Global PaedSurg Research Training Fellowship



**Session 3: 25th January 2019**

**Ethical considerations, gaining study approval and undertaking patient consent.**

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Overview for this Session

**Ethical considerations:**

Historical background,

Guiding resolutions,

Ethical principles

**Study approval and consent:**

Responsibility of researchers and ethics review boards;

Consent from parents and children

Learning Objectives

* Recognise ethical issues
* Identify regulations
* Define principles
* Describe consent
* Paediatric angles
* Describe IRB (institutional review board)

Why is this all necessary?

The advent of strict conduct in research is because historical abuses in many countries have occurred under the name of research, also associated with human exploitation and injury as well as researchers cheating.

Misconduct of research has placed us all at risk of the misfortune associated with it. We may fall prey to career and incitement structures, velocitation, tunnel vision, dehumanisation, indifference, ignorance and lack of oversight and control.

The Nurnberg Code

Established during the Nurnberg Trials (1947), in response to the atrocities perpetrated by Nazi researchers. This Nurnberg Code postulates 10 research ethics principles, including:

* Voluntary at all time
* Informed consent
* Rational and societal benefit
* No other way than having a human subject research
* Proportionality (where the risk/benefit ratio is high)
* Stop when dangerous
* Skilled personnel to perform research

Most of the international and national regulations and laws are based on this code.

The Helsinki Declaration

Declaration of Helsinki was established in 1964 under the authority of the World Medical Association (WMA) and the latest amendment for it was made in 2013. The declaration acknowledges the existence of a conflict of interest amongst researchers as we play a double role of being interested in the study and patient care. This led to the development of an ethics review board to take away judgement from the researchers alone to a board that could make an independent evaluation. Discussion about vulnerable populations having less say in the research was also incited along with talks on how international collaboration could be designed. As good as this declaration is, the only drawback is that it is not legally binding.

This can be accessed from the following link:

<https://www.wma.net/policies-post/wma-declaration-of-helinskiethical-principles-for-medical-research-involving-humansubjects/>

Convention on Human Rights and Biomedicine - The Oviedo convention

An international legally binding document was enacted by the Council of Europe, 1997 updated in 2005, signed by many nations. They talk at length about informed consent where the human subject is duly informed of having the right to choose to participate in the research or not.

The Belmont Report

The National Research Act was established in 1974 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research. The Belmont Report was drafted and it poised the fundamentals of international agreements on what is considered ethical in terms of research. This report states three ethical principles which are: Respect for persons [Autonomy and informed consent]; Beneficence [ Do not harm, Maximise the risk/benefit ratio]; Justice [Fair selection of study subjects, fair share of benefits]

This can be accessed via the following link: <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html>

The Common (and Final) Rule

From the USA, last updated 2017. To be followed as a federal law if one gets funding from the FDA (Food and Drug Association), NSF (National Science Foundation) and National Institutes of Health (NIH). Specifies and defines how to go about the informed consent and institutional review boards in the following ways:

1. Informed consent:
* Purpose and choice
* risks and benefits
* rights
* privacy
* responsible
1. Institution Review Series:
* Human Subjects Research
* Ethical Committee Review

Definition of terms (The Common Rule, 2017)

Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

A human subject is a **living** individual about whom an investigator (whether professional or student) conducts research:
1.  Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyses the information or biospecimens; ***or***2.  Obtains, uses, studies, analyses, or generates identifiable private information or identifiable biospecimens

The diagram on the right can be used to assess if the proposed study will be a human subjects research or not.

In Sweden, IRB approval is required if the personal information handled is *sensitive,* such as:

* Race or ethnicity
* Political opinion
* Religion or philosophy
* Trade unions
* Sexuality
* Health (in its broadest sense)

You have to approach the IRB at your institution so that they can approve, require modification in research to secure approval, defer action or disapprove all research activities, including proposed changes in ongoing, and previously approved human subject research. IRB also has the power to suspend or terminate the approval of ongoing, previously approved research that is not being conducted in accordance to the board’s requirements or could cause more harm than good on the subjects. For a research to be approved it needs to fulfil the following requirements:

* Risks to subjects are minimised
* Risks are reasonable in relation to anticipated benefits
* Selection of subjects equitable
* Informed consent is sought from each subject
* Informed consent is appropriately documented
* Data collection is monitored to ensure subject safety
* Privacy and confidentiality of subjects is protected
* Additional safeguards are included for vulnerable populations
* Benefits should always be more than the risk – assessment of methodology

Respect and protect the subjects from harm:

* Physical harm
* Mental harm
* Integrity harm
* Social harm – stigmatisation
* Financial and legal

Is a review required?

In some cases, an expedited review can be done with one getting a quick go ahead. But in any case, if you have to file an application, wait for approval before you commence the study.

Data safety

How do you store and protect your data? Code the data and encrypt it using a separate key. If the data forms are paper based then have all the material securely locked away. E-safety platforms like REDCap (used in Global PaedSurg) can be used for data storing as it is safe.

Information to study subjects can be given in the following 12 steps

1. Background and Aim – description of the purpose of study
2. Why we ask you – justification of why this particular person or family
3. Details of the study – how will this study influence standard of care or follow-up
4. Standard of care
5. Risks – are there any risks associated with
6. Benefits
7. Data handling – who can they appeal to if they are concerned about their data
8. Study results information – will they be relayed to the participants, or will it just be a publication.
9. Insurance – to cover whatever happens
10. Voluntary and withdrawal – Explicitly indicate that participants can choose to join or quit with no need to justify why.
11. Responsible personnel to contact if they need any clarifications
12. Consent form – agreement

Informed consent

* Who should give consent? In a family, should it be the mother, child or both parents?
* When to obtain informed consent? Sometimes it can be very acute/emergencies, how do you go about that?
* How should consent be obtained?
* How should consent be recorded?
* Are inducements acceptable? Is it okay to give financial remuneration for participants?

Exemption from informed consent may apply in the following scenarios:

* When impossible to contact participants, but having the data that you need.
* When not feasible with a huge number of people in the database. You can put an advert in the national newspapers to inform participants on the research, allowing them the freedom to choose to continue or opt out of the study.

Special considerations must be made in the following scenarios:

* Incompetence, where there is cognitive impairment such as unconsciousness, dementia, young age
* Child assent – where child can give their consent if they agree or object (at any age their objection to participation in the study should be respected)

Free will and benefits

Although participation is said to be voluntary, is it really voluntary? How much pressure is implicit in the situation? Do not persuade or keep asking for individuals to join the study, this is extremely unethical. In some situations, patients may feel that the level of care they will get will depend on their participation in the study or not. Are there any financial or material benefits (such as better care, follow-up, preventative care, interviews with therapeutic potential and remuneration) for one who participates in the study.

Equipoise – control group treatment

If you do an RCT, there should be uncertainty as to which of the two treatment arms is the best. If you *know* that one of the treatment modalities is much better than the other then the study has no equipoise, and may therefore be considered unethical. The provision of non-universal standard of care to half the patients may appear advantageous to having no patients getting anything, but such experiments are viewed as exploitive and unethical by many. A better way would be to use a non-inferiority approach. In this model, the control group gets perfect treatment with local modification as to the intervention to see if there is no difference with what is considered universal standard of care.

Other treatment considerations

In a study where you map disease, will treatment be offered to those found to have a disease after a screening is done? After study is finished how do you deal with the group just started to have a medical interaction? Do the results from the research benefit the study population or reciprocate the efforts received from burdening the participants?