

Incidence of Substudies Publication After Originally Negative Clinical Trials and Rate of Positivation: a Call for Scientific Integrity

Diego Rabelo, Janine Magalhães, Thiago Taniguchi Alessandra Caldas, Bruno Goes, Camila Verônica Freire, Daniel Medina, Denise Matias, Gabriel Grisi, Larrie Laporte, Mariana Cruz, Luis C. L. Correia



Medical and Public Health School of Bahia, Brazil



Key Findings and Conclusion

No. of **Negatives** RCTs = **34%** | Incidence of **Republication** = **30%** | **Positivation** Ratio = **93%**

Subsequent publication of subanalysis from originally negative trials is frequent, commonly not defined a priori, commonly not explicit about the exploratory nature and highly successful in positivating results. This suggests lack of ecosystem scientific integrity.

Objectives

- 1) Describe the incidence of substudies testing the same hypothesis over a period of 5 years after publication of a primarily negative randomized clinical trial;
- 2) Access the rate of successful result positivation.

Rational

- After a negative study, substudies may emerge providing a positive spin on the hypothesis, based on subgroup or secondary outcome analyses;
- This approach suffers from multiplicity problem, imprecision and higher risk of type I error.

Methods

Research in NEJM

- Search of all negative randomized trials published in the *New England Journal of Medicine (NEJM)* during 2014.

