

Reproducibility and Experimental Design

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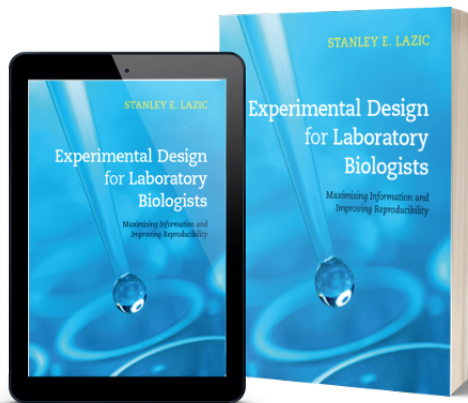
15.04.2020

Overview

- ▶ What is reproducibility?
- ▶ Source of bias
- ▶ Experimental Design
- ▶ Replication ($n = ?$)
- ▶ Recommendations

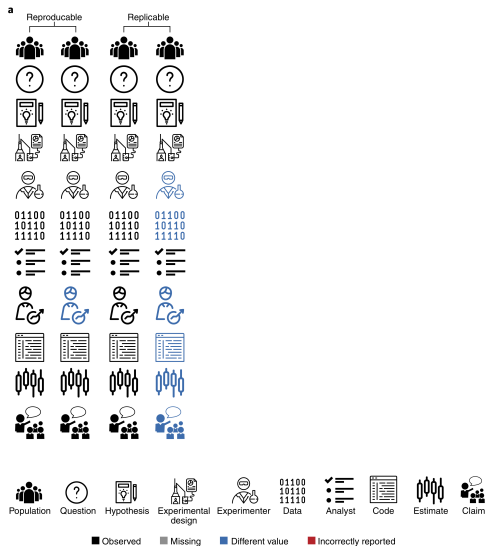
Source: <https://github.com/tschauer>

Reference Book



Patil, Peng and Leek, 2019

Reproducibility vs. replicability



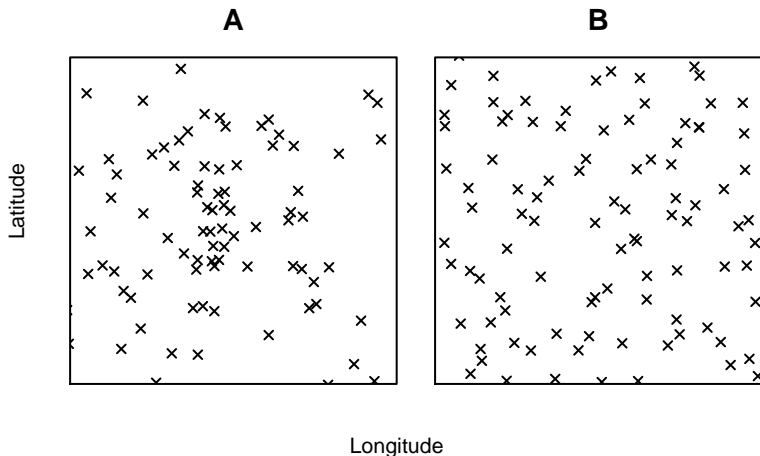
Patil, Peng and Leek, 2019

Reproducibility by Lazic

- ▶ **analytical:** original data and analysis (code!)
- ▶ **direct:** same conditions, materials, methods
- ▶ **systematic:** different conditions (e.g. cell line, KD vs drug)
- ▶ **conceptual:** general under diverse conditions (paradigm)

Source of bias

- Strategy: which location was bombed randomly?

