



# The cumulative effect of reporting and citation biases on the apparent efficacy of treatments: the case of depression

Jojanneke Bastiaansen, PhD

Interdisciplinary Center Psychopathology and Emotion regulation

Department of Psychiatry

University Medical Center Groningen

The Netherlands



@BastiaanseJACJ

# Disclosures



**No conflicts of interest to report**

# Evidence-Based Medicine



**Best Research  
Evidence**



**Researchers**

**Policy makers**

**Health professionals**

# Forms of Bias



## 1. Publication bias



*“File drawer effect”*

# Forms of Bias



1. Publication bias
2. Outcome reporting bias



# Forms of Bias



1. Publication bias
  2. Outcome reporting bias
- Affecting  
*meta-analytic*  
effect

# Forms of Bias



1. Publication bias
2. Outcome reporting bias
3. Spin / Selective focus

# Forms of Bias



1. Publication bias
2. Outcome reporting bias
3. Spin / Selective focus

No spin: “Treatment X plus CAU was not more effective than CAU plus placebo in patients with depression”.

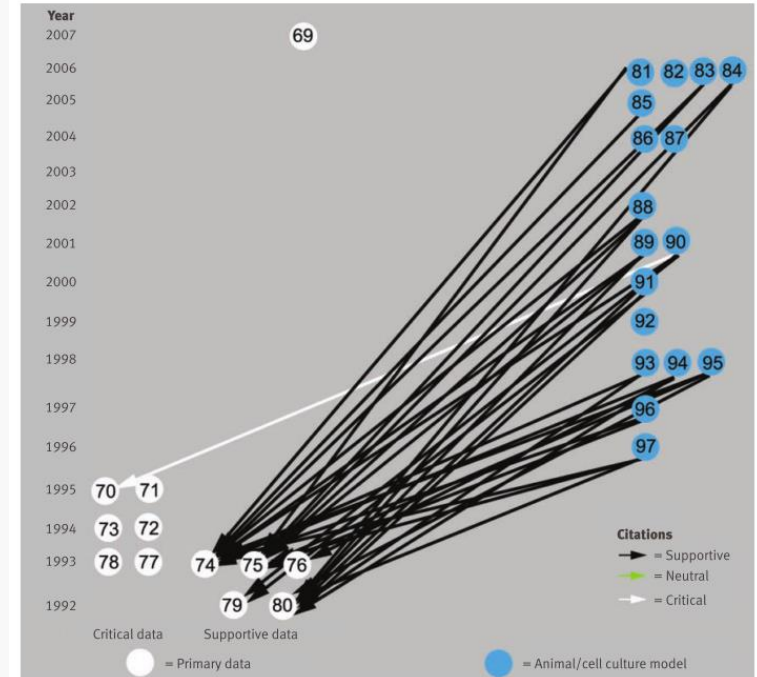
Spin: “Treatment X plus CAU was well tolerated and is suggested to have efficacy in patients who had not received prior therapy”.



# Forms of Bias



1. Publication bias
2. Outcome reporting bias
3. Spin / Selective focus
4. Citation bias



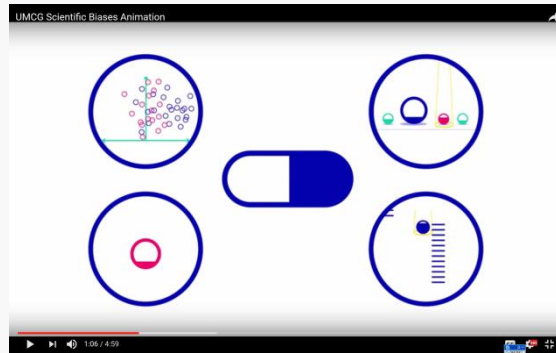
Greenberg, BMJ, 2009

# Forms of Bias



1. Publication bias *Affecting meta-analytic effect*
2. Outcome reporting bias *Affecting meta-analytic effect*
3. Spin / Selective focus *Affecting apparent effect*
4. Citation bias *Affecting apparent effect*

## UMCG Biases Animation



[goo.gl/dsvSzu](https://goo.gl/dsvSzu)

# Methods



- **Dataset: 105 antidepressant trials** Turner et al., 2008, NEJM
  - Food and Drug Administration (FDA) database
  - Matched journal articles (if available)
  
- **Duplicate coding**
  - FDA outcome, article outcome, abstract conclusion

# Methods



- **Dataset: 105 antidepressant trials** Turner et al., 2008, NEJM
  - Food and Drug Administration (FDA) database
  - Matched journal articles (if available)

## Publication bias:

positive trials are more likely to be published than negative trials

## Outcome reporting bias:

mismatch between FDA outcome (negative) and article outcome (positive)

## Spin:

mismatch between abstract conclusion (positive) and article outcome (negative)