Detection of Republication

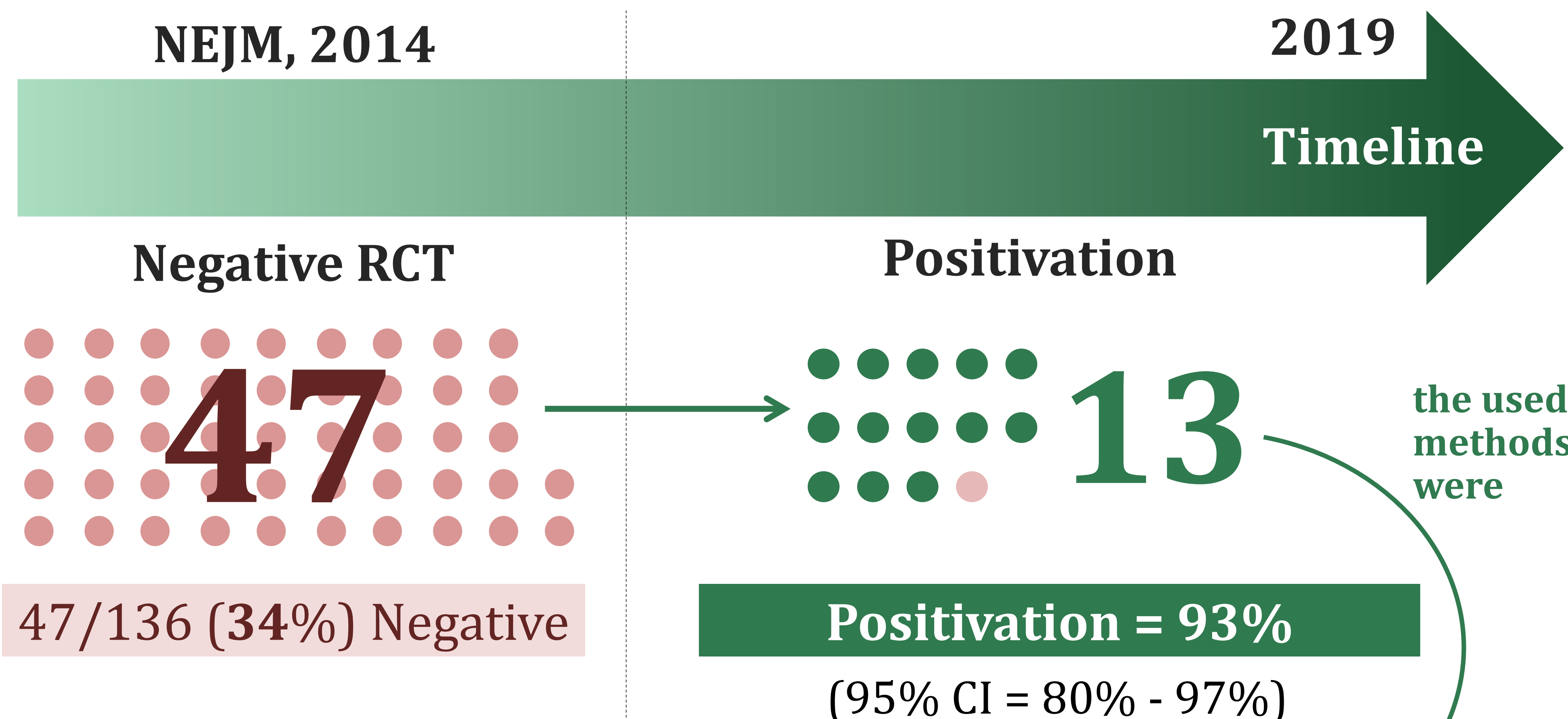
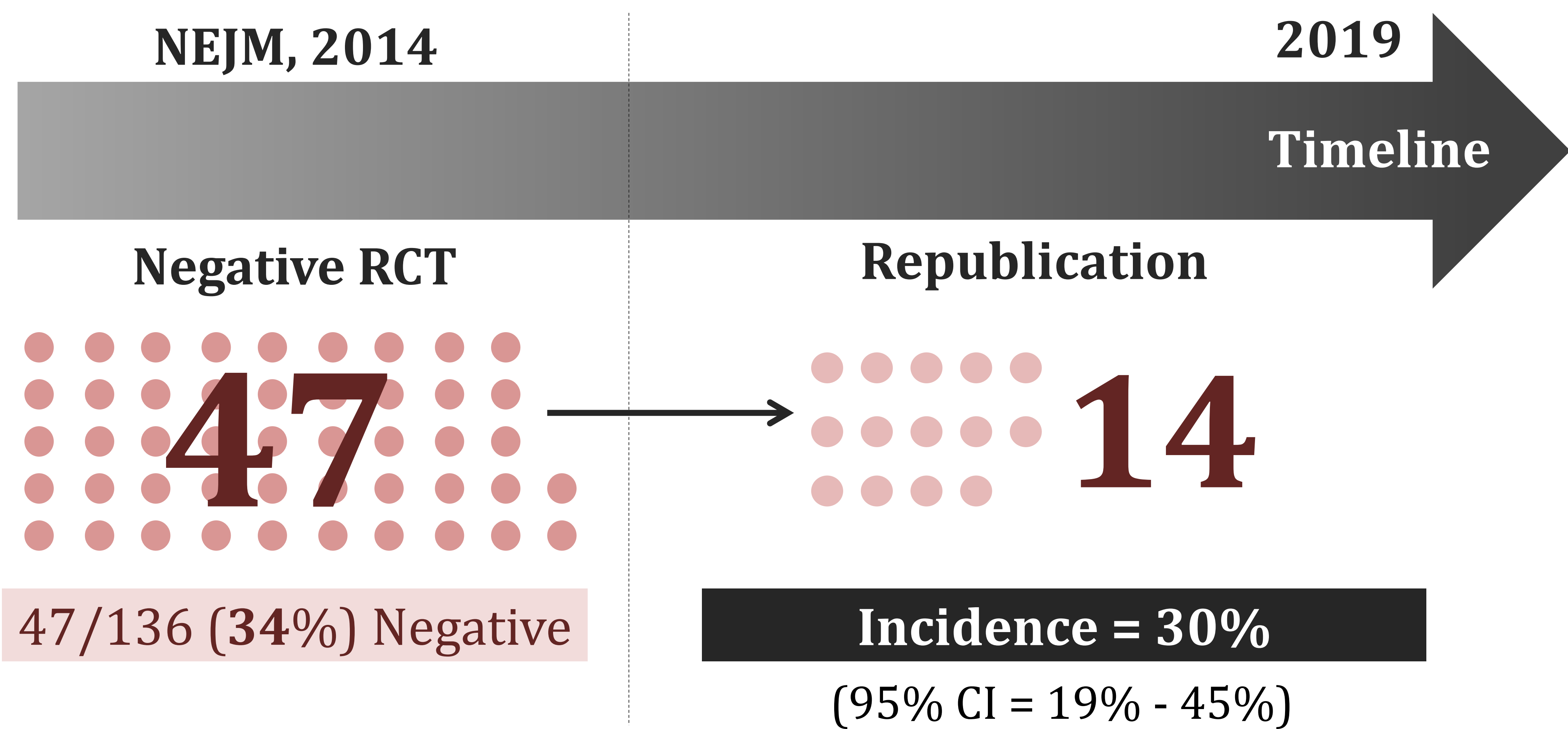
- Highly sensible PUBMED search over the following 5 years;
- Searching for substudies testing the same hypothesis using:

Study acronym (when available);
Names of first and last author;
PICO terms.

What Was Analyzed

- Methods utilized;
- Lack of identification as a secondary analysis;
- Rate of positivation.

Results



SPECIALTY	N (%)
Cardiology	13 (65%)
Oncology	2 (10%)
Infectology	2 (10%)
Pneumology	2 (10%)
Intensive Medicine	1 (5%)
REGION	N (%)
North America	10 (50%)
Europe	8 (40%)
Africa	2 (10%)
TYPE OF STUDY	N (%)
Pharmacological Intervention	15 (75%)
Procedural Intervention	4 (20%)
Both	1 (5%)

9 secondary end-point

5 subgroups analysis

(1/2 post-hoc)