Research Methodology In Medical Research

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What Is Research?

- Research is a logical and systematic search for new and useful information on a particular topic
- Research is a planned activity leading to generation of information that will help in answering a specific question

Types of Research

- Conventional research includes descriptive studies and analytical studies.
- Unconventional research, which is gaining more importance nowadays, includes operational research, evaluation of health systems, economic studies (cost benefit, cost-effectiveness, *etc.), qualitative research,* and research synthesis (reviews and meta-analysis)

What are the Objectives of Research?

The prime objectives of research are:

1. To discover new facts
2. To verify and test important facts
3. To analyze an event or process or phenomenon to identify the cause and effect relationship
4. To develop new scientific tools, concepts and theories to solve and understand scientific and nonscientific problems
5. To find solutions to scientific, nonscientific and social problems
6. To overcome or solve the problems occurring in our every day life

Laake, P., Benestad, H. and Olsen, B. (2018). Research Methodology in the Medical and Biological Sciences - 1st Edition. [online] Elsevier.com. Available at: https://www.elsevier.com/books/research-methodology-in-the-medical-and-biological-sciences/laake/978-0-12-373874-5 [Accessed 1 Oct. 2018].

Basis of RM In Medical Research

Every patient is different in the way the disease manifests and also in the response to treatment

- An effective treatment for 90% of the population may not work for the other 10%. Thus, medicine is said to be inherently experimental
- Even the most widely accepted treatments need to be monitored and evaluated to determine whether they are effective for specific patients or for patients in general.
- This is one of the functions of medical research

Basis of RM In Medical Research

- Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their efficacy, accessibility and quality
- Another function is the development of new treatments, especially new investigational drugs, medical devices and surgical techniques
- In other words, the purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and understanding of the etiology and pathogenesis of disease

Steps in Medical Research

1. Research
2. Identify the problem
3. Formulating a research question
4. Refining the research question: Literature review
5. Formulate hypotheses and research objectives
6. Decide the study population and setting
7. Decide on the study design & methodology
8. Writing the protocol
9. Collecting the data
10. Analyze the data and apply statistical significance
11. Write the report

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1. Identify the problem

❑**Interest and expertise:**

❖The topic should be interesting to the investigator, funding agency, and the medical community

❑**Relevance and applicability:**

❖Research should add new information to the scientific society or expected result is likely to alter clinical decisions in future

❑**Feasibility:**

❖Should be feasible in terms of time, manpower and money

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2. Formulating a research question

- Research question is a formal statement of the goal of the study
- Foremost among these is whether the question is interesting
- It is important that the investigator is genuinely curious about the question being investigated, so that he or she can remain motivated till the successful completion of the study
- Curiosity is also an asset in terms of stimulating questions for future studies

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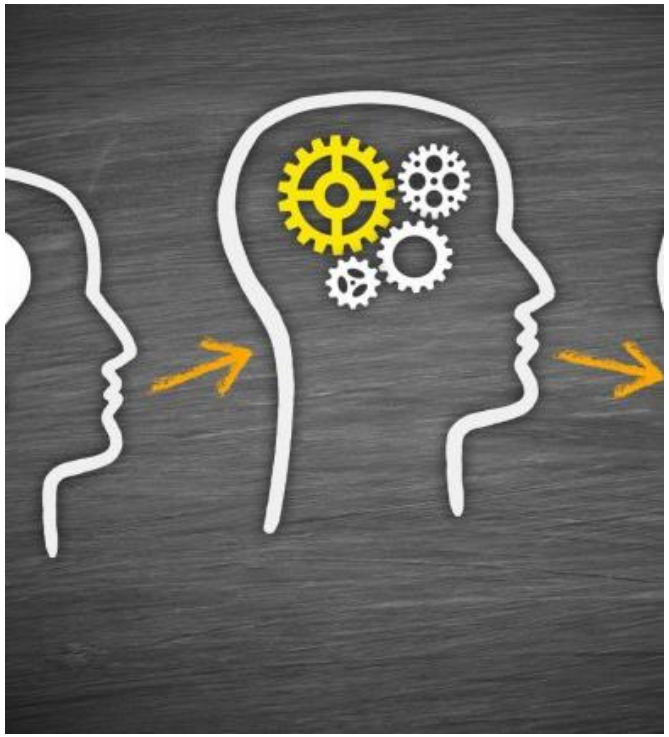
2. Formulating a research question

