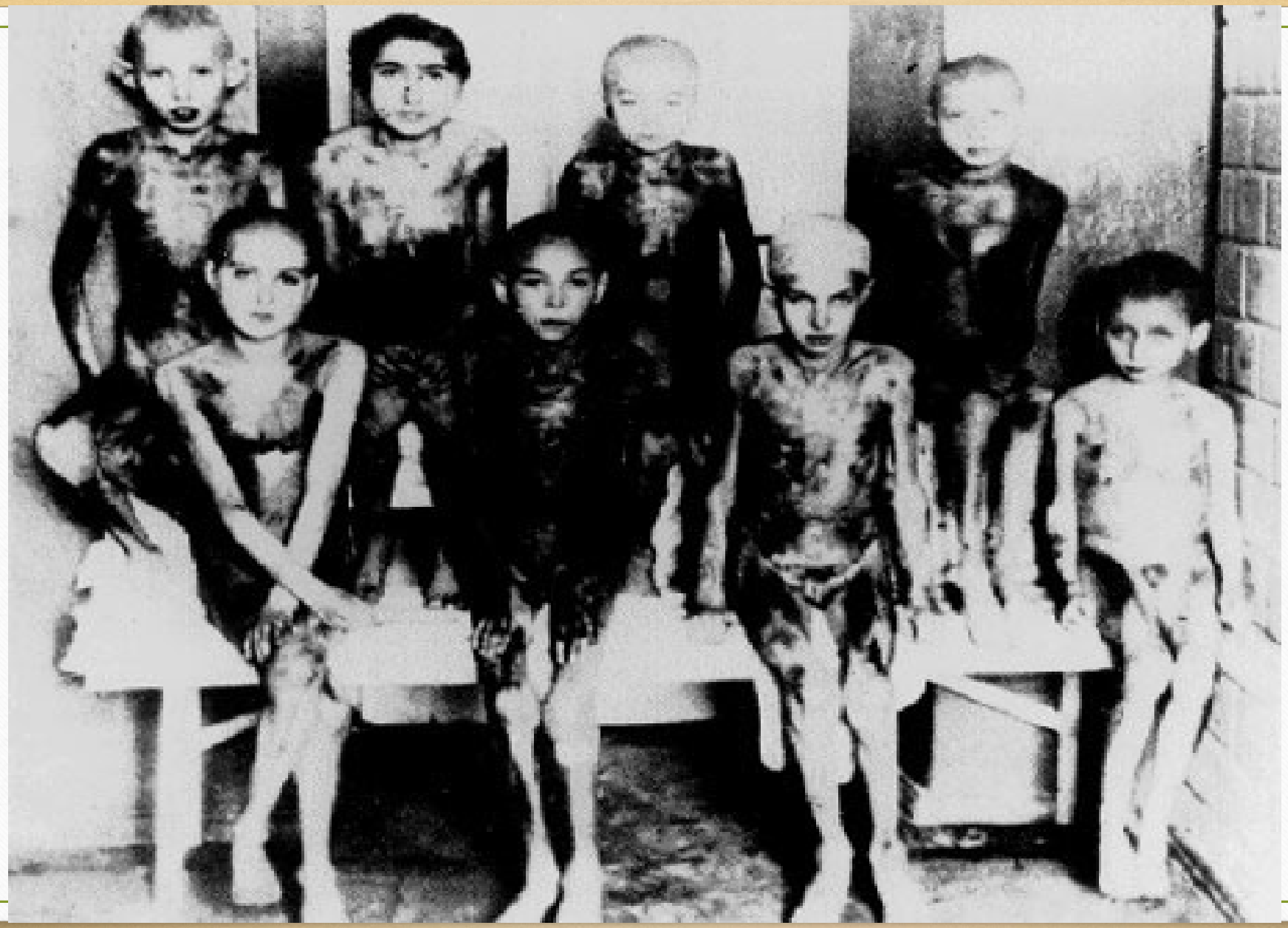
- Even very early experiments with humans had positive outcomes:
  - 1700's James Lind, and scurvy studies
  - 25 years later, Edward Jenner's smallpox vaccine.

