Replicability in Science: Day 3, Paper 6: Replicability in Cancer Science

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RESEARCH ARTICLE

Investigating the replicability of preclinical cancer biology

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"The Reproducibility Project: Cancer Biology was set up to provide evidence about the replicability of preclinical research in cancer biology by repeating selected experiments from high-impact papers."

"A total of 50 experiments from 23 papers were repeated, generating data about the replicability of a total of 158 effects. Most of the original effects were positive effects (136), with the rest being null effects (22)."

study selection

(1) Studies were selected by searching Scopus and Web of Science for the most cited papers in the field of cancer biology using the search terms (cancer, onco*, tumor*, metasta*, neoplas*, malignan*, carcino*).

(2) The top 400 most cited papers from Web of Science in 2010, 2011, and 2012 and the top 400 most cited papers from Scopus in 2010, 2011, and 2012 were combined to make the sampling frame. Many papers were present in both the top 400 from Web of Science and the top 400 of Scopus, yielding a total of 584 papers from 2010, 548 papers from 2011, and 543 papers from 2012.

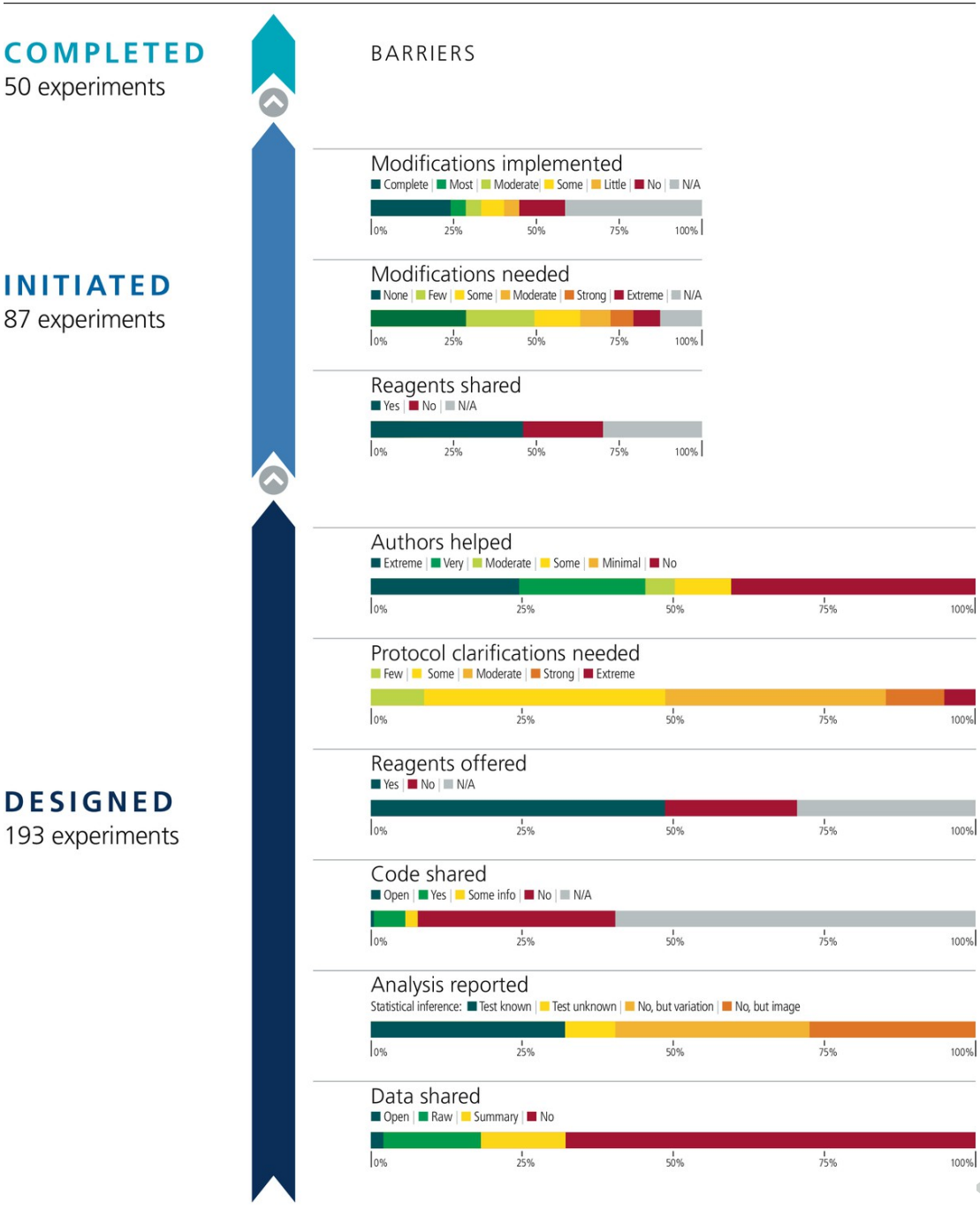
(3) Altmetrics scores from Mendeley and Altmetric.com were collected for the entire dataset.

