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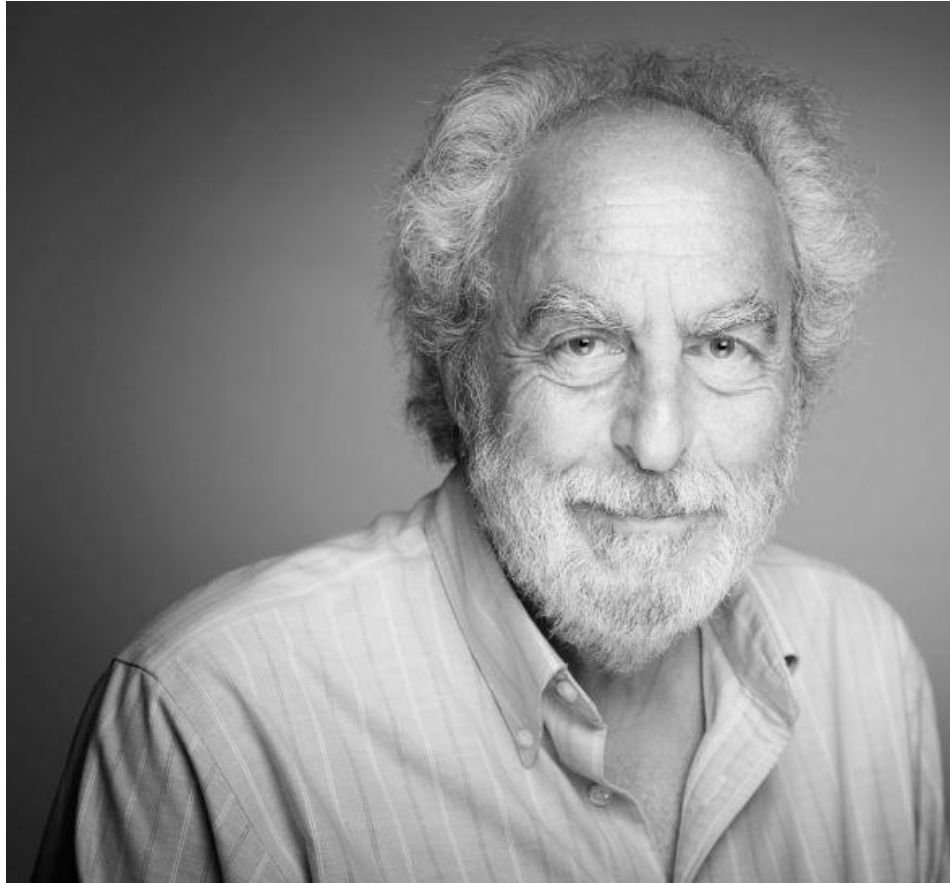
SCIENCE BEFORE STATISTICS

Jose Andres Calvache MD MSc PhD

Department of Anesthesiology, Universidad del Cauca, Colombia

Department of Anesthesiology, Easmus University Medical Centre, Rotterdam, The Netherlands

