Meta-analysis and network meta-analysis

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Let's roll back in history

William G. Cochran (1909-1980)

https://magazine.amstat.org/blog/2016/09/22/sih-cochran/

Ronald A. Fisher (father of modern statistics) conceptualized way back in 1944 a framework to aggregate probability values (famously p-values)

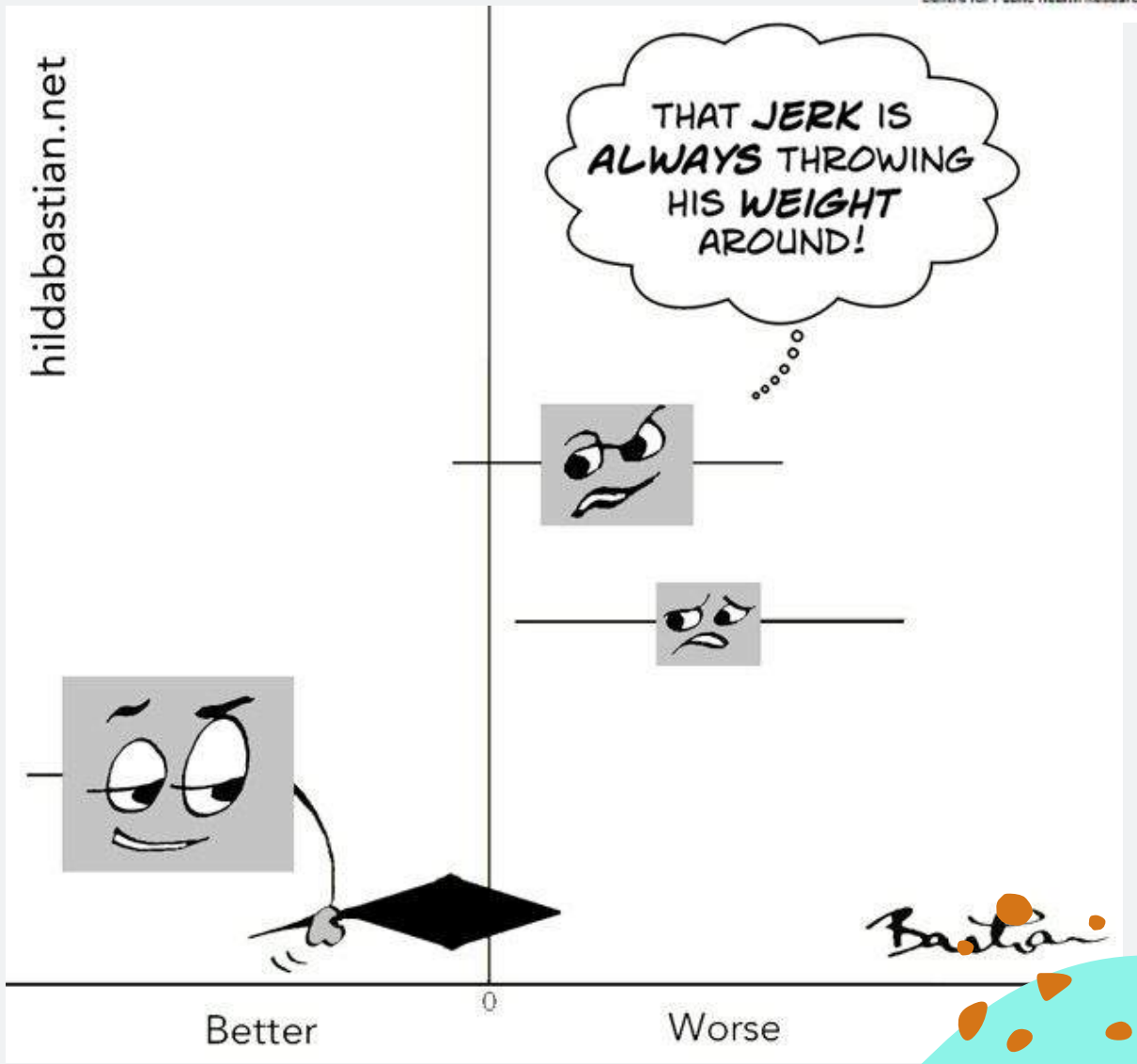
Hans J.Eysenck concluded that psychotherapy was not effective using available literature but created a huge array o debates which lasted power the next 20 years.

However, the most relevant framework was proposed by W.G. Cochran (1953). Discussed the method of averaging means across independent studies. Even laid out the statistical foundation that modern meta-analysis is built upon (e.g., inverse variance weighting and homogeneity testing)

In 1978, Gene V. Glass was able to conclude by aggregating the findings of over 375 studies in psychotherapy that it indeed worked. He coined the method "meta-analysis"

The logic behind meta-analysis

- Traditional review methods focus on statistical significance and hypothesis testing (for example, we can hypothesize “there is no relationship between a family history of depression and the person will attempt suicide”) and test it by sampled data.
- However, meta-analysis changes the focus to the direction and magnitude of the effect sizes (odds ratio, relative risk, etc.) across several studies comparing the same intervention and comparator.
- Interestingly, meta-analysis provides a robust statistical combinatorial framework to represent the direction and magnitude of effect.