- *SUCCESSES NOT WITHOUT COST*

SOME REALITIES

Foto: PRIVAT





POSNER'S TESTIMONY

"In the workroom next to the dissecting room, fourteen Gypsy twins were waiting and crying bitterly. Dr Mengele didn't say a word to us, and prepared a 10cc and a 5cc syringe. From a box he took Evipal and from another box he took chloroform, and put these on the operating table. After that the first twin was brought in … a 14 year old girl. Dr Mengele ordered me to undress the child and put her head on the dissecting table. Then he injected the Evipal into her right arm intravenously. After the child had fallen asleep, he felt for the left ventricle of the heart and injected 10cc of chloroform … . After 1 little twitch the child was dead … in this manner all 14 were killed."

Mengele then removed the eyes from the dead twins and shipped them off to Berlin for further study.

Japanese Experiments: Unit 731 “Germ doctors” cut up a live Chinese girl … .

Ethics in research was:

“ … born in scandal and reared in protectionism”.

Levine C. Has AIDS Changed the Ethics of Human Subjects Research?” Law, Medicine and Health Care. (1998); 16: 163-73.

Some Pertinent International Instruments & Guidelines

- Nuremberg Code – ***1947***
- International Covenant on Civil and Political Rights – ***1966:*** *"No one shall be subject to torture or to cruel, inhuman or degrading treatment or punishment. In particular, no one shall be subjected without his free consent to medical or scientific experimentation"*
- WMA Declaration of Helsinki – ***1964*** (updated x 7). Latest version ***2013***
- Council of International Organisation of Medical Scientists (CIOMS)- ***1993 ; 2002, 2016***
- International Conference on Harmonisation (ICH) Good Clinical Practice Guidelines – ***(1995 ; 2002; 2017)***
- Singapore Statement on Research Integrity - ***2010***
- WMA Declaration of Taipei regarding Human Databases and Biobanks - ***2016***

South African Instruments & Guidelines

- Bill of Rights of the Constitution of South Africa
- National Health Act (No.61 of 2003)
- Protection of Personal Information Act
- Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa – *2020 (3ed)*
- Ethics in Health Research: Principles, Structures & Processes – *2004; 2015 (2ed)*
- Health Professions Council of South Africa Ethical Guidelines

Bill of Rights

- 12(2)
  - "Everyone has the right to bodily and psychological integrity which includes the right …
    - (c) not to be subjected to medical or scientific experiments without their informed consent."

- Some other applicable rights:
  - 9 – Equality;
  - 10 – Human Dignity;
  - 11 – Life;
  - 14 - Privacy;
  - 15 – Freedom of religion, belief and opinion;
  - 32 – Access to information

Health Research – NHA s1

- Any research which contributes to the knowledge of:
  - Biological, clinical, psychological, social processes
  - Improved methods for provision of health services
  - Human pathology
  - Causes of disease
  - Effects of environment on human body
  - Development of new applications of pharmaceuticals, medicines, related substances
  - Development of new applications of health technology

National Health Research Ethics Council (NHA s72(2))

- determine guidelines for the functioning of health research ethics committees,
- register and audit health research ethics committees,
- set norms and standards for conducting research on humans and animals, including norms and standards for conducting clinical trials,
- adjudicate complaints about the functioning of the health research ethics committees,
- refer to the relevant health professional councils any violations
- institute disciplinary actions,
- advise the national department and provincial departments on any ethical issues concerning research.

Clinical Trials (NHA – sec 71)

- "… a systematic study involving human subjects that aims to answer specific questions about the safety or efficacy of a medicine or method of treatment."

Health Research Ethics Committees (NHA)

- 73(1) Institutions at which health research is conducted, to establish / have access to health research ethics committee, registered with the NHREC.

