

A Very Small Introduction to Research Methods (Day 2)

Prepared for the Brilliant
Fourth Year FRMS Students

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Learning Outcomes

By the end of this workshop, participants will be able to:

- Evaluate and appreciate the relevancy and importance of research in Health Sciences.
- Formulate and manipulate several hypotheses pertaining to the topic of interest according to the different research designs.
- Choose an appropriate research design based on research topic of choice.
- Construct the different components of a research proposal

Why Do Research???

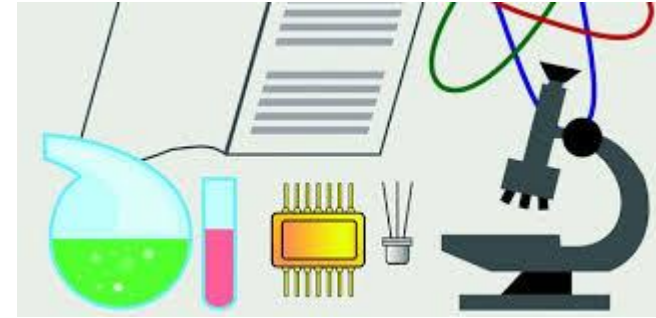
- Answer questions
- Satisfy curiosity
- Correcting old/wrong ideas
- Further ideas
- Add to the body of knowledge
- Makes you smarter

Why Do **Clinical** Research??

Passing on the ball to
HELP MANKIND

Types of Research

Basic Science (Lab)



Translational
(connecting the two
above)



Population
(surveys/stats/patterns)

Translational Research

T1 – Bench-to-bedside (lab to clinical trials)

- Must fill the gap of knowledge between the two sciences (Basic and Clinical)
- Researcher must be able to understand both sciences
- Collaborate

T2 – Clinical Trials-to-population

- ID the correct population
- Follow up

T0

T1

T2

T3

T4

**BASIC SCIENCE
RESEARCH**

Preclinical
and animal
studies



Defining
mechanisms,
targets, and lead
molecules

**TRANSLATION TO
HUMANS**

Proof of
concept
Phase 1
clinical
trials



New methods
of diagnosis,
treatment, and
prevention

**TRANSLATION TO
PATIENTS**

Phase 2
and 3
clinical trials



Controlled studies
leading to
effective care

**TRANSLATION TO
PRACTICE**

Phase 4
clinical trials
and clinical
outcomes
research



Delivery of
recommended
and timely care to
the right patient

**TRANSLATION TO
COMMUNITY**

Population-
level
outcomes
research



True benefit
to society

Translation from basic science to human studies

Translation of new data into the clinic
and health decision making

Philosophy: The study of problems concerning anything

- Epistemology: The theory of knowledge
 - how did you come to know
 - What justifies knowledge?
 - How much truth, and how did you get to it to make it a belief (knowledge)?
- Methodology: The applied particular procedures
 - Logic: Valid demonstration and inference.
 - Validity: best approximation to the truth of a given proposition, inference, and conclusion.

By the way, Do you know the difference
between inference and conclusions?



Let's challenge you

Which of the two Sentences is true? Or are they both true or both false?