## Citation bias:

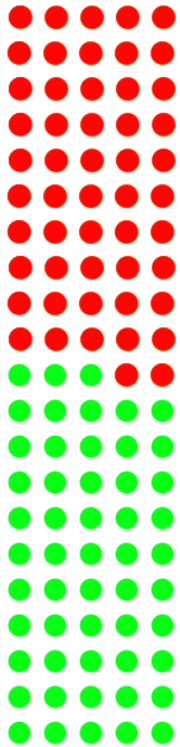
positive and positively presented trials receive more citations than negative trials (average number in Web of Science, Jan 2016)

# Results



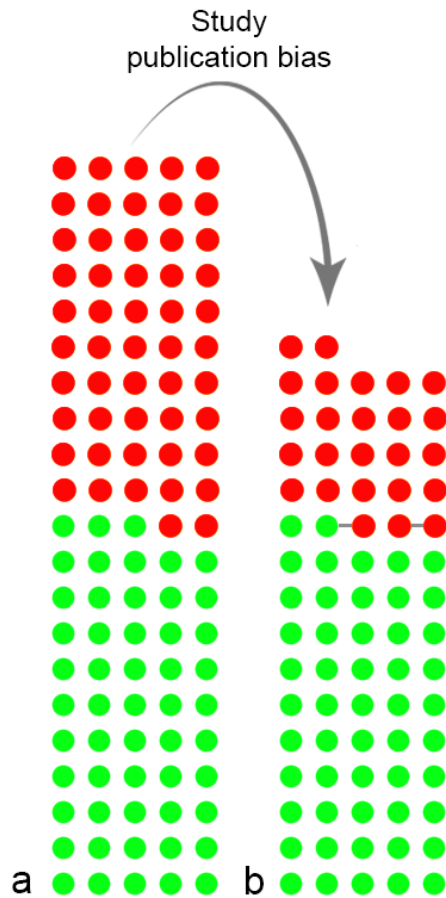
- Negative trial
- Positive trial
- Spin
- Mild spin
- No abstract

**a) Original cohort (n=105)**  
- positive-negative trial ratio is 50/50



a

# Results



- Negative trial
- Positive trial
- Spin
- Mild spin
- No abstract

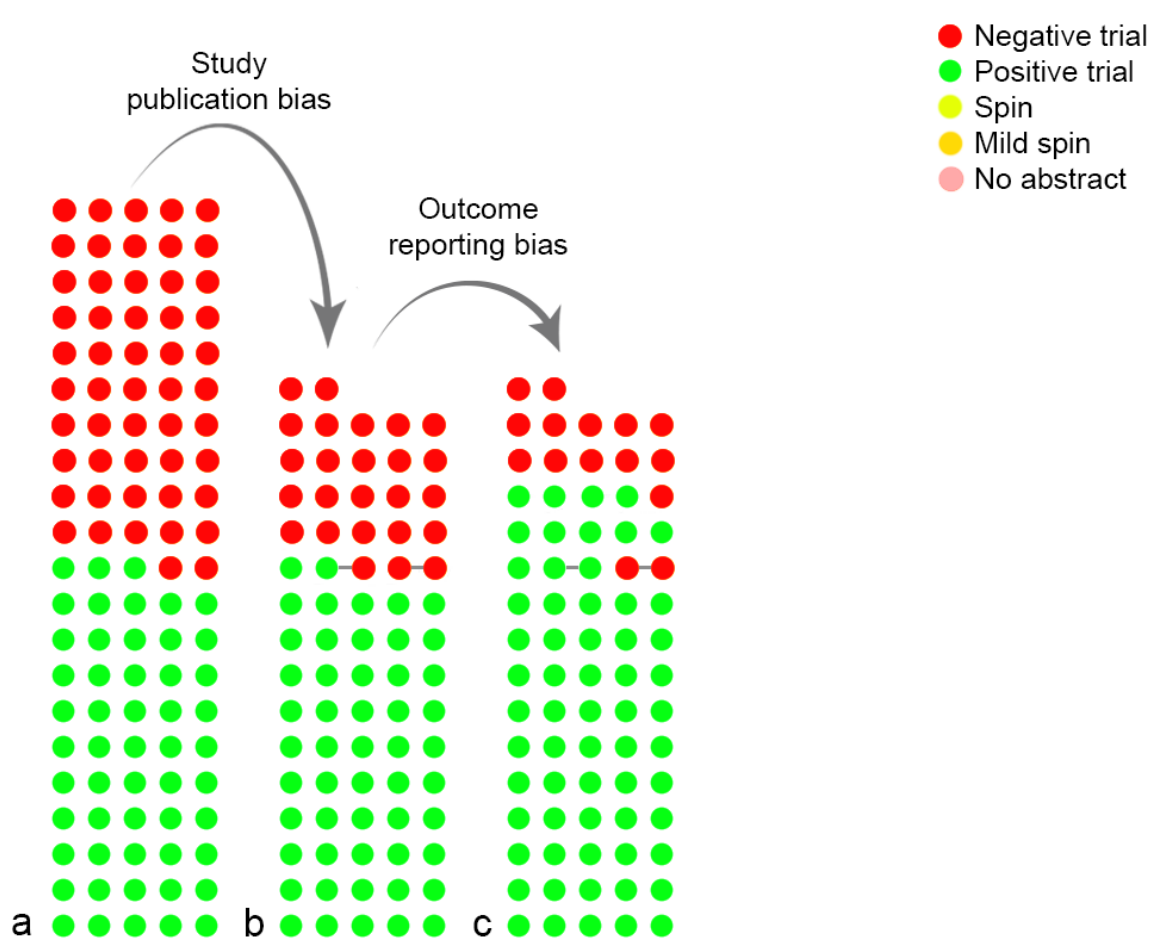
## a) Original cohort (n=105)