- Next is feasibility
  - The third consideration is the novelty factor, or the potential of the study to contribute something new to the knowledge base
  - Related to novelty is the relevance of the research question.
- It should add to existing knowledge, guide future studies, or have implications for education, clinical practice or health care policy.



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2. Formulating a research question

- Finally, the idea must be ethical
  - Studies that invade people's privacy or create possible physical or psychological risks are ethically unacceptable

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A good research question could thus be described by the acronym

F: Feasible

I: Interesting to the investigator

N: Novel

E: Ethical

R: Relevant

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An useful format to use in the development of a specific research question is the PICO format

- Format the population (P) of interest the intervention (I) being studied, the comparison (C) group (the intervention being compared) and the outcome of interest (O)
- Often timing (T) is added to PICO, indicating the time frame in which the study will be completed
- In patients with pneumonia (P) whether treatment with X (I) compared to Y (C) reduces the number of days of hospital stay (O)

3. Refining the research question: Literature review

Once the problem or question is specified, the next step is to collect as much related information as possible

- Literature review will help to determine
- To what extent the issue or research question has been previously researched,
- To identify the past relevant studies as well as methods used,
- To refine the research question and
- Also to put the project and methodology into A relevant context

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4. Formulate hypotheses and research objectives

The research hypothesis is developed from the research question

- For example, in the research study comparing treatment X versus treatment Y in patients with pneumonia, the experimental group would be treatment X and the control/ conventional group would be treatment Y

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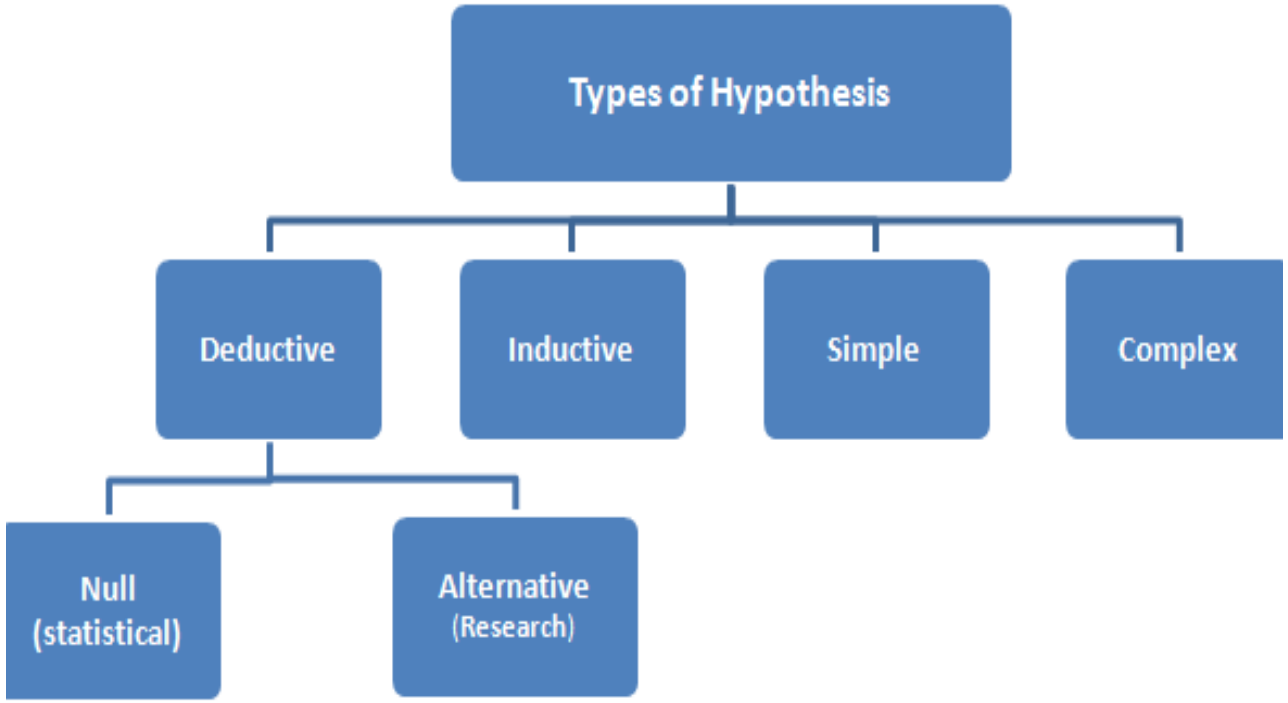
4. Formulate hypotheses and research objectives