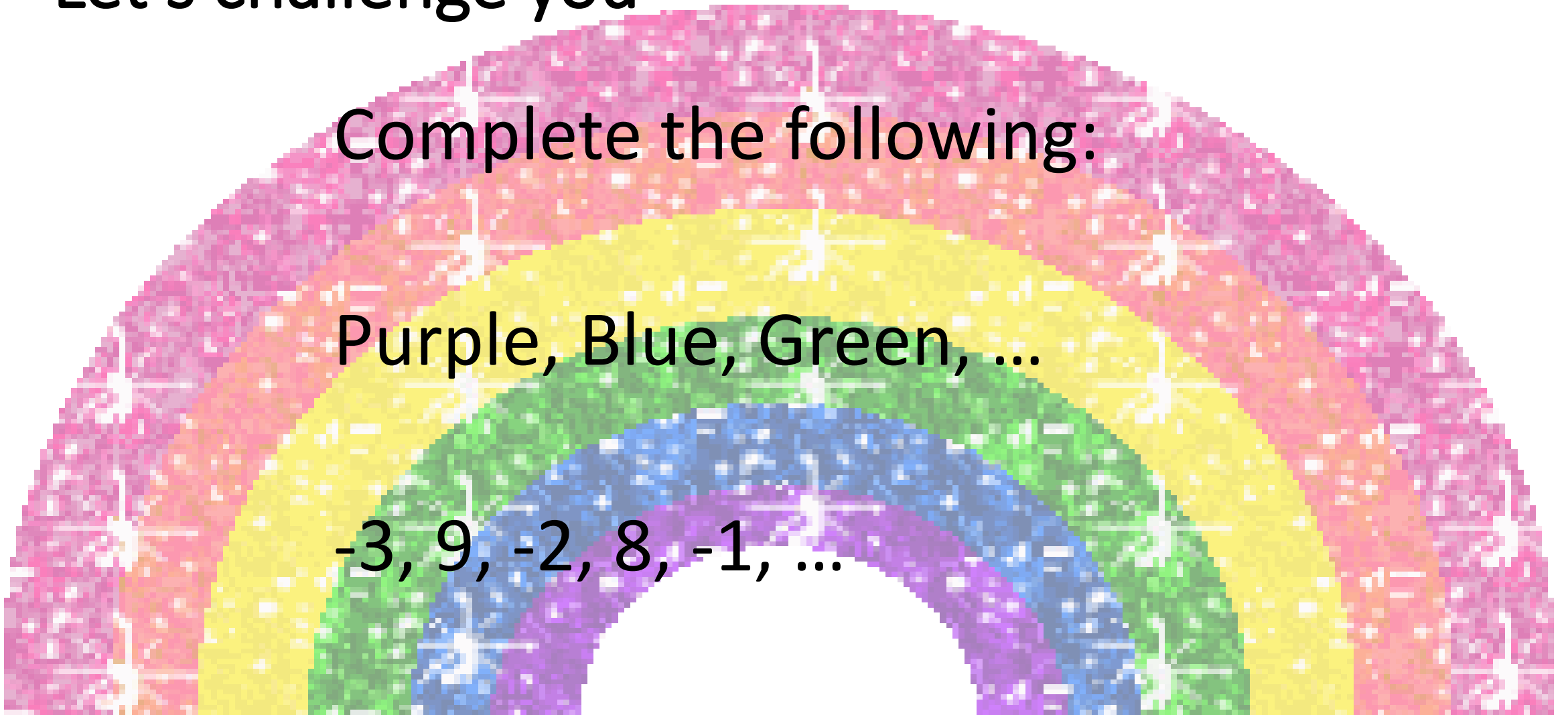
- If all FRMS students have above-average IQ score and Sarah is an FRMS student, then Sarah has an above average IQ score.
- If all FRMS students have above-average IQ score and Sarah has above average IQ score, then Sarah is an FRMS student.

Let's challenge you

Complete the following:

Purple, Blue, Green, ...

-3, 9, -2, 8, -1, ...



Source of Knowledge

- Deductive Reasoning
 - Making sense and logic
- Inductive Reasoning
 - Finding patterns



Let's challenge yet another time

Which question one is deductive and which is inductive?

