Reasoning About the Design and Execution of Research

The Scientific Method

- This is a set of steps that defines the appropriate order of events to structure and carry out an experiment.

1. Generate a Testable question 2. Gather Data & Resources 3. Form a Hypothesis 4. Collect New data 5. Analyze the data 6. Interpret the data and existing hypothesis 7. Publish 8. Verify the results

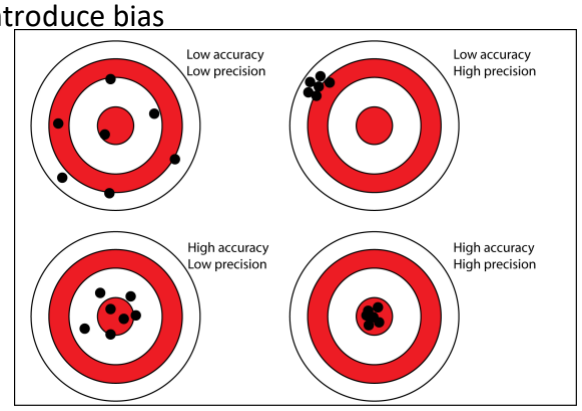
The FINER Method

Method to determine whether the answer to one's question will add to the body of scientific knowledge in a practical way.

- Is the necessary research going to be **feasible?**
- Do other scientists find the question **interesting**?
- Is this particular question **novel?**
- Would the study obey **ethical** principles?
- Is the question **relevant** outside the scientific community?

Basic Science Research

- Conducted in a laboratory and not on people.
- Controls: conditions can be applied to multiple trials of the same experiment that are as near identical as possible. This acts as a standard to verify results.
    - Positive Controls: those that ensure a change in the dependent variable when it is expected.
    - Negative Controls: Ensure no change in the dependent variable when no change is expected. (**Placebo Effect)**
- Causality: **Independent variable** is manipulated and **dependent variable** is measured or observed.
    - If there is a theoretical or known mechanisms that links the two variables, a causal relationship can be investigated. If change in the independent variable always precedes the change in the dependent variable, and the change in the dependent variable does not occur in the absence of the experimental intervention, then the relationship is said to be causal.
- Error Sources: Not much source of bias unless intentionally done so by the researcher.
    - Accuracy: ability of an instrument to measure a true value (**Validity**)
    - Precision: ability of the instrument to read consistently (**Reliability**)
    - Systematic Errors: only an inaccurate tool will introduce bias
    - Random Errors: introduce by an imprecise tool.



Human Subjects Research

Experimental Approach

- Randomization: method used to control for differences between subject groups in biomedical research. Ideally, each group is perfectly matched on conditions such as age and gender.
- Blinding: Researchers do not have information about which group the subject is in.
    - Single-Blind: Only the patient or the **assessor** is blinded.
    - Double Blind: The investigator, assessor and subject are blinded.
- Data Analysis: must account for variables outside the independent and dependent variables considered. Some variables can be accounted for, but sometimes **confounding variables** may exist.
    - Programs can use **binary**, **continuous, or categorical variables** to create a **Regression model**. The model may be used to demonstrate relations.

Observational Approach

- Studies conducted when experiments cannot be conducted for ethical or practical reasons. These cannot demonstrate causality, can only be used to look for possible connections.
    - Cohort Studies: subjects are sorted into groups based on differences in risk factors (**exposures**), and then assessed at various intervals to determine how many subjects in each group had a certain **outcome**.
    - Cross-Sectional Studies: Attempts to categorize patients into different groups at a single point in time.
    - Case-Control Studies: Identify subjects with or without a particular outcome, and then looks backward to assess how many subjects in each group had exposure to a particular risk factor.

Hill's Criteria

- Describes the component of an observed relationship that increase the likelihood of causality in the relationship. Only first criterion is absolutely necessary for relationship to be causal, the more that are satisfied, the better.
- Do not provide an absolute guarantee of causation, should instead state that relationship demonstrates **correlation**.
    - Temporality: exposure must occur before the outcome
    - Strength: More variability in the outcome that is explained by the variability in the independent variable, the more likely the relationship is causal.
    - Dose Response Relationship: As independent variable increases, there is a proportional increase in the response.
    - Consistency: relationship is similar in multiple settings
    - Plausibility: reasonable mechanism for the independent variable to impact the dependent variable.
    - Consideration of alternative explanation: Determine if all other plausible explanations have been eliminated
    - Experiment: see if an experiment can be performed

    - Specificity: change in outcome variable is only produced by an associated change in the independent variable
    - Coherence: New data and hypothesis are consistent with the current state of scientific knowledge.

Error Sources

- **Bias** is a result of flaws in the data collection phase and is a systematic error which skews the results in one direction or another.
- **Confounding** is an error during analysis.
- Selection Bias: Subject used for the study are not representative of the target population. Most prevalent
- Detection Bias: educated professionals using their knowledge in an inconsistent way.
- Observation Bias: **The Hawthorne effect** posits that the behavior of study participants is altered simply because they recognize that they are being studied.
- Confounding: data analysis error where an incorrect relation is characterized. Where two variables are related, but they are not the cause of the relation.

Ethics

- Four basic tenets of ethics in medicine: **beneficence** (the obligation to act in the patient's best interest); **nonmaleficence** (avoid treatments or interventions in which the potential for harm outweighs the potential for benefit); respect for patient **autonomy**; and **justice** (treat similar patients with similar care). These are slightly changed when it comes to research.

Respect for Persons

- The need for honesty between the subject and the researcher. Included process of **informed consent**.
- Investigator cannot assert coercive influence over subjects
- Confidentiality also a part of this
- Need to respect participants wishes to continue or cease participation in study.

Justice

- **Morally relevant differences** are the differences between individuals that are considered an appropriate reason to treat them differently. Things like age, population size are examples.
- Important in selection of participants and execution of research. Must make sure that no specific group is put in any excess harm.

Beneficence

- It must be the researcher's intent to cause a net positive change for both the study population and the general population, and all measures must be taken to minimize any potential harms.
- Equipoise: one cannot approach the research with the knowledge that one treatment is superior to the other when comparing two or more options.

Research in the Real World

- **Population** is the complete group of every individual that satisfies the attributes of interest
    - Information from populations are called **parameters**
- **Sample** is any group taken from a population that does not include all individuals. These samples would ideally be representative of the population as a whole.
    - **Random samples** are generally the gold standard for ensuring this.
    - **Statistics** are the information gathered from a sample.
- Generalizability: also called **external variability**, studies with low generalizability have a very narrow set of conditions for sample selections that does not reflect the target population.
- Want to generate results that are **statistically significant**. But sometimes mathematical significances will not cause a noticeable change in patient outcomes. As such, it must be assessed whether there is **clinical significance** (a notable or worthwhile change in the health status as a result of an intervention).