- The investigative team would first state a research hypothesis.
- This could be expressed as a single outcome, e.g., treatment X leads to improved functional outcome



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5. Decide the study population and setting

The definition of the subject of study and the target population should be clearly spelt out

- The inclusion and exclusion criteria should be decided in the beginning itself
- Sample size is very important
- The smaller the sample, the more will be the uncertainty
- Sample size should be chosen in such a way that the finding in the study accurately reflects what is going on in the population

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5. Decide the study population and setting

- A well designed study, poorly analyzed, can be rescued by re analysis but a
- Poorly designed study is beyond the redemption of even sophisticated statistics

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5. Decide the study population and setting

- To get valid and reliable answer to the questions, appropriate research design and method is a prerequisite
- Study design is the frame work in which investigation is planned and carried out
- Selection of design is necessarily based on type of research question

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6. Research designs

Observational

Studies in which subjects are observed-includes:

- Case study/case series
- Case-Control
- Cross Sectional
- Cohort/Longitudinal

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6. Research designs

Experimental

Studies in which the effect of an intervention is observed

- Controlled trials
- Diagnostic Test

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Research Study Designs

1. **Case Reports**
2. **Case Series**
3. **Analyses of Secular Trends**
4. **Case – Control Studies**
5. **Cohort Studies**
6. **Randomized Clinical Trials**

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Case Reports

- **Are simply reports of events observed in single patients.**
- **Useful for raising hypotheses about drug effects. Leads to the drug test with more rigorous study design.**
- **Very rare to use to make a statement of causation.**
- **Exception to this is when the outcome is very rare and so characteristic that one knows that it is due to the exposure.**
- **Is accepted when challenge situation is very fatal.**

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Case Series

- **Collections of patients, all of whom have a single exposure, whose clinical outcomes are then evaluated and described.**
- **Alternatively case series can be collection of patients with a single outcome, looking at their antecedent exposure.**
- **Useful for quantifying the incidence of an adverse reaction or whether occurs in larger population.**
- **Just provides clinical descriptions of a disease or of patients who receive an exposure.**

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Analyses of Secular Trends

- **Called as ecological studies.**
- **Examines trends in an exposure that is a presumed cause and trends in a disease that is a presumed effect and test whether the trends coincide.**
- **Vital statistics and record linkage are often used in these studies.**
- **Useful for rapidly providing evidence for or against a hypothesis.**
- **Unable to control confounding variables. E.g. lung cancer might be the cause of cigarettes but chance of occupational hazards can still not be ruled out**

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Case – Control Studies

- **Compare cases with the disease to controls without the disease, looking for differences in exposure.**
- **Multiple possible causes of a single disease can be studied.**
- **Helps in studying relatively rare disease requires smaller sample size.**
- **Informations are generally obtained retrospectively from the medical records, by interviews or questionnaires.**
- **Limitations are validity of retrospective information and selection of control is challenging task. Inappropriate control selection can lead to incorrect conclusion.**

