

## Research, Evidence and Ethics

ORCA  
Brussels 2<sup>nd</sup> July 2015  
Ingegerd Mejàre

ingegeerd.mejare@sbu.se  Malmö University 

## Items



- What is ethics?
- Some declarations, protocols and guidelines
- The hierarchy of evidence
- How to deal with the non-randomized study
- Knowledge gaps.

2

## What is Ethics?



Ethics (from Greek *ethos*) is synonymous with moral philosophy, that tries to answer questions such as: *What is good?, What is right?, How should one act?*

Ethical aspects in a health-care mainly address:

- things that benefit or harm the individual patient
- questions concerning respect for patient autonomy and integrity
- questions on equity regarding who should be offered different types of health-care intervention.

3

## Ethics - different levels



- Universal morals or ethics – fundamental beliefs: stealing, lying, harming or murdering another are wrong
- Personal – beliefs that an individual has and maintains over time; how a universal moral is interpreted and used by each person
- **Professional – formal standard or code that guides a person in work activities and decision making.**

4

## Sharing the same values



5

## From the Nuremberg Code (1947).

- The voluntary consent of the human subject is absolutely essential.
- The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
- The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
- During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage.

6



## Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects Adopted in 1964. (WMA Declaration of Helsinki)

7

## Declaration of Helsinki



It is a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

8

## Declaration of Helsinki, under General Principles:

While the primary purpose of medical research is to generate new knowledge, this goal can **never** take precedence over the rights and interests of individual research subjects.



**The end can never justify the means.**

9

## Declaration of Helsinki – paragraph 12:



**“Medical research involving human subjects must be justifiable on scientific grounds.”**

- This requirement is meant to eliminate projects that are unlikely to succeed, for example, because they are **methodologically inadequate**
- or even if successful, will likely **produce trivial results**
- even where risk of harm to patients is minimal, there should be an expectation that **important scientific knowledge will be the result.**

From World Medical Association **Medical Ethics Manual**. 2nd edition 2009

10

## Guidelines for reporting studies.

- The **CONSORT STATEMENT** (Statement on Consolidated Standards of Reporting Randomized Trials)
- **STARD** (Standards for Reporting of Diagnostic Accuracy)
- **STROBE** (STrengthening the Reporting of OBServational studies in Epidemiology)
- **PRISMA** (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).



11

## Guidelines for editors



12

## The Vancouver Protocol

Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals ("The uniform requirements").



Issued by the International Committee of Medical Journal Editors (ICMJE).

13

## From the recommendations:

### "Protection of Research Participants"

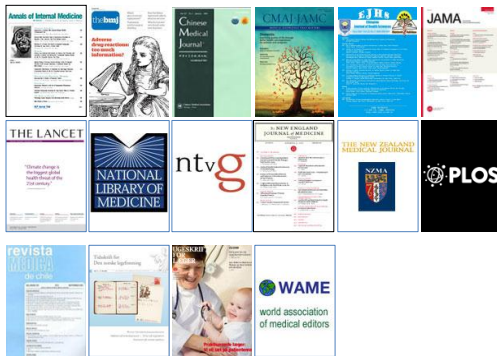
When reporting experiments on people, authors should indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national), or if no formal ethics committee is available, with the Helsinki Declaration as revised in 2008..."



"Approval by a responsible review committee does not preclude editors from forming their own judgment whether the conduct of the research was appropriate."

14

## Member Publications & Organizations



15

## Ethics and methodology

Good methodology prevents waste of resources and risk of bias.

16

## Evidence based medicine

The practice of evidence based medicine means integrating individual clinical expertise with the best available external evidence from systematic research.

Sackett *et al.* BMJ 1996. January 13;312:71-2.



David Lawrence Sackett

17

## The hierarchy of evidence according to study design

1. Systematic reviews and meta-analyses
2. Randomized controlled trials (RCT)
3. Non-randomized controlled trials (cohort, case-control, cross-sectional, case series)



18

## The hierarchy of evidence according to study design

- **Systematic reviews and meta-analyses**
- Randomized controlled trials (RCT)
- Non-randomized controlled trials (cohort, case-control, cross-sectional, case series)



19

## Systematic mapping of systematic reviews in pediatric dentistry. PlosOne. Mejare et. al 2015.

About half of the identified systematic reviews were considered to have high risk of bias, i.e.:

- not at least two independent data extractors (duplicate reading)
- scientific quality of included studies not reported
- scientific quality of included studies not used appropriately in formulating conclusions.

20

## The hierarchy of evidence according to study design

- **Systematic reviews and meta-analyses**
- **Randomized controlled trials (RCT)**
- Non-randomized controlled trials (cohort, case-control, cross-sectional, case series)



21



- **The randomized controlled study has methodological advantages**
- For some questions the best available evidence may come from non-randomized (observational) studies:
  - effects (benefit or harm) of interventions that cannot be randomized/unethical to randomize
  - large samples/long term follow-up time required (rare outcomes).

22

Question: Any differences in intra-and post-operative morbidity, effectiveness and cost-effectiveness between sedation and general anaesthesia?

Main result: No study was eligible for inclusion.

Conclusion: RCT's are required to quantify differences such as morbidity and cost.



23

## Cohort studies with comparison groups on sedation or general anaesthesia.

1. Children chose between the two treatment options.
2. Children treated under sedation were compared with historical data on general anaesthesia.
3. Children previously treated under general anaesthesia were offered treatment under sedation.

**Outcomes:** Post-operative morbidity, patient satisfaction, cost. Sedation was superior to general anaesthesia for all outcomes.

### Potential biases:

- Selection bias (e.g. different treatment needs)
- Confounding (childrens' baseline anxiety)
- Incomplete reporting (historical data).

24

## Risk of bias in non-randomized trials

- **Selection bias** = differences in the baseline characteristics of individuals in different intervention groups (e.g. baseline differences in treatment needs, socio-economy)
- **Confounders** = allocation to groups depends on other factors (e.g. degree of anxiety or other unknown factors). Result in imbalances between intervention and control groups
  - **Study design** = historic controls (risk of overestimating effects of intervention).

25

## Knowledge gaps

26

## A worried voice...



Voltaire

### From Epigrams 1760

Doctors are men who prescribe medicines of which they know little, to cure diseases of which they know less, in human beings of whom they know nothing.

Every patient is different and what is an effective treatment for 90 % of the population may not work for the other 10 %. Thus, medicine is inherently experimental.

## Knowledge gaps



- At some level there will always be uncertainties and knowledge gaps
  - e.g. fluoride toothpaste – what amount is appropriate for pre-school children?
- Important knowledge gaps should be taken care of (James Lind Alliance)
- How can that be accomplished?

28

## The James Lind Alliance (JLA)

- JLA is a non-profit making initiative established in 2004. It brings **patients, carers** and **clinicians** together to identify and prioritize the [Top 10 uncertainties](#), or 'unanswered questions', about the effects of treatments that they agree are most important.
- The aim of this is to help ensure that those who fund health research are aware of what matters to both patients and clinicians.

29

## Conclusions

- Research workers must be aware of the need to conduct ethical research
- Ethical principles must always be considered.
  - Read Instructions to authors carefully!
- Randomized trials are more likely to provide unbiased information than other study designs
- If a question cannot be answered by a randomized trial, a non-randomized trial (NRT) can be a reliable alternative
  - The potential for selection bias and confounding in NRT's must, however, be considered.

30