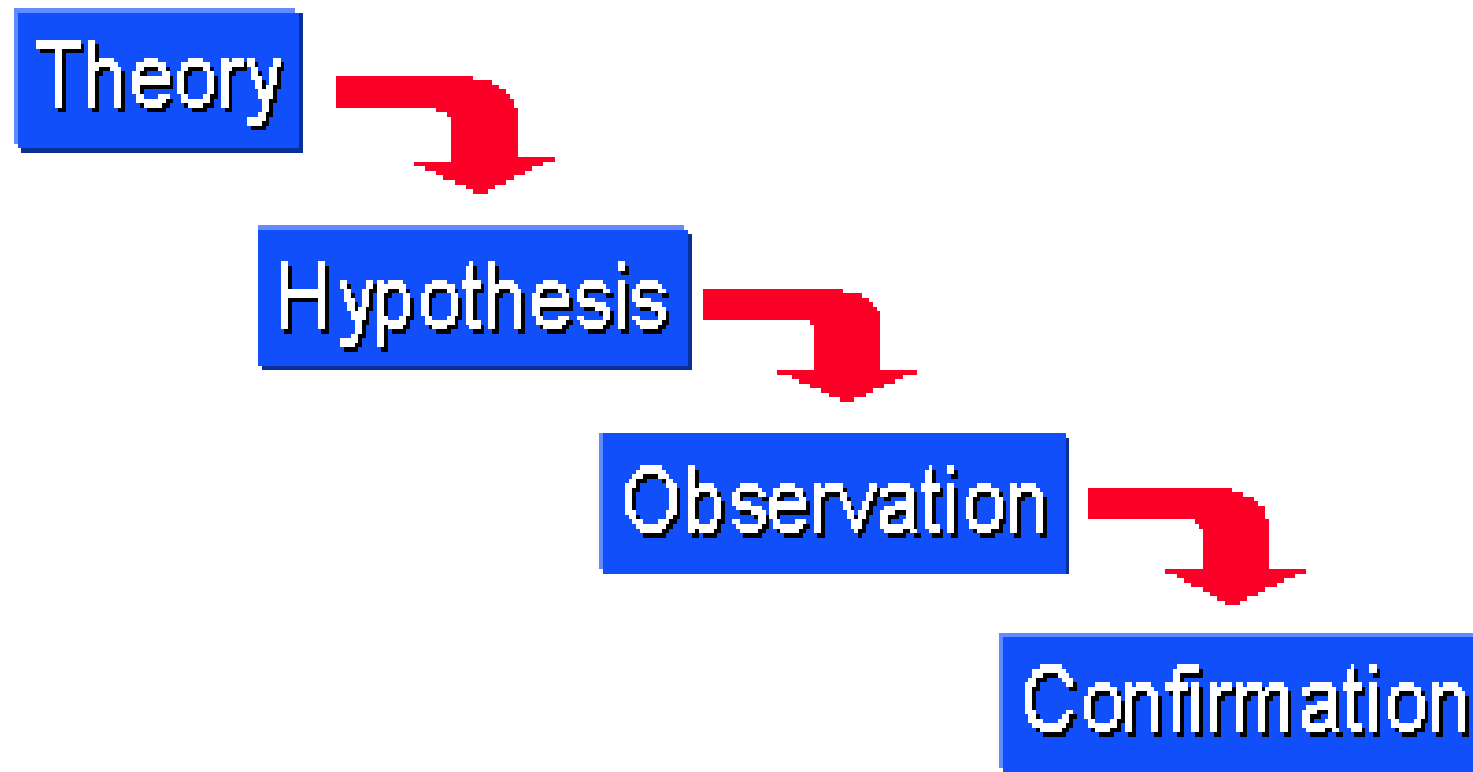
Complete the following:



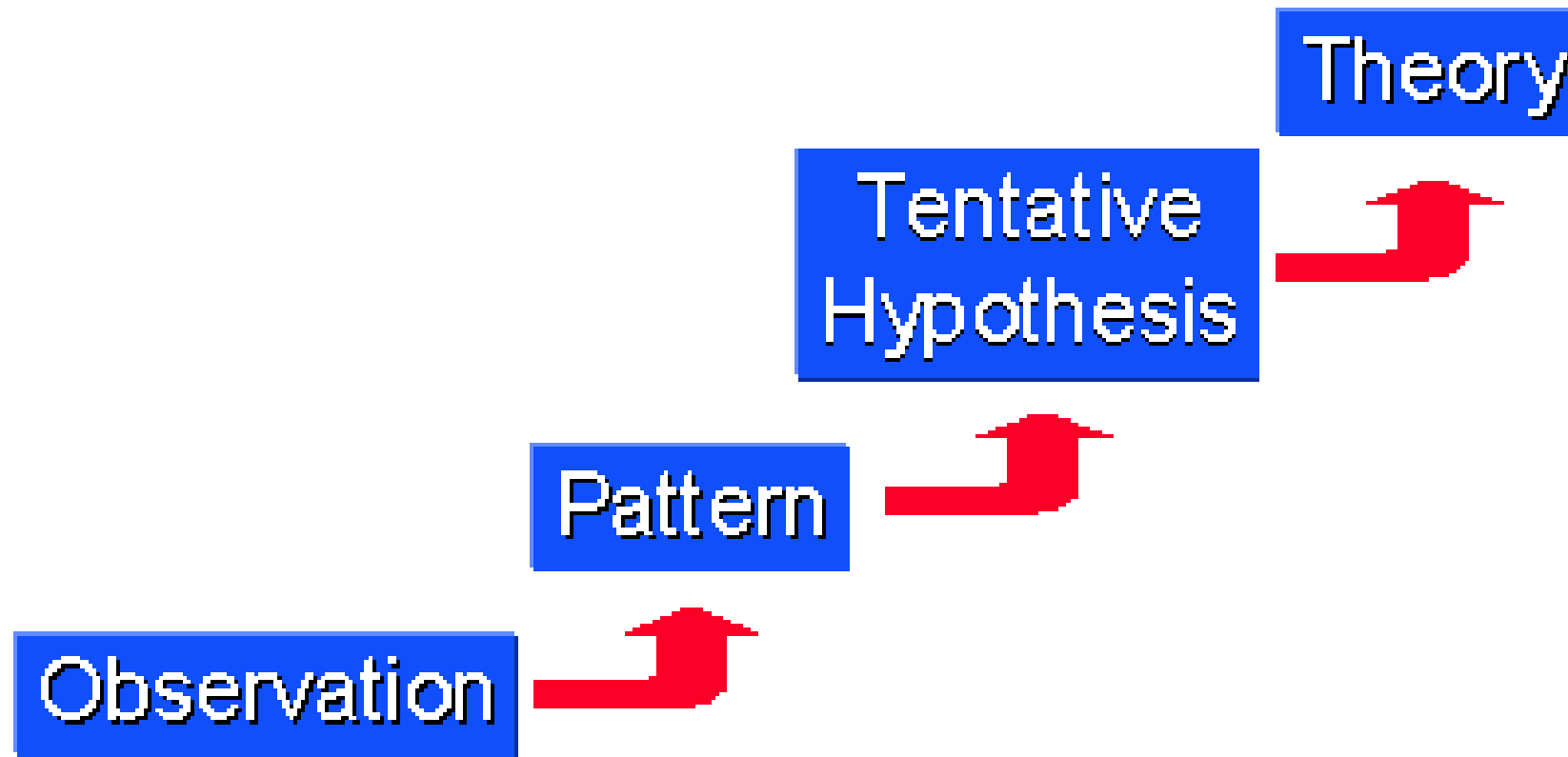
Which of the two Sente
true or both false?