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Cohort Studies

- **Identify subsets of a defined population and followed them over time, looking for differences in their outcome.**
- **Used to compare exposed patients to unexposed patients, can also be used to compare one exposure to another or when multiple outcomes from single exposure is to be studied.**
- **Either done prospectively or retrospectively.**
- **More reliable causal association.**
- **But requires large sample size (even for an uncommon outcome) and can require prolonged time period to study delayed outcomes.**

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Differences between Cohort study and Case – Control study

		Case – Control Studies ↓ Disease	
Cohort studies ↓ Factor		Present (Cases)	Absent (Controls)
	Present (Exposed)		
	Absent (Unexposed)		

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Randomized Clinical Trials

- **An experimental study – the investigator controls the therapy that is to be received by each participant.**
- **Major strength is the randomization.**
- **Problems might include the ethical issues and are expensive. They are not of big importance after marketing.**

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Meta-Analysis Studies

DEFINITION

Meta-analysis has been defined as the statistical analysis of a collection of analytical results for the purpose of integrating the findings

USE OF META-ANALYSIS ?

Identify sources of variation among study findings

To provide an overall measure of effect as a summary of those findings

Meta-analysis is most often used to assess the ***clinical effectiveness of healthcare interventions;***

it does this by combining data from two or more randomized control trials.

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Meta-Analysis Studies

Meta-analysis of trials provides a ***precise estimate of treatment effect,*** giving due weight to the size of the different studies included.

Important: Studies chosen for inclusion in a meta-analysis must be sufficiently similar in a number of characteristics in order to accurately combine their results.

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Where does meta analyses fit in the research process ?

- The graphical elements of the meta-analysis, such as the forest plot, provide a mechanism for presenting the data clearly, and for capturing the attention of the reviewers.
- Some funding agencies now require a meta-analysis of existing research as part of the grant application to fund new research.

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Evidence Based Medicine

EBM is an approach to medical practice that uses the results of patient care research and other available objective evidence as a component of clinical decision making.

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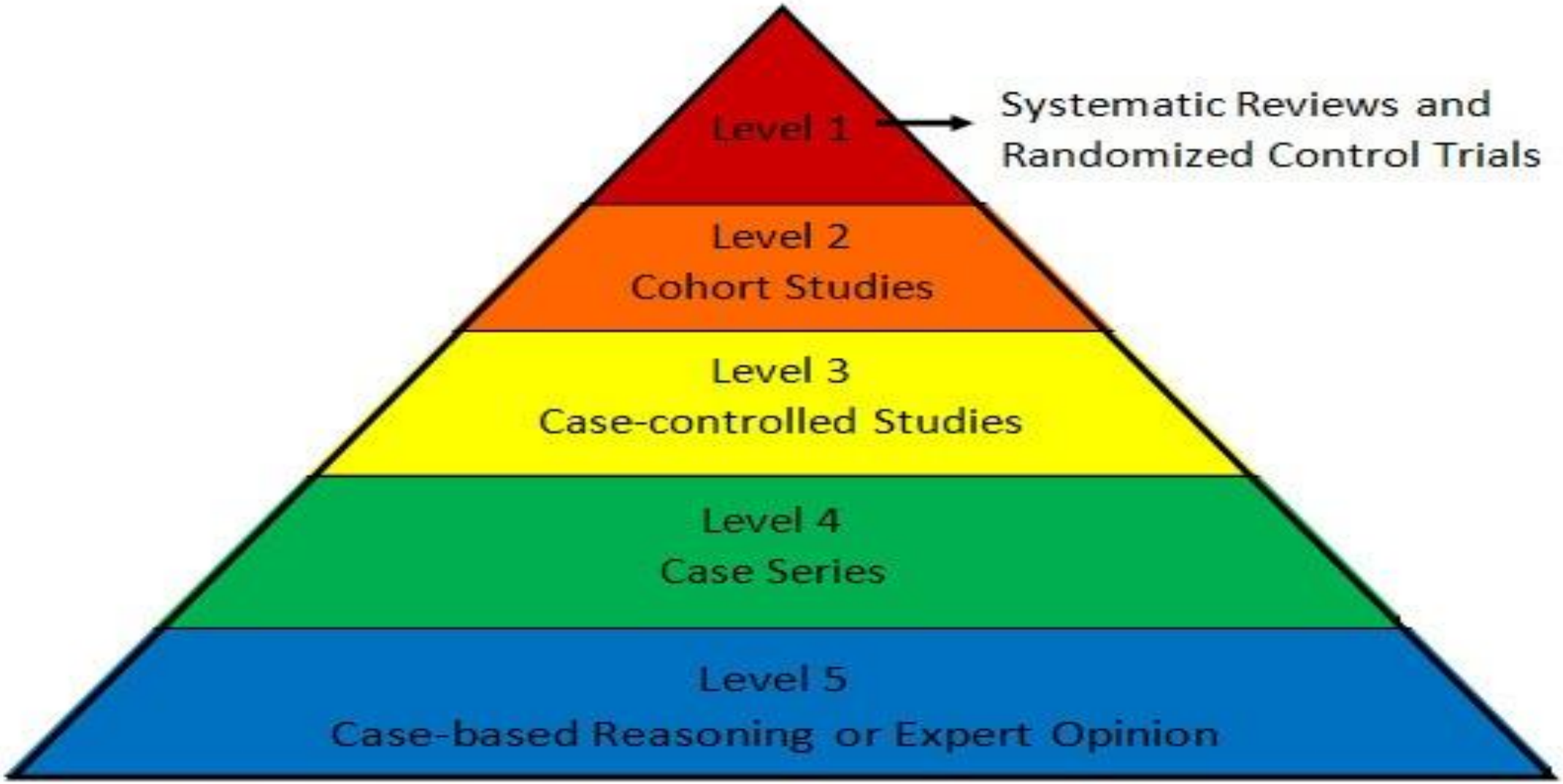