@jacalvache



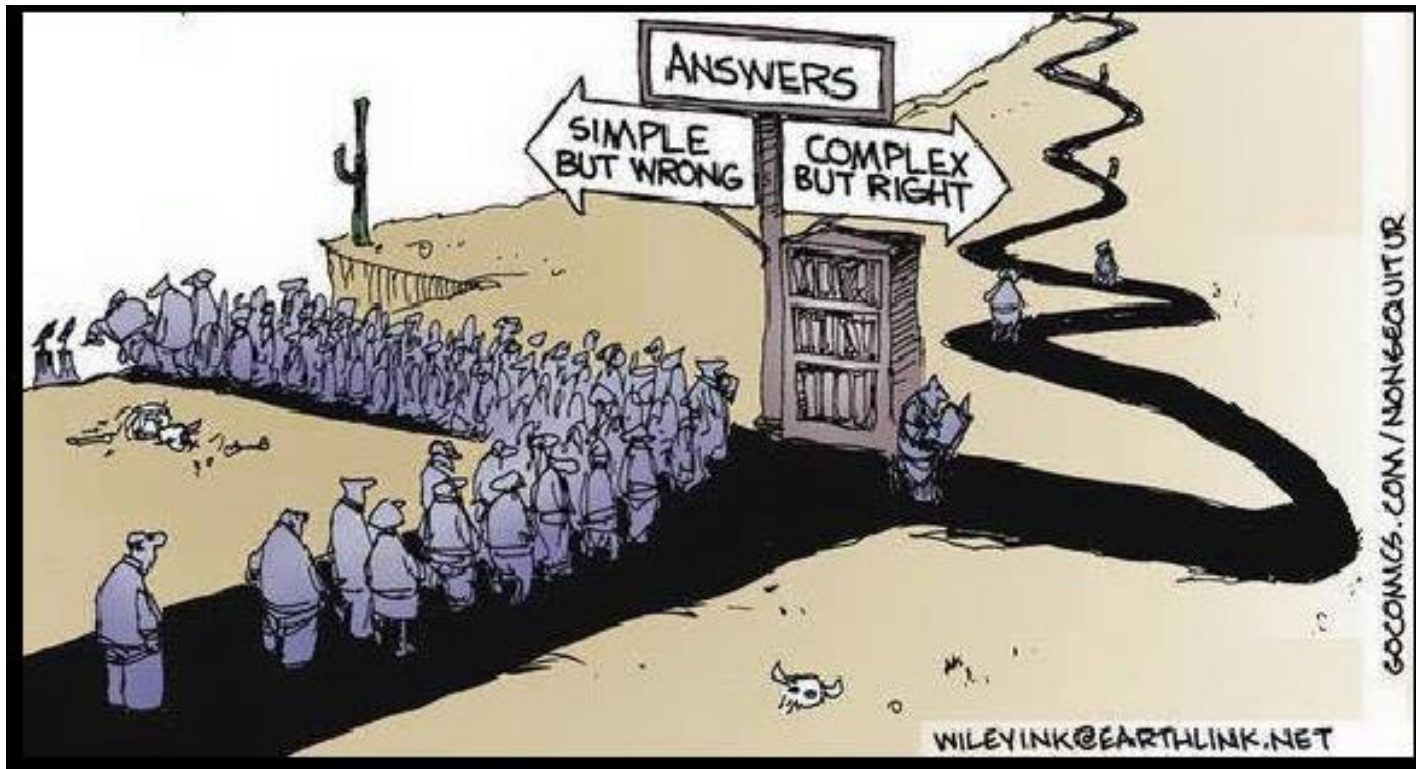
“

**To maximise the benefit to
society, you need to not just
do research but do it well.**

- Professor Doug Altman

Medical research hero and statistics game-changer

1948 - 2018



Training in statistics and methodology should discuss how studies are designed and how research questions are translated into study procedures, data collection processes, and analysis tools.



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COMMENTARY

Methodology over metrics: current scientific standards are a disservice to patients and society

Ben Van Calster^{a,b,c,*}, Laure Wynants^{a,c,d}, Richard D Riley^e, Maarten van Smeden^f,
Gary S Collins^{g,h,i}

- Research incentives focus on quantity, rather than methodological quality
- Funders and journals prioritize novelty over incremental and replication research
- Researchers' agendas are dictated by short-term deadlines
- Peer review remains unacknowledged
- Methodological illiteracy is still accepted
- Transparent and complete reporting remains rare

Practices resulting from prioritizing publication appearance over publication quality

- Poor study preparation and design
- Data or analysis tweaking (e.g. p-hacking)
- Incomplete reporting
- Selective reporting
- To use exaggerated claims when disseminating research results (over or wrong interpretation)
- Publication bias
- HARKing (hypothesizing after the results are known)
- Reluctance to take corrective action post hoc.