Applicability of meta-analysis

Applicable when the collection of research is –

- empirical than theoretical.
- produces quantitative results than qualitative (needs mean and standard deviation for each study)
- produces comparable statistical measures (for example, odds ratio, correlation coefficients)
- can examine the constructs, design, and relationships that are comparable given the question at hand.

Table 2 | Questions answered according to types of synthesis methods and types of data used

		Minimum data required			
Question answered	**Synthesis method**	**Estimate of effect**	**Variance**	**Direction of effect**	**Precise P value**
What is the common intervention effect? What is the average intervention effect? Which intervention, of multiple, is most effective? What factors modify the magnitude of the intervention effects?	Meta-analysis of effect estimates and extensions (eg, sub-group analysis, meta-regression, network meta-analysis)	✓	✓	-	-
What is the range and distribution of observed effects?	Summarising effect estimates	✓	-	-	-
Is there evidence of an effect in at least one study?	Combining P values	-	-	✓	✓
Is there any evidence of an effect?	Vote counting based on direction of effect	-	-	✓	-

Abbreviated from table 12.2.a of McKenzie and Brennan 2019.[11]

Strengths

Strengths-

- A disciplined and quantitative approach to compare empirical findings
- Can handle many studies in a single quantitative framework.
- Allows us to evaluate what attributes of a study are related to smaller vs. larger effect sizes (concepts like meta-regression can handle this)
- Allows us to plan smarter, more sensitive, and more useful studies!
- Can involve both Randomized controlled studies (RCTs) and observational studies

Weaknesses

- Requires a huge amount of effort.
- May sometimes compare apples with oranges; comparability of studies is often in the “eye of the beholder” (Wilson)
- Issue of subjectivity-
  - ❑ Which studies to include or exclude
  - ❑ Is population heterogeneity a key concern
  - ❑ What study attributes to code

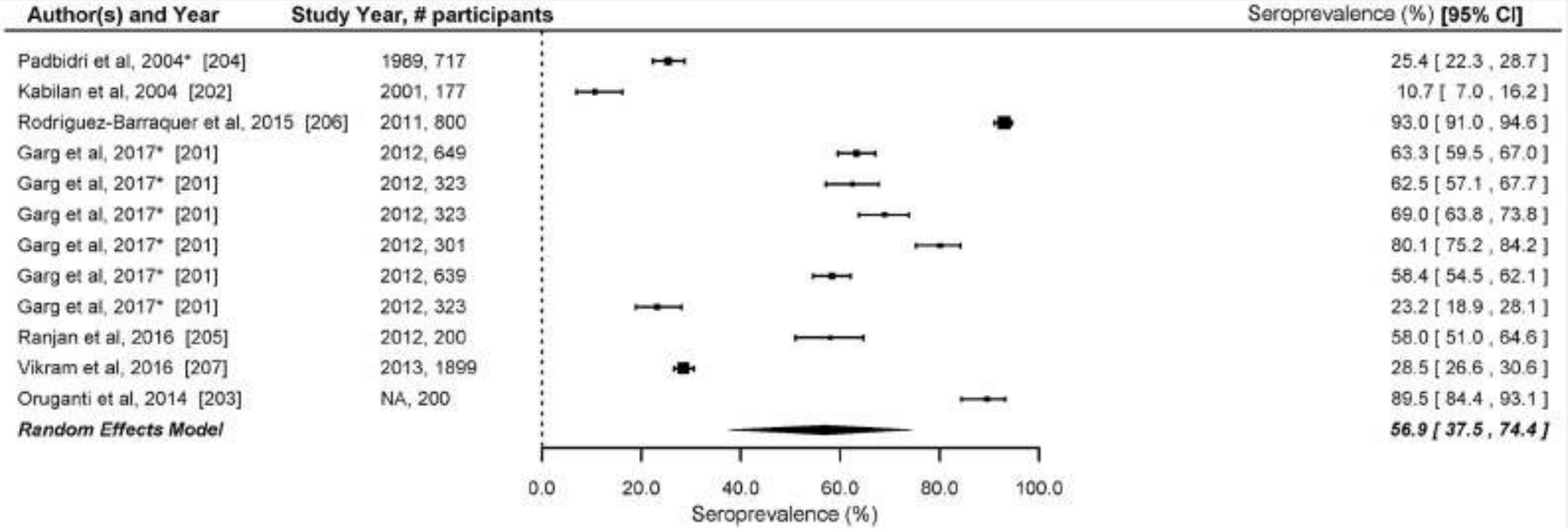
Types of meta-analysis [outcome-specific]

- Binary outcome data
- Incidence rates
- Single correlations
- Single proportions
- Rate data
- Continuous outcome data

Special Note - Most standard software packages such as R, and RevMan can easily handle most forms of meta-analysis