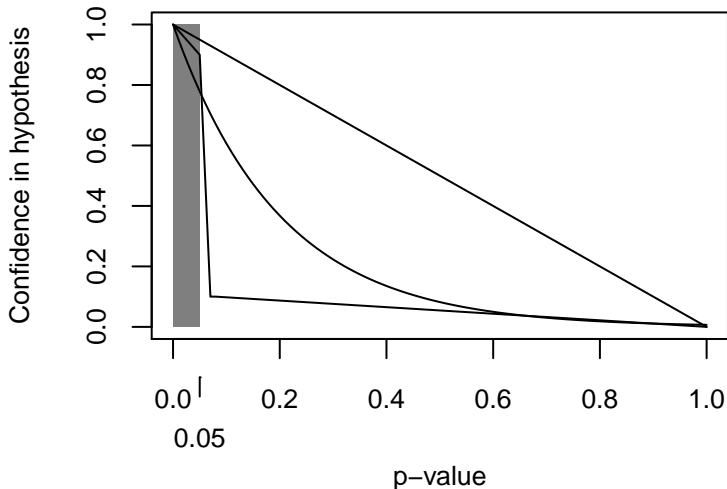


Source of bias

- ▶ seeing pattern in randomness
- ▶ not wanting to miss anything (what else can we get out?)
- ▶ *if a hypothesis is derived from the data, then the ability of the data to support that hypothesis is diminished*
- ▶ exploratory vs. confirmatory research

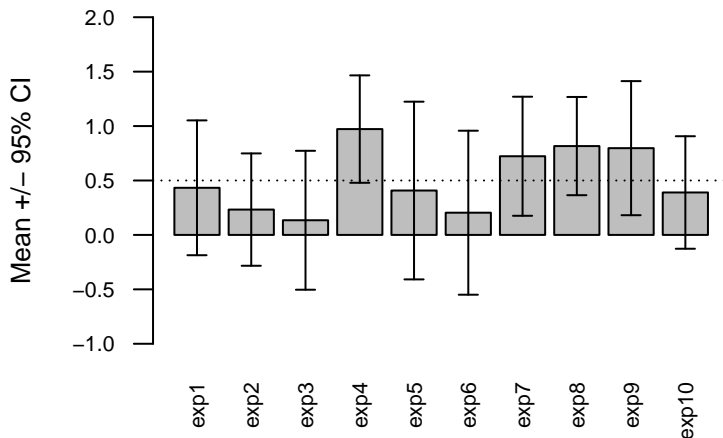
Source of bias

- ▶ psychological cliff at $p = 0.05$



Source of bias

- neglect of sampling variability



- mean = 0.5, standard deviation = 1, n=10 each

Source of bias

- ▶ lack of independence
 - ▶ repeated measures
 - ▶ observations are close together in space or time
 - ▶ same animal, litter, cell culture dish, fly vial
 - ▶ correlated variables
 - ▶ different measures of a single underlying effect
 - ▶ co-regulated genes, proteins, metabolites
 - ▶ disease severity

Source of bias

- ▶ confirmation bias
 - ▶ Pubmed search: disease + gene name
 - ▶ what about studies which do not find the association?
 - ▶ neglecting negative results
 - ▶ data transformation until it “gets” significant
 - ▶ selecting data to tell the story (data that do not fit excluded)

Source of bias

- ▶ expectancy effects (measurements are influenced)
- ▶ hindsight bias ('I knew it all along')
- ▶ herding effect (scientific inbreeding)

Common problems

- ▶ Experimental Design
 - ▶ confounding (conditions ~ biological, technical effects)
 - ▶ experimental unit (replicates)
 - ▶ lack of randomization
 - ▶ low statistical power
- ▶ Conducting experiments
 - ▶ lack of blinding
 - ▶ lack of randomization
 - ▶ optional stopping

Common problems

- ▶ Analysis
 - ▶ experimental unit (inflated sample size)
 - ▶ inappropriate model (normal distribution)
 - ▶ incorrect interpretation
 - ▶ selective reporting

Experimental Goal

	Exploratory	Confirmatory
Question	General	Specific
Hypothesis	Generating	Before
Order	Before	After (independent data)
Analysis	Data dependent	Data independent
Minimize	False Negatives	False Positives
P-value	No Diagnostic Value	Diagnostic Value

- Pre-registration: <https://cos.io/prereg/>

Experimental Goal

	Exploratory	Confirmatory
Subjects	Heterogeneous	Homogeneous
Environment	Varied	Standardised
Treatments	Many	Few
Levels	Many	Few
Time points	Many	Few
Outcome	Many	Few
Controls	Few	Many
Blinding	Possibly	Yes
Randomization	Yes	Yes
Blocking	Yes	Yes