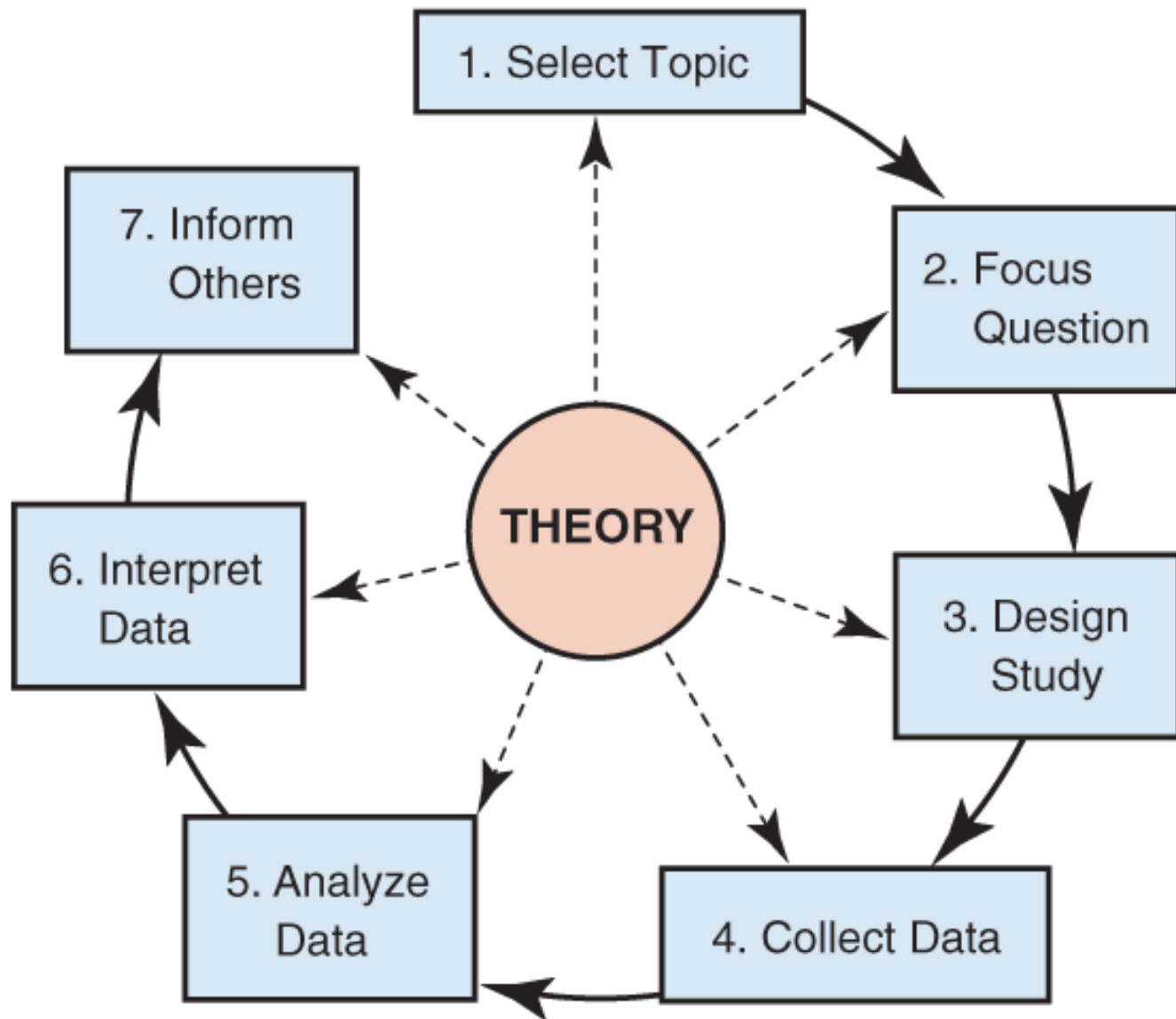


Figure 1.1 Steps in the Research Process

What is Science?

- **Oxford Dictionary definition:** A branch of knowledge conducted on objective principles involving the systematized observation of and experiments with phenomena, especially concerned with the material and functions of the physical universe.
- **Science More simply:** Science is the acquisition of reliable but not infallible knowledge of the real world, including explanations of phenomena.

What Science is not! (popular myths)

1. The practice of Science leads to the truth
2. Science can prove things
3. Science can only be done whenever experimental manipulation can be carried out


The essence of science is the testability of hypotheses
and the reproducibility of findings

Knowledge comes in many forms

- Science is one approach to gaining knowledge through research
- Science includes anything observable in the universe
 - Must be measurable
 - Empirical - relies on observation and experience

Areas of Science

- Physical Sciences
 - Chemistry
 - Physics
- Biological Sciences
 - Ecology
 - Evolution
 - Molecular Biology
- Behavioural Sciences
 - Animal behaviour
 - Human behaviour
- Earth Sciences



Can rely heavily
on observation
outside the
laboratory

Why understand science?

- To be informed
- To make decisions
- Pseudoscience
 - Silly to dangerous
 - Need to separate sense from nonsense

Why we need to understand

- Link between MMR vaccine & Autism 1998
- Study in The Lancet
 - Sample size of 12 children
 - Parents of 8 noted symptoms of Autism after vaccination
 - Study recommended further investigation to examine possible link
- Press conference with lead author **who suggested a link**
- Major health scare
- Children getting MMR vaccine dropped considerably

Major flaws with this study

- Small sample size
- Patients were not chosen randomly
- No control group to compare
- Most importantly, despite these flaws the study did not observe a link. Importance of communication of findings
- Lead author
 - Received large amounts of money from lawyers
 - Applied for patent for a vaccine to rival MMR
 - As a result, 10 of the 12 authors published a retraction
- Since then... All following studies have been definitive on the conclusion that **there is no link between MMR** vaccine and autism

Philosophy of Science

- Philosophy: How we understand the world
- Science: A method for understanding
 - Developing a theory
 - Formulation of hypotheses
 - Explanations and predictions
 - Design and analyses

Four terms: four meanings

- Fact
- Law
- Hypothesis
- Theory

A fact (National Academy of Sciences)

- In science, an observation that has been repeatedly confirmed and for all practical purposes is accepted as “true”.
- Truth in science, however, is never final, and what is accepted as a fact today may be modified or even discarded tomorrow.