(4) All metrics were normalized by dividing each metric by the highest in the dataset for that given year. The sum of the normalized metrics were used to create a final impact score assigned to each paper.

(5) Content of the articles were reviewed. Clinical trials, case studies, reviews, and studies reporting sequencing of cancer samples (mainly TCGA studies), and basic research papers not explicitly about cancer, yet still appearing in the results, were excluded. Studies were also excluded if they included unique instrumentation or samples that would be difficult or impossible to obtain. (Total exclusions for 2010 = 83; 2011 = 104; 2012 = 105)

(6) From the remaining set of articles (2010 = 501; 2011 = 444; 2012 = 438), we selected the top 17 papers in 2010, top 17 in 2011, and top 16 in 2012 based on the within year impact score from step 4 to form the 50 studies chosen for inclusion.

Barriers to conducting replications

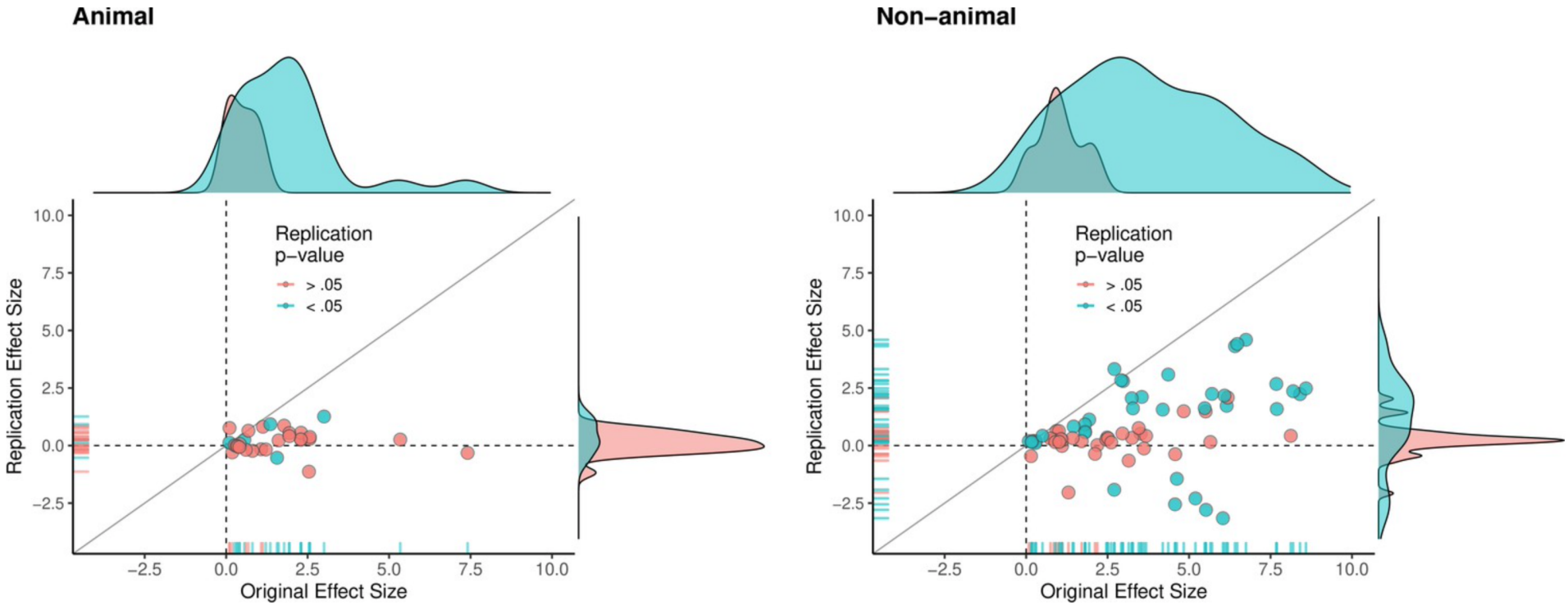


Summarizing across five dichotomous replication success criteria

- 47%: Same direction and statistically significant
- 25%: Original effect size in the replication 95% confidence interval
- 48%: Replication effect size in the original 95% confidence interval
- 61%: Replication effect size in the 95% prediction interval
- 63%: Meta-analysis of original and replication

replicability of preclinical cancer biology

Errington etal



Replication effect sizes compared with original effect sizes for animal and non-animal experiments. Graphs for animal experiments (n = 30 effects; left) and non-animal experiments (n = 70 effects; right) in which each circle represents an effect for which an SMD effect size could be computed for both the original effects and the replication. Blue circles indicate effects for which $p < 0.05$ in the replication, and red circles indicate $p > 0.05$. Animal experiments were less likely to replicate than non-animal experiments and this may be a consequence of animal experiments eliciting smaller effect sizes on average than non-animal experiments (see main text for further discussion). Twelve effects in the non-animal experiments for which the original effects size was >10 are not shown. SMD: standardized mean difference

regression to the mean

Lecture notes

Interpreting failures to replicate

- A failure to replicate could mean:
  - The original finding was a false positive
  - The replication was a false negative
  - Both are “true” and key conditions in the experimental design differ

replicably wrong results

A scientific claim is said to be replicable if it is supported by new data. However, it is often not straightforward to decide if a claim is supported by new data or not. Moreover, the success or failure of an attempt to replicate rarely provides a definitive answer about the credibility of an original claim. When the replication attempt is successful, confidence in the reliability of the claim increases, but that does not mean that the claim is valid: a finding can be both replicable and invalid at the same time. Repeated successful replications can help to eliminate alternative explanations and potential confounding influences, and therefore increase confidence in both reliability and validity, but they might not eliminate all confounding influences. It is possible that the original experiment and all the replication attempts could be invalidated by a common shortcoming in experimental design.