*based on the Oxford Centre for Evidence-based Medicine – Levels of Evidence

Need for Evidence based medicine

1) **Daunting number of diseases.**
2) **Availability of broad number of therapeutic options**
3) **To Keep ourselves updated in the field of expertise.**
4) **Addition in number of information sources.**
5) **To remain competent throughout the careers.**

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7. Writing the protocol

- All the efforts put into preceding steps culminates into the draft of the research protocol that incorporates all the information regarding the research in a concise manner

- The protocol should contain background information on the study, objectives, ethical aspects, study design, study procedures, method of assessment, statistics and evaluation, administrative issues and references

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7. Writing the protocol

- Once the protocol is ready, approval from the Ethics committee should be obtained before the start of the study
- Along with the protocol, the informed consent form and other documents required should also be submitted to Ethics committee for approval

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8. Collecting the data

- Once the protocol is finalized, the data should be collected
- The data forms should be legibly filled, and they should be fully completed
- Ethical issues must be taken care of from the beginning to the end of study
- In drug trials care must be taken to document the details of adverse events if any
- Proper documentation through out the study is important to ensure credibility of data

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9. Analyze the data and apply statistical significance

- The data should be scrutinized for internal consistency and external validity
- Data should be analyzed using the already decided data management plan

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10. Write the report

- The report should be sufficiently detailed that can remove any doubt a reader might have about any aspect of the results
- It should be properly worded, should be adequately illustrated by charts or diagrams or tables which enhance the clarity
- All the limitations need to be described openly

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Ethical Considerations in Medical Research

Definition of Scientific Misconduct

Scientific misconduct is fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

The Basics of Ethics in Research

Dishonest, fraudulent, or unethical researchers can circumvent the scientific method

Notable examples:

1. Nazi Germany Experimentation

- Charges brought against 23 German physicians in the Nuremberg War Crime Trials for their medical experiments – included:
  1. Freezing Experiments
  2. Malaria Experiments
  3. High-Altitude Experiments

- Led to the development of

Nuremberg Code

The Basics of Ethics in Research

2. The Tuskegee Syphilis Study

Was investigation of long-term effects of untreated syphilis on AA males in Macon County,AL

Decision was made to do long-term prospective study and follow long-term effects until death

Participants were never told real nature of study – were not afforded informed consent

Treatment for syphilis was withheld (even after discovery of penicillin to treat syphilis) – study continued for 40 yrs.