A law (National Academy of Sciences)

- In science, a descriptive generalization about how some aspect of the natural world behaves under *specified circumstances*.
- e.g. the second law of thermodynamics

A scientific hypothesis (National Academy of Sciences)

- A tentative statement about the natural world leading to deductions or predictions that can be tested. If the deductions are verified, it becomes more probable that the hypothesis is correct.
- If the deductions are incorrect, the original hypothesis is abandoned or modified.
- Research hypotheses must refer to concepts that can be studied scientifically (can be observed)
 - Living organisms are purposely designed by a maker: no way to test for this hypothesis

A theory (National Academy of Sciences)

- The goal of science
- In science, a well substantiated explanation of some aspect of the natural world that incorporates facts, laws, and tested hypotheses.

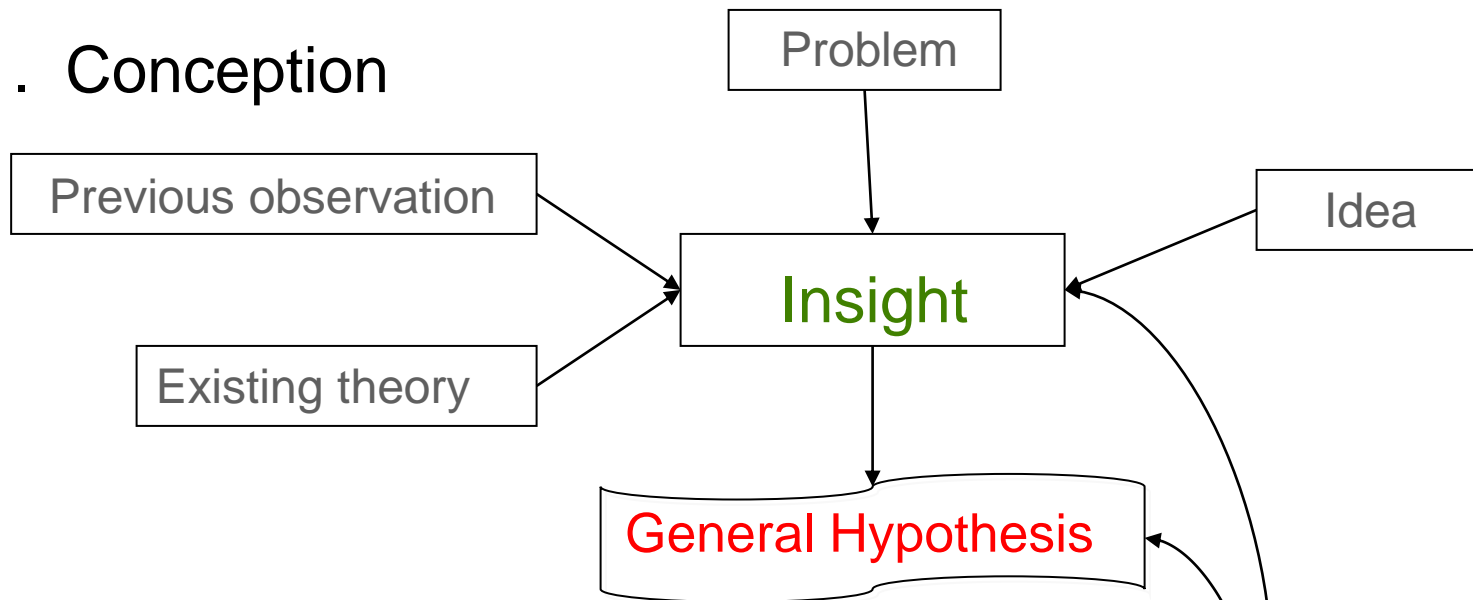
A key element of scientific theories is that they must be
FALSIFIABLE (refutability)

Evidence or “pruebas”