Meta-analysis conclusions

- Replication effects were much weaker than originals
- "Success" was low across replication criteria with variability due, in part to liberalness of the test
- Positive results were half as likely to replicate as null results
- Animal and non-animal declines similar magnitudes - animal effects lower success rate because small original effect sizes
- There is room for improvement

Conclusions

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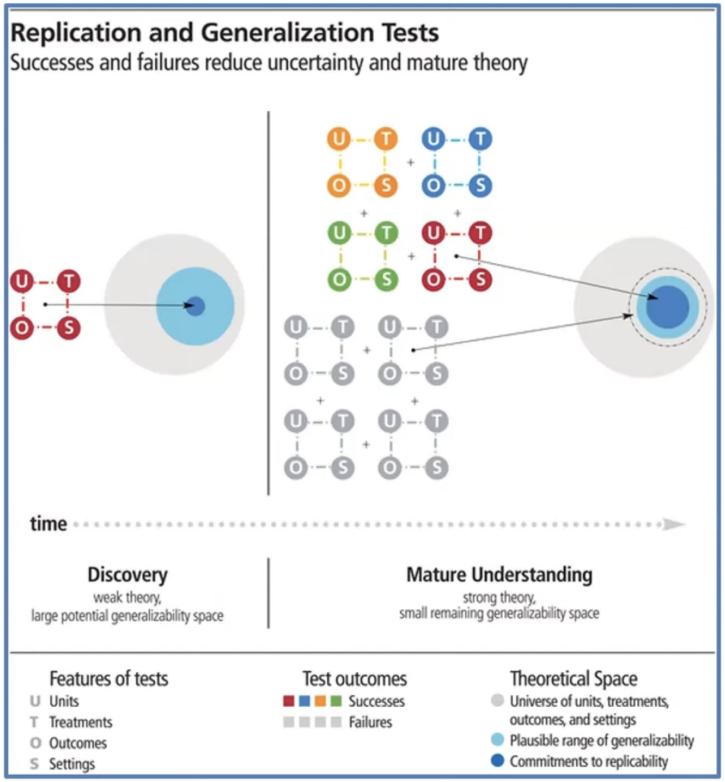
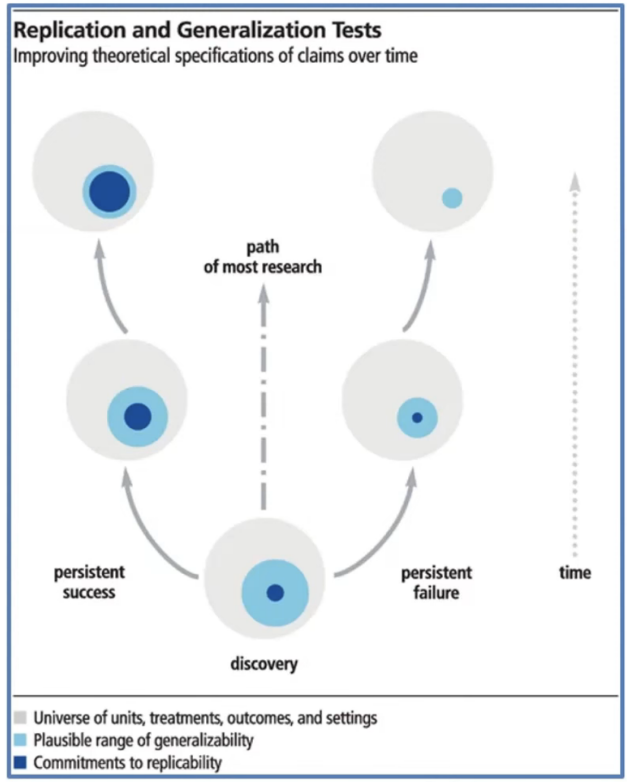
Do we know the conditions necessary to observe a finding?





Nosek & Errington, 2020a

What can we do?

- Incentivize open science practices in your community
  - Aligning institutional policies with open science practices (e.g., NASEM Roundtable)
  - Journal polices that incentivize open practices (e.g., TOP Guidelines)
  - Assessment of researchers and scholarly research (e.g., DORA)
  - Training on reproducible and open science practices

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What can we do?

- Incorporate open science practices in your research
  - Share data/code/etc using repositories (e.g., NIH GREI Repositories)
  - Deposit reagents in repositories (e.g., addgene)
  - Make detailed protocols open (e.g., ELNs)
  - Try preregistration/Registered Reports