(Courtesy National Archives)

Regulation of research and protection of research participants:

Proponents of situational ethics argue that no general rules can be applied to all situations – each action is unique

Belmont report – serves as a fundamental document for current federal regulations for protection of human subjects – 3 principle:

1. *Respect for Persons*
2. *Beneficence*
3. *Justice*

**Code requires that protocols involving human subjects be reviewed by an IRB.*

Informed Consent

Inherent to this principle are 4 elements:

1. Subjects are made fully aware of the nature and purpose of the research project

2. Consent is voluntarily given

3. The person involved has the legal capacity to give ***consent***

4. The responsibility for obtaining consent rests with the ***researcher***

* Sometimes, because of the Hawthorne Effect, it may be necessary to use some deception in telling subjects about the study.

Privacy and Confidentiality

Privacy refers to capacity of individuals to control when and what conditions others have access to their behaviors, beliefs, and values.

Confidentiality refers to linking information to a person's identity

- **CAN YOU THINK OF EXAMPLES WHERE CONFIDENTIALITY WOULD BE IMPOTANT?**

Informed consent should indicate how researcher will protect confidentiality of participants

Privacy and Confidentiality

Some procedures that can ensure confidentiality:

- Obtaining anonymous information
- Code data so that identifying info is eliminated
- Substitute other names
- Do not release or report individual data
- Limit access that could reveal individual identity
- Report data only in group form
- Used computerized methods for encrypting data

Six Areas of Scientific Dishonesty

1. Plagiarism—using the ideas, writings, and drawings of others as your own
2. Fabrication and falsification—making up or altering data
3. Nonpublication of data , also called “cooking data”
4. Faulty data-gathering procedures

Six Areas of Scientific Dishonesty

5. Poor data storage and retention

6. Misleading authorship—who should be an author?

- Technicians do not necessarily become joint authors.
- Authorship should involve only those who contribute directly.
- Discuss authorship before the project!

CONSTITUTION OF IRB

The IRB should consist at least SEVEN members, who collectively have the qualifications and experience to review and evaluate the science, medical aspects, and ethics of the proposed trial. viz.

1. Chairperson – Appointed (who is from outside the institution)
2. 1-2 basic medical scientists (i.e. Clinical Pharmacologist)
3. 1-2 clinicians from same institute
4. One legal expert
5. One social scientist
6. One philosopher or ethicist
7. One lay person from community
8. Member secretary – Appointed

Drugs & Cosmetic Act 1940, Schedule Y

QUORUM OF IRB

For reviewing and making decision on each protocol the quorum of IRB should be at least FIVE members with the following representations:

1. Basic medical scientists (preferably one pharmacologist)
2. Clinicians
3. Legal expert
4. Social scientist / Representative of non-governmental voluntary agency / Philosopher / Ethicist / Theologian or a similar person
5. Lay person from the community

Drugs & Cosmetic Act 1940, Schedule Y

QUORUM OF IRB

In any case, the IRB must include

1. At least one member whose primary area of interest / specialization is nonscientific
2. At least one member who is independent of the institution / trial site
3. Besides, there should be appropriate gender representation on the IRB
4. If required, subject experts may be invited to offer their views
5. Further, based on the requirement of research area, e.g. AIDS, genetic disorders etc. Specific patient groups may also be represented in the IRB

Drugs & Cosmetic Act 1940, Schedule Y

Conclusion

- Research is a scientific method used to collect and analyse information to increase our understanding or solve issue on particular field.
- The research topic should be Feasible, Interesting, Novel, Ethical and Relevant.
- The ethical consideration should be taken care of conducting the research.
- The research result should not be biased, both the negative and positive results should be reported/published.


Thank
you