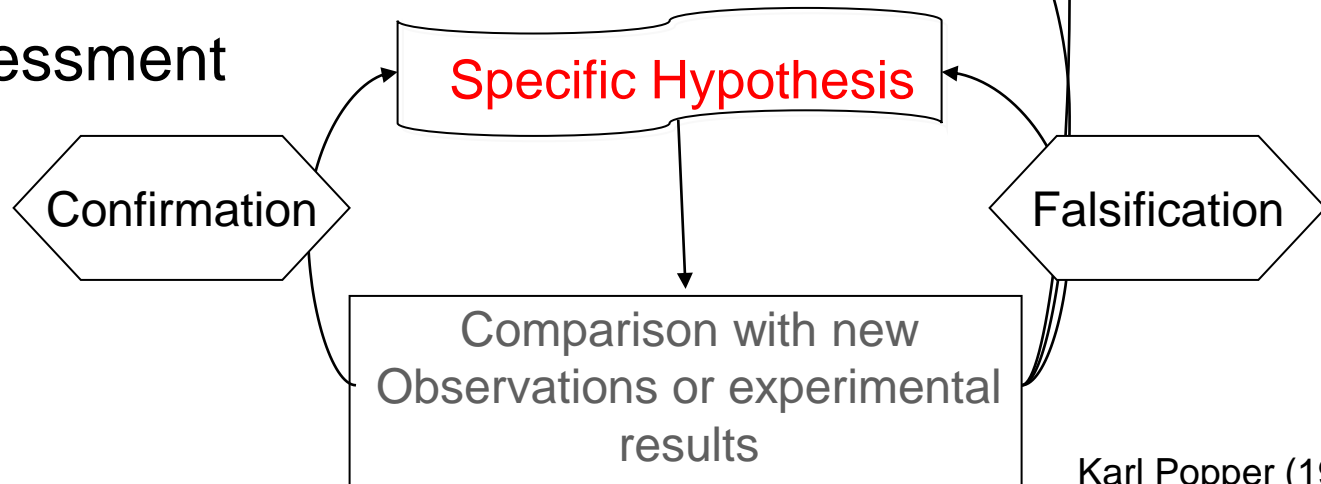
- Hypotheses are usually tested through experimentation
- Two types of evidence accepted by scientists
 - Confirmation of hypotheses by data strengthens their validity
 - Repeated inconsistency of data with a hypothesis leads to rejection
- When a hypothesis is not verified, ask: is it because the hypothesis is incorrect or is it because of problems in the statement of the hypothesis, or problems in the experiment
- Repeat testing in many different ways

Hypothetico-deductive reasoning

1. Conception



2. Assessment



Example

1. Observation

- Individuals taking Echinacea say that it reduces the intensity and duration of a cold

2. Hypothesis

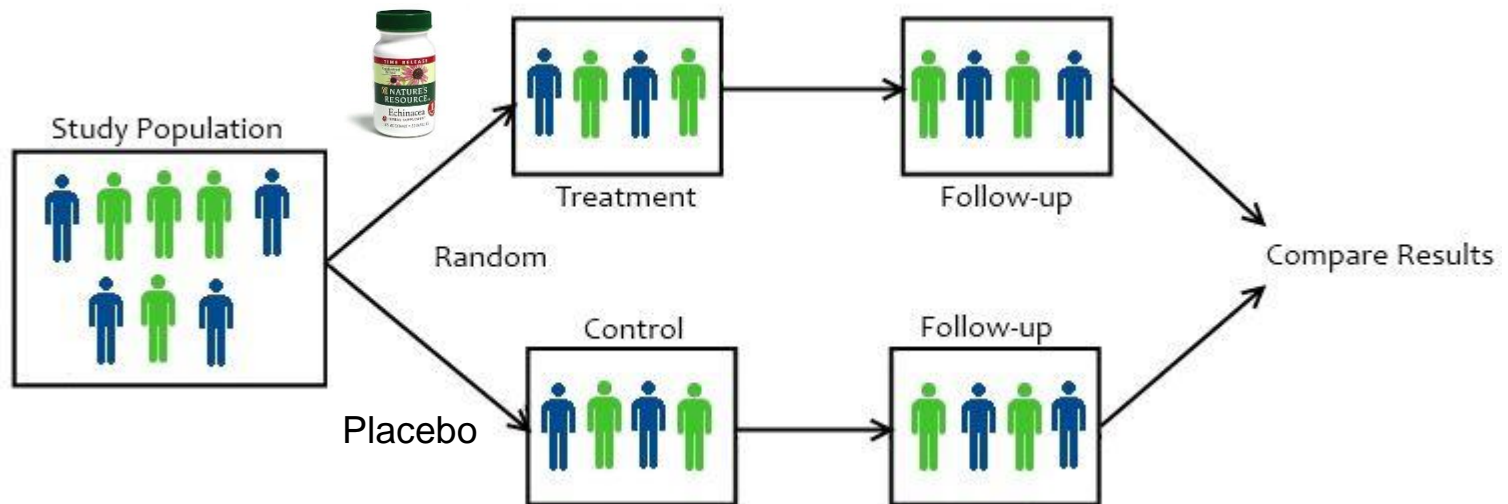
- Echinacea reduces the severity and duration of a cold (how is it defined)
- Null: Echinacea has no effect on the duration or severity of the common cold