- If all FRMS students have ab
is an FRMS student, then Mc
- If all FHS students have abov
has above average IQ score,

- Top-down
- More general to more specific
- Exploratory



- Bottom-up
- More specific to more general
- Confirmatory



And so, if I want to turn the argument below to inductive, it would be ...

- If all FHS students have above-average IQ score and Mohammed is an FHS student, then Mohammed has an above-average IQ score.
- Because we conducted an IQ test on all students admitted to our college and found that Mohammed like the rest of the students has an above-average IQ score

Who is controlling who???

- Studying the correlation between car accidents and texting
Texting → car accidents
- The excellent grades of a student as a relationship with studying hours
Studying → excellent grades
- The later side effects of steroid use with regards to heart muscle enlargement, heart failure and liver damage
Steroids → heart and liver problems

Some Definitions

Variables

- **Independent** (Predictor): it is what you or nature is manipulating
- **Dependent** (Outcome): it is dependent on/effected by what you or nature manipulated
- Qualitative vs. Quantitative
- Subject (sample) vs. population

Validity

- Internal Validity: Making the correct conclusion within the findings of your experiment

Measuring the fasting glucose of a patients, finding it high, and inferring that they are diabetics

Concluding the average IQ of FRMS Students by testing this classroom

Validity

- External Validity: Making the correct generalization to subjects outside the study.

IQ in Jeddah by testing the classroom

Validity

- External Validity: Making the correct generalization to subjects outside the study.

IQ in Jeddah ~~by testing the classroom~~

Conceiving the Research Question

Why Do Researchers Ask?

- Resolve a problem
 - Clear Uncertainty
 - Make money
 - Curiosity
 - In health, help mankind
-
- *To answer an uncertainty about something in the population that you (the researcher) want to resolve by measuring/experimenting on subjects that represent the population.*

Where Do Questions Come From?

- Literature
 - Journals
 - Old Data
 - Media
- Looking for New ideas or techniques
 - Skepticism
 - Don't be shy

- Imagination
 - Keeping an open mind
 - Creativity
 - SiFi movies and TV
- Advisors
 - *(I believe this is the simplest most important)*

Characteristics of Good Research

FINER

- **F**easible: can it be done
 - Subjects
 - Techs
 - Cost
 - Time
 - Scope (*early recognition and backing off*)

- **I**nteresting

- Must pass the “*So what?*” Test

- **N**ovel

- Don't reinvent the wheel unless in a new way

- **E**thical

- **R**elevant

- Must pass the “*Why should my grandmother care?*” Test

When Thinking about a question...