- 73(2) A health research ethics committee must –
  - (a) review research proposals to ensure that research will promote health, contribute to the prevention of communicable or non-communicable diseases and or disability or result in cures
  - (b) grant approval for research where proposals meet the ethical standards

Principle-based Ethics

- Autonomy
  - Informed consent
  - Confidentiality
- Beneficence
  - Benefits
- Non-maleficence
  - Decrease risks
- Justice
  - Compensation for study participation
  - Compensation for Research Related Injury
  - Standards of Care
  - Post Trial Access

Informed Consent - Grounding

- Philosophical basis
  - Respect for persons – autonomy
  - Beneficence, nonmaleficence, justice
- Legal basis
  - International human rights law, national legal systems, outcome of litigation

Autonomy

- Greek origin
  - *Autos* - "self"; *nomos* - "rule"
- Conditions fundamentally indispensable for autonomy:
  - Liberty – independence from controlling influences;
  - Agency - capacity for intentional action.

Autonomy

- Acknowledges:
  - right of autonomous agents to hold views
  - make choices
  - take actions based on their values and beliefs.
- Respect includes
  - where necessary, individual is assisted in developing ability to competently make autonomous choices.

Autonomy

- Negative and positive obligations included in this principle.

- Negative obligation
  - broad
  - Entails : for action to be truly autonomous there should be no constraints by controlling influences of others.
    - in health research - avoid coercion during recruitment to ensure voluntariness not interfered with.

Autonomy

- Positive obligation
  - autonomous decision making to be facilitated by treating individual with respect when disclosing information and assisting with actions that promote autonomous decision making.
  - gives recognition for possible need for involvement of others to bring to fruition respecting the principle.
    - health research - disclose all essential information
    - ensure understanding of enrolment and implications.
    - voluntariness of decision making to be probed for and ensured.
    - community involvement coupled with innovative methods of information sharing prior to and during enrolment of participants in health research - examples of positive obligations.

Autonomy

Assisting participants in achieving their ends and building up their capacities as agents go a long way in avoiding treating research participants exclusively as a means to researchers' ends.

Benefit

- a good that contributes to and promotes the welfare of an individual or community
- determined by taking into account needs, values, priorities and cultural experiences
- prior consultation with individuals and communities of great value in determining benefits.
- CIOMS - benefit refers to added value that the research may bring to the individual or community.

Benefit: Ethics in Health Research: PPS

- *"That which positively affects the interest or welfare of an individual or group, or the public generally"*

- *"A risk/benefit analysis of the study should precede the research itself. Risk/benefit analysis should take full notice of benefits and harms beyond the duration of the research, particularly in the case of chronic, life-threatening conditions. Alternate ways of providing benefits to participants might be available. The principle investigator has the ethical duty to exclude participants who might be placed at undue risk."*

CIOMS - Potential benefits

- Directly associated with study participation:
  - Generation of knowledge to protect and promote health of future patients;
  - Prospect of clinical benefit where previous studies have provided evidence that the intervention's potential clinical benefits will outweigh its risks;
  - Generation of data and biological materials for future health-related research; and
- Benefits not directly associated with study participation:
  - improving health infra-structure;
  - training laboratory personnel;
  - educating the public about the nature of research and the benefits resulting from a particular study;
  - and contributing to the overall scientific environment in that locale or region. *Capacity-building should be a part of any research project involving international collaborative partnership with researchers in low-resource settings.*

Harm / Risk: Ethics in Health Research: PPS

- HARM: *"That which adversely affects the interest or welfare of an individual or group; harm extends to physical harm, discomfort, anxiety, pain, psychological disturbance and includes placing a person at social disadvantage."*

- RISK: *"The magnitude of a harm and the probability of its occurrence."*
  - Minimal Risk: *"This anticipates that the probability and magnitude of harm or discomfort to be experienced in the research will not be greater than those ordinarily encountered in daily life"*
  - More than Minimal Risk
  - Minor Increase above Minimal Risk (CIOMS): "… the increment in risk must only be a fraction above the minimal risk threshold and considered acceptable by a reasonable person." There must be full regard to context when making this determination.