3. Testable predictions, clear outcomes

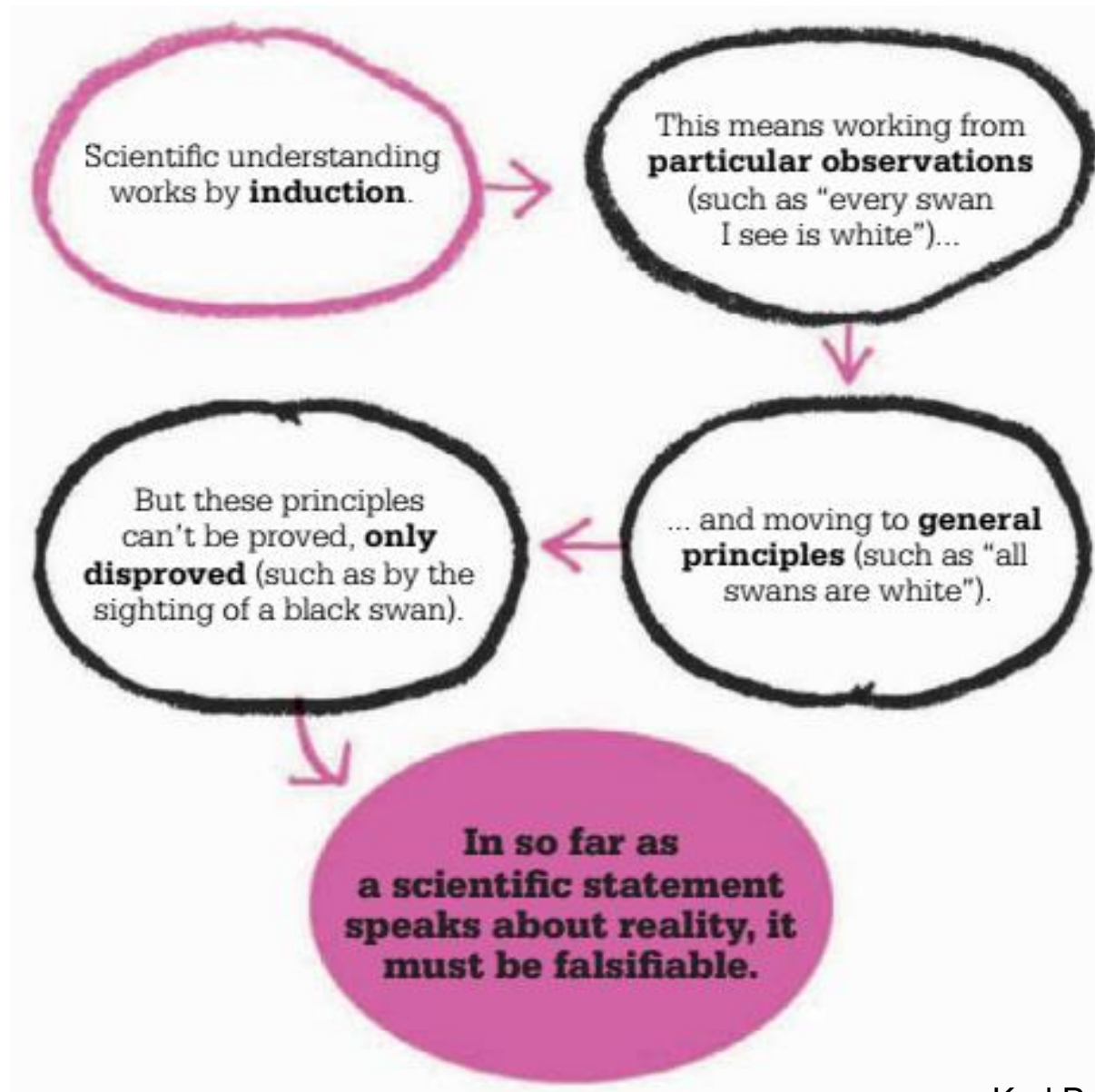
- If Echinacea reduces the duration & severity, then...
- Individuals taking Echinacea should get sick less frequently and should recover more quickly.