- Background and Significance
- Design
- Study Subjects: excluded or included according to a criteria.
- Variables
 - Independent Variables (Predictor): What is being manipulated
 - Dependent Variables (Outcome): What is measured
- Statistical Tools

First Exercise

Write your research question
and why it is a FINER question

The Hypothesis

What is a Hypothesis

- A statement
- Claiming a tentative fact
- But still needs to be tested
- A provisional idea whose merit requires evaluation (wiki)
- Specific version of the research question that summarizes the main elements of the study.

Types of hypotheses

- **Null Hypothesis:** There is no association between the variables.
- **Alternative Hypothesis:** There is an association
- **One sided (one tailed):** The association is directional
- **Two sided (two-tailed):** only states that there is an association

When are they used?

One-Sided

- When the results are meaningful in one direction only
- When other studies indicated similar results
- Effect of smoking on lungs

Two-Sided

When both sides could be interesting and can be published regardless to the outcome as meaningful results.

Exercise for children with DMD

Characters of Good Hypotheses

- Specific and focused: state the test, subject and outcome. Go to the point
- Short: do not tell a story of how and why
- Simple: One predictor and one outcome
- Written in advanced: helps keeping the research concise and focused

Some Bad examples...and a couple of good ones... find them 😊

Innate immune receptors participating in bacterial recognition pathways, such as Toll-like receptors (TLRs) on the cell surface and NOD-like receptors (NLRs) in the cytosol, sense the types of bacteria present in Bacterial Vaginosis, and play a role in pathogenesis of this common condition.

Decreased expression of CD59 allows the binding of C5b-7 and of C9 leading to destruction of red and white blood cells in hyperhemolysis syndrome of acutely and chronically diseased patients.

Since SBP1 was evidenced to be an autoantigen, the presence of this autoantigen could mean possible risk for cancer; hence, the detection of this antibody against SBP could also suggest the risk for ovarian cancer.

The length of the telomere in HIV infected subjects is comparable to uninfected elderly individuals.

The diagnosis of ovarian cancer involves the examination of the cell nucleus morphology. The nucleus undergoes morphological changes as it differentiates into a cancerous cell. These tumor-related transformations are recognized as an early event in malignancy and result in modification of nuclear matrix proteins at the molecular level. An autoimmune response is triggered when the nuclear matrix proteins are released into circulation.

- individual's with sarcopenia will have more insulin resistance than individuals without sarcopenia.
- Influenza infection during pregnancy does not increase the risk of developing schizophrenia.

- Studies have reported anti-ovarian autoantibodies in sera of humans and hens with ovarian cancer. Researchers have also observed nuclear morphological changes associated with early stage ovarian cancer in hens. Thus it is hypothesized that anti-nuclear matrix protein antibodies will predict nuclear morphological changes in cells associated with early ovarian cancer in the spontaneous laying hen and will be correlated with ovarian tumor angiogenesis.

- There is an association between the use of statins and the prevention of secondary myocardial infarctions.
- caffeine consumption can increase one's risk of certain types of cancer, specifically colon cancer.
- Prolonged use of oral contraceptives such as those containing DRSP or LNG significantly increases the incidence of deep vein thrombosis.

Exercise 2

Turn your research question into a valid alternative hypothesis and state the null

Statistical Error

Type I

- False Positive
- Rejection of the null
- Erroneous acceptance of the alternative hypothesis

Type II

False Negative

Failure to reject the null hypothesis

Erroneous rejection of the alternative hypothesis

Statistical Significance

- The probability of committing a type I error (false positive) is known as the alpha (α) value
- Small value that gives an upper limit of the chance of incorrectly rejecting the null hypothesis
- ~0.01- 0.05

The probability of committing a type II error (false negative) is known as the beta (β) value

Failure to reject the null when it is actually incorrect

~0.05 -0.20

Depends on the situation

- Studying the efficacy of biopsies to diagnose OVCA

- $\alpha = 0.20$

- 20 out of every 100 women will be subjected to a dangerous and invasive technique for nothing

Using CA125 as a biomarker to detect early stage OVCA

$\beta = 0.30$

30 out of every 100 women with OVCA will be misdiagnosed/under diagnosed

Jury Decision

- | | |
|---|------------------------------------|
| • Innocence: ----- | Null |
| • Guilt: ----- | Alternative |
| • Beyond reasonable doubt: --- | Significance (α) |
| • Acquit an innocent person or
convect a criminal: ----- | Correct inference |
| • Convect an innocent person: | Type I error (<i>false pos</i>) |
| • Acquit a criminal: ----- | Type II error (<i>false neg</i>) |

POWER

- The quantity of $1-\beta$ is power
- The probability of correctly rejecting the null hypothesis and accepting the alternative
- A power of 0.90 means that the samples will fall under the predicted outcome by the alternative hypothesis 90% of the time.