Risks/Harms linked to Justice:
Declaration of Helsinki 2013

- *"15. Appropriate compensation and treatment for subjects who are harmed as a result of participating in research must be ensured."*

Risks/Harms: Conflicts of Interest

- *"set of conditions in which professional judgement concerning a primary interest tends to be unduly influenced by a secondary interest."* Thompson

- *"set of circumstances in which a clinician's or investigator's own interests conflict with those with whom he/she has a fiduciary relationship"* Sugarman

- *"when a secondary interest compromises or appears to compromise or has a potential to compromise an individual's professional judgement towards the primary interest."* AAU

Characteristics

- must be undue influence or that one interest must conflict with another for conflict of interest to occur

- COI sets in when a potential exists that one interest (especially the secondary interest) will supersede the other (usually the primary interest) and unduly influence the professional judgement of the person involved.

Levels of COI in Research

- community
- investigator
- supervisor
- institutional conflicts
- Research Ethics Committee
- journals
- political
- media

Standards for assessing conflict of interests

- **<u>Likelihood of influence:</u> depends on extent of the secondary interest; scope of conflict; extent of discretion by the scientist**

- **<u>Seriousness of the harm</u>**

Justice

- Ethical obligation to treat each person in accordance with what is right & proper
- Study should leave participant / community better off / no worse off
- In health research closely linked to beneficence, nonmaleficence

Justice - Notions

- Equality:
  - Equals should be treated equally
- Distributive:
  - Distribution of burdens and benefits should be fair
- Procedural:
  - Process in which decisions are made and the manner in which actions are carried out
- Compensatory:
  - The way in which people are compensated in relation to injuries inflicted upon them

From Ethical Principles to Norms & STDS : PPS

- Relevance and value
- Scientific integrity
- Role-player engagement
- Fair selection of participants
- Fair balance of risks and benefits
- Informed consent
- Ongoing respect for participants, including privacy and confidentiality
- Researcher competence and expertise

Regulatory : PPS

- Purpose and Status of PPS:
  - To provide minimum national benchmark of norms and standards for conducting ethical responsible research
  - Endorse ethical principles laid down in international guidelines
  - To be read in conjunction with other guidelines

Regulatory : PPS

- REC review process
  - Independent, objective assessment of potential effect of proposed research on potential participants and *general day-to-day functioning of infrastructure that provides research site*
- Review ensures ethical & scientific standards maintained to
  - Protect participants from harm
  - Hold researchers accountable for research activities
  - Promote important social & ethical values

Regulatory : PPS

- Researchers to be suitably qualified & technically competent
- Primary responsibility of PI / research leader to ensure
  - safety & well being of participants
  - scientific integrity of protocol
  - responsible implementation of protocol
- Competence includes research competence & *research ethics competence*
  - Researchers to produce evidence of appropriate research ethics training within previous 3 years
- International multicentre research, at least 1 (co-) PI must be SA based.

Regulatory : PPS

- No need for formal ethics review for
  - Quality assurance and improvement studies
  - Program evaluation
  - Performance reviews
- Prudent to obtain ethics approval before activity commences if publication desirable

- 1.6.9: "*Retrospective review and approval or clearance is not permitted*" (all research)

Regulatory : PPS

- Reciprocal recognition of review decisions:
  - REC, *at its own discretion* may recognise prior review and approval by another registered REC – avoids duplication of effort
  - REC must determine nature of documents to be filed locally – must include copy of approval letter from other REC
  - REC may revise decision if justifying circumstances arise.

REC Roles & Responsibilities

- Primary Role – protect rights and welfare of research participants.
- Primary responsibility of member – to decide independently whether opinion on conduct of research will protect participant.
- Responsibility of Institutions undertaking research – to ensure adequate resources for optimal REC functioning
- Institutions to accept legal responsibility for REC decisions and advice and to indemnify REC members

Some Benchmarks

- Consultation and meaningful collaboration
- Worthiness
- Justifiable and Defensible Study Design, Methodology & Processes
- + Benefit / Risk ratio
- Respect for persons
- Avoidance / Ethical Management of Conflicts of Interest