4. Conduct an experiment



5. Draw conclusions

- Cold symptoms lasted for the same amount of time in experimental and placebo groups
- Echinacea had no effect on the duration or severity of the cold
- Causally related
- What next?...
 - Repeat the experiment using different variant cold viruses, use larger dose, other populations



Failure of falsification

- Null models not unique
- Science versus no science based on falsification
- It is a criteria of demarcation, not about the method
- Should falsify the explanatory model, not the null

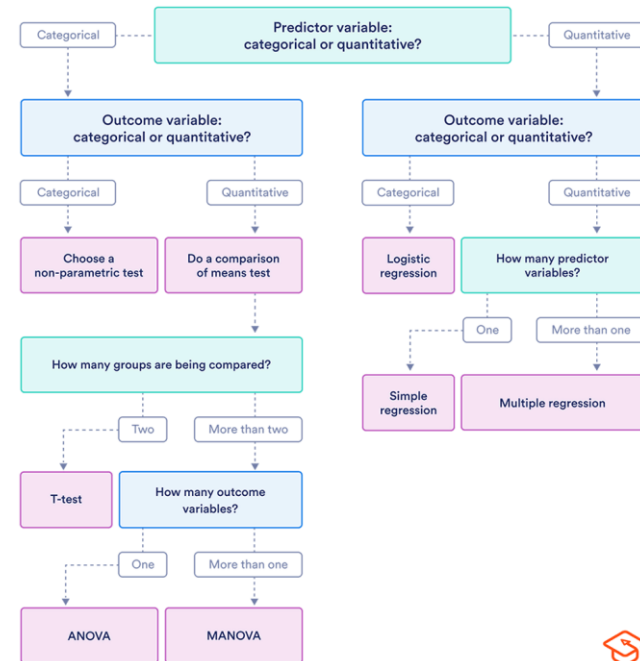
- To build some amount of theory at some point
 - No statistical procedure is sufficient
 - It is called: “confirmation”
 - Models should be consistent with observed

Against ...selection of... test

- Test and (selection of test) are specialized procedures
- Most developed in early 20th century, fragile, initial and eclipsed by more recent tools
- Users are using models (usually linear models)
- Falsifying *null* model not sufficient
- Against dichotomization of choices
 - P-values wrong interpretations
- Inference is not decision

Choosing a statistical test

This flowchart helps you choose among parametric tests



Philosophy of Science



- Inductivism:
 - Empirism: concept developed by Hume (1777)
 - Causes of events can be determined by observation
 - Generalization from observations
 - Unlike deduction, the conclusions of inductive reasoning are probable given the evidence, in contrast to being certain.
- When events not following the rule occur – the theory becomes a probability rather than a certainty.
 - This is where Bayesian statistics can play a huge role
 - Principle of the Uniformity of Nature “The future will resemble the past”
 - Extend the ordinary logic (true/false) to *continuous plausibility*

Some forms of inductivism

- Positivism (19th Century)
 - Science can rise above superstition by specializing in the description and analysis of observable phenomena, leading to discovery of natural laws.
- Logical positivism
 - Science progresses toward truth by observation, formulation of hypotheses, empirical verification, leading to additional hypotheses.
 - Scientific questions are referred to as “positive” while unscientific ones are “normative”

Problems with inductivism

- The theory chosen is not necessarily the right one
- The observed data can be biased (quite common)
 - Measurement error
- Difficult to come up with an experiment without an underlying theory
- In other words, we are born Bayesian....

Hypothetico-deductive and falsification

- Background
 - Fisher with p-values (nil-null hypothesis testing)
 - Pearson with hypothesis testing (alternative hypothesis)
 - Neyman with 95%CI
- Applies Popper's theory to statistics
 - *"The null hypothesis is never proved or established, but is possibly disproved, in the course of experimentation. Every experiment may be said to exist only in order to give the facts a chance of disproving the null hypothesis"* (Fisher, 1947)
- Issues with this theory
 - The hypothesis is true or false, there is no probability...
 - *"Scientific hypotheses can be rejected (i.e. falsified), but never established or accepted the same way."*

The Bayesian approach

- Refutation and hypothetico-deductive approaches were developed to avoid the concept that theories in sciences can be appraised in terms of their “probabilities”
- Theories usually lie between being certainly right or certainly wrong, we cannot tell...
 - *“It is often stated that one should experiment without preconceived ideas. This is simply impossible; not only would it make every experiment sterile, but even if we were ready to do so, we could not implement this principle. Everyone stands by his own conception of the world, which he cannot get rid of so easily.” (Poincaré, 1905)*

The Bayesian approach

- Bayesian statistics have an inductive approach
 - Start with a prior distribution (prior knowledge, multitude of observations)
 - Get data (observe under different condition)
 - Obtain a posterior distribution (update prior knowledge)