P-Value

- The chance (%age) of null is true
- The null hypothesis is rejected in favor of its alternative **only** if the P value is smaller than α (significance)
- In other words, the results cannot be explained by the alternative hypothesis alone, but it could NOT be explained by chance as well.
- The smaller the P -value the better.

Literature Review

Why Review the Literature?

1) What's been done so far

- Should provide you with the following:
 - The latest trends in your topic
 - Any gaps that you may answer
 - A concept for how you will answer your question

2) Level of Existing Knowledge and theory

- Determine the level of knowledge
 - Descriptive
 - Explanatory
 - Predictive
- The methodology applied to gather data
- How relevant to your topic

3) Relevance and rational to your investigation

- A well written lit review should
- Very good story, that...
- Flows directly into your research plan, and...
- Supports your choice of topic due to its relevance and choice of study design due to its innovation

How to Conduct a Lit Review

- **When?**

- Start early to get an idea or to fine tune one that you already have.
- Keep searching while conducting research
- In case using databases and previous results it can be part of your results
- And always remember, three months in the lab will save you one hour in the library.

What?

- Journals: Latest work and techniques
- Books: Basic fundamental concepts

How?

- **Set Parameters**
 - Your topic
 - Related topics
 - Related methods
 - Start from a central point and branch off
 - Use good keywords

Organization makes a world of difference

- You are not going to read everything at first
- Abstract:
 - directly related: good for latest findings
 - Indirectly related: good for techniques, approach, sitting

Organization makes a world of difference

- Take short notes to remind yourself what's useful in that paper
- Highlight key points
- Periodically skim over the papers you thought useful.
- Learn the names of the authors

Write up

- Start with an outline
- Specific points
- Smooth flow
- Fill in the large details then smaller and smaller..

Efficient PubMed Search

Learning Outcomes

By the end of this session, the participant will be able to:

- Employ the PICO approach for searching a topic
- Employ Boolean operators to narrow down a search in PubMed
- Use “truncation”, “quotation”, and “parentheses” to aid in literature search in PubMed
- Use the “advanced” search option in PubMed
- Employ filters to refine literature search
- Retrieve articles from the Saudi Digital Library

How do I start

PICO

- Focus on most important issues and outcomes
- Used to identify key terms for search

P	I	C	O
Problem Population	Intervention	Comparison	Outcome
What is the problem in question?	Am I exposing them to something?	Who are they going to be compared with?	What did it affect?
Who is my subject?	Am I looking for something in them?	Controls?	

- **P**atient (Problem)

- Patient or problem (patient population – such as COPD, CHF, Sickle Cell Anemia, asthma)

- **I**ntervention

- What are you considering (a medication, diagnostic test, gene, mutation)?

- **C**omparison

- What are your alternatives, if any? A different drug or therapy? No treatment? Different gene than normal?
- A comparison **may not** be required for your question

- **O**utcome

- What outcome are you hoping for?
- Decreased symptoms, improved test results, improved function, etc.?

Current example

P: PTH measurements

I: tube type

C: effects of additives on the stability of PTH (compared at different tubes)

O: identify the best tubes to draw for PTH

Exercise 1

Identify PICO for your research

P:

I:

C:

O:

Boolean Operators

- AND
 - Myeloid AND PKI
- OR
 - Duchanne OR Becker Muscular Dystrophy
- NOT
 - Muscular dystrophy NOT Becker

Database Search tricks

- Best match sort order
- Truncation: using * at the end of the word
Incubat* = incubate, incubation, incubating, incubated
- Quotation: using “ ” to specify a term
“Acute Myeloid Leukemia”
- Parentheses: executing a command inside the parentheses before outside (similar to math)
Leukemia AND (myeloid OR lymphoid) similar to $3 \times (3+5)$

English vs. American English

- **Leukemia vs. Leukemia**

Use OR

- “Similar articles” suggestion

Great for early exploration of the literature