A simple example

The below forest plot summarizes the seroprevalence of dengue in India (Ganeshkumar 2018)

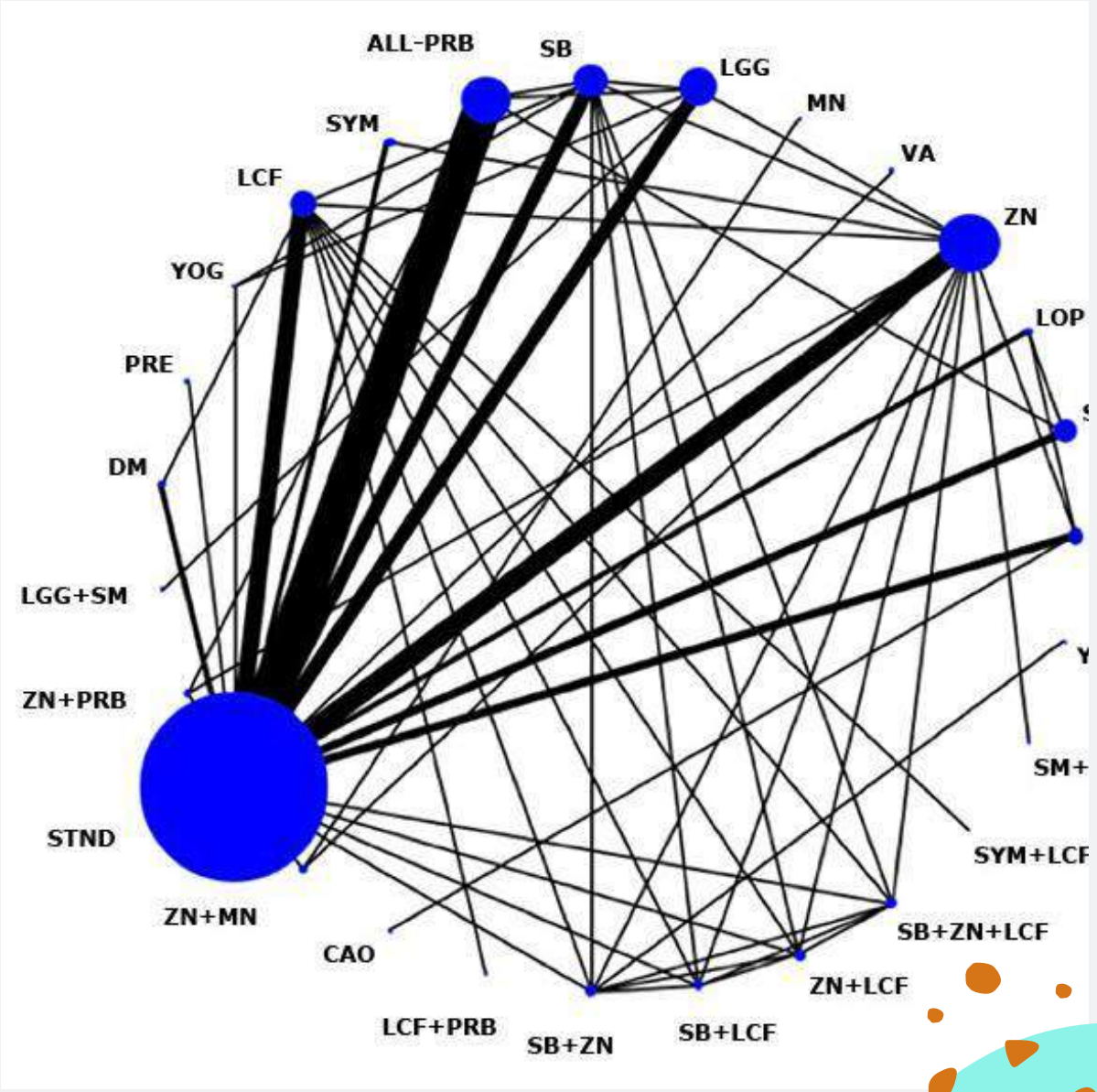


Note-

- Error bars indicate 95% confidence intervals.
- Diamonds show the pooled estimates with 95% confidence intervals based on the random effects (RE) model.

Network meta-analysis

- First proposed by Lu and Ades (2002, 2004)
- Statistical extension of meta-analysis.
- Can compare several interventions not studied at a single time using a network diagram.
- Generally applied to handle Randomized controlled studies (RCTs) in a network.
- More complex statistical framework than meta-analysis.
- Requires even more effort than meta-analysis.



The network diagram visually conveys the size and complexity of the network in NMA. This example shows the network diagram for an NMA that evaluated 62 clinical trials (20,256 participants) evaluating different treatments for acute diarrhea in children. The "nodes" (blue dots) represent different treatments; the size of each node corresponds to the number of participants who received that treatment. The "edges" (black lines connecting different pairs of dots) represent trial(s) directly comparing the 2 treatments; the thickness of the line corresponds to the number of trials.