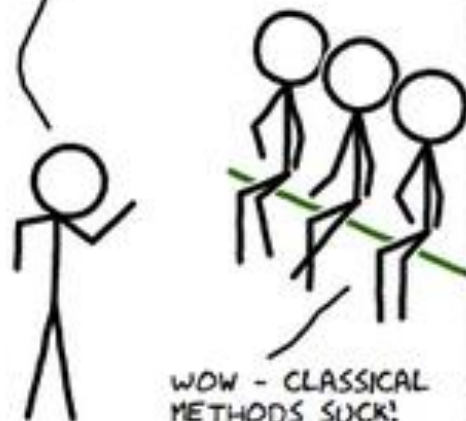
The Bayesian approach

The Posterior	The Evidence	The Prior
	The probability of getting this evidence if this hypothesis were true	The probability of H being true, before gathering evidence
$P(H E)$	$P(H E)$	$P(H)$
The probability that the hypothesis (H) is true given the evidence (E)	$P(E)$	The marginal probability of the evidence (Prob of E over all possibilities)

<i>Frequentist</i>	<i>Bayesian</i>
Data is a repeatable random sample - there is a frequency	Data is fixed, probably a few samples.
No expression of belief (formally not present) => Objective view on probability.	Approach deals with belief (Formally present) => Subjective view on probability. It helps to update their beliefs in the evidence of new data (thus creating posterior distribution).
Provides us with a point estimate using MLE and Least Squares Estimate.	Provides us with a posterior distribution with high density interval with mean, mode and median stats.
Parameters are fixed and unknown.	Parameters are unknown, random and described probabilistically.
Confidence Interval: Over an infinite sample size taken from population, 95% of these contain the true population value.	Credible Interval: A 95% probability that the population value is within the limits of the interval.
Statistical Hypothesis Testing with p-value and significance level is employed to deduce a solution in the decision-making process.	Bayes Factor considered a direct test of null and alternate hypothesis, yielding a measure of strength of evidence.
Less Computationally intensive	Computationally intensive

SOMEWHERE. DURING CLASS ...

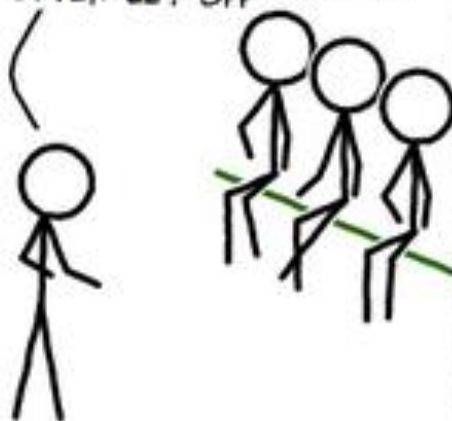
... AND THAT SUMARISES WHY
BAYESIAN STATISTICS HAS MANY
ADVANTAGES OVER FREQUENTIST
METHODS



WOW - CLASSICAL
METHODS SUCK!

BUT IT MUST BE CONCEDED
THAT BEING FREQUENTIST
SOMETIMES HAS ADVANTAGES

FOR EXAMPLE, WHEN UP IN
FRONT OF A MAGISTRATE FOR A
MINOR OFFENCE, FREQUENTISTS
ARE OFTEN LET OFF

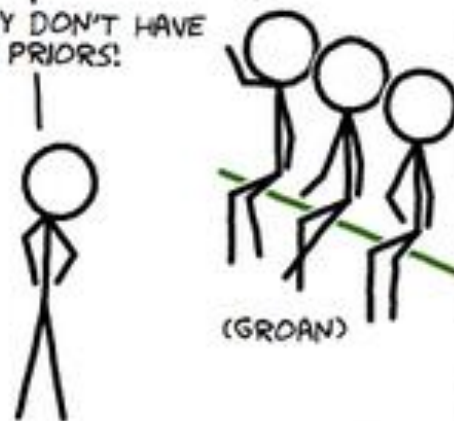


IS THAT BECAUSE THEY CAN MAKE
PROBABILITY STATEMENTS SOUND
MORE SIMPLE TO THE JUDICIARY?

NO - IT'S BECAUSE

(PAUSE)

THEY DON'T HAVE
ANY PRIORS!



(GROAN)

REVBAYES #008

A few words on: Pseudoscience

- Ideas often put forward as scientific when they are not
- Examples
 - Astrology
 - Creation Science/ Intelligent Design Theory
 - Paranormal phenomena
 - UFOs
 - Cryptozoology: e.g. Bigfoot, the Ogopogo and Loch Ness Monster
 - And many many many more. Some in health care!
- Can be dangerous

How to recognize Pseudoscience

- Driven by cultural, ideological or **commercial goals**
- Changed very little since first established
- Challenge to dogma is considered heresy
- Observations not consistent with beliefs are ignored
- Vague and ambiguous