- positive-negative trial ratio is 50/50

**b) Publication bias:** 98% of the positive and 48% of the negative trials were published

- positive-negative trial ratio of the 77 published trials is 68/32

# Results



## a) Original cohort (n=105)

- positive-negative trial ratio is 50/50

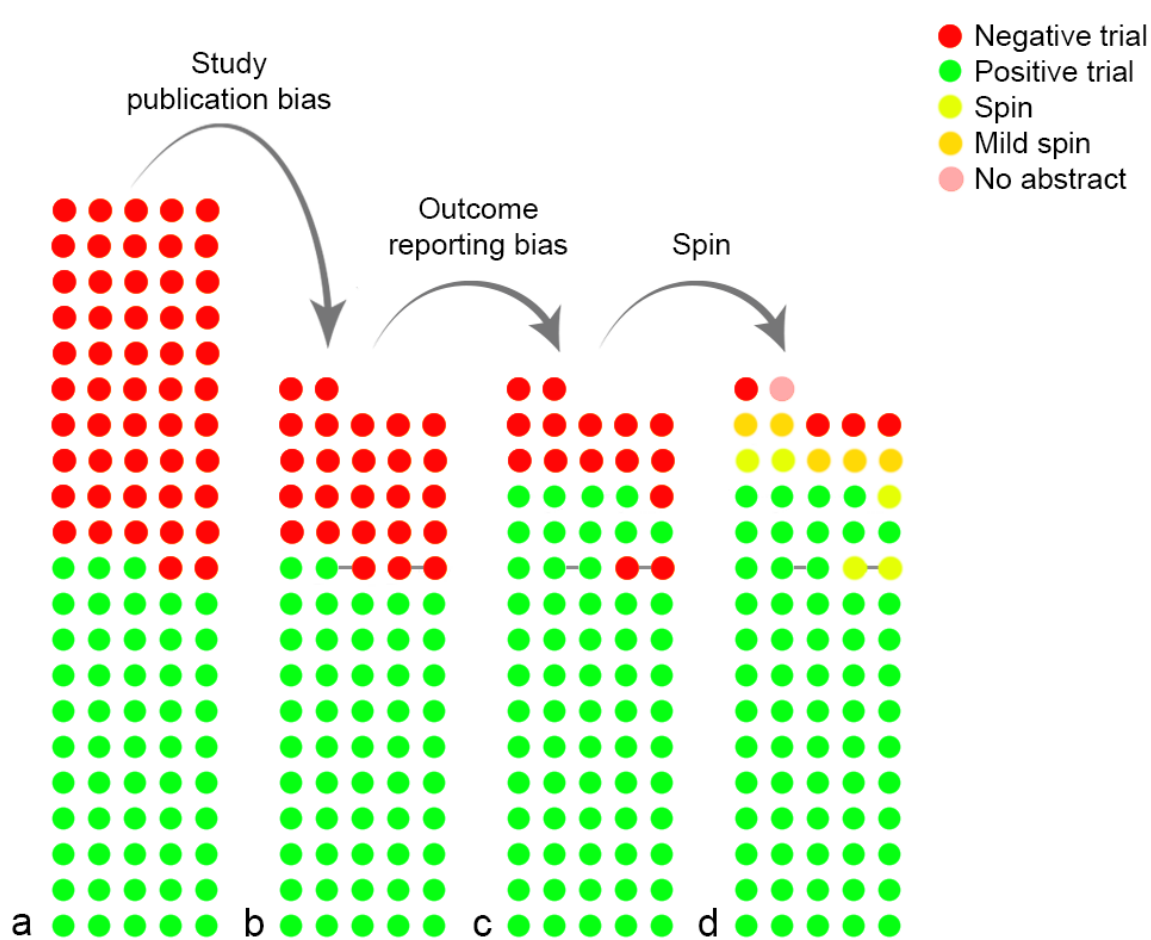
**b) Publication bias:** 98% of the positive and 48% of the negative trials were published

- positive-negative trial ratio of the 77 published trials is 68/32

**c) Outcome reporting bias:** 10/25 negative trials were published with positive primary outcomes

- positive-negative trial ratio 81/19

# Results



## a) Original cohort (n=105)

- positive-negative trial ratio is 50/50

**b) Publication bias:** 98% of the positive and 48% of the negative trials were published

- positive-negative trial ratio of the 77 published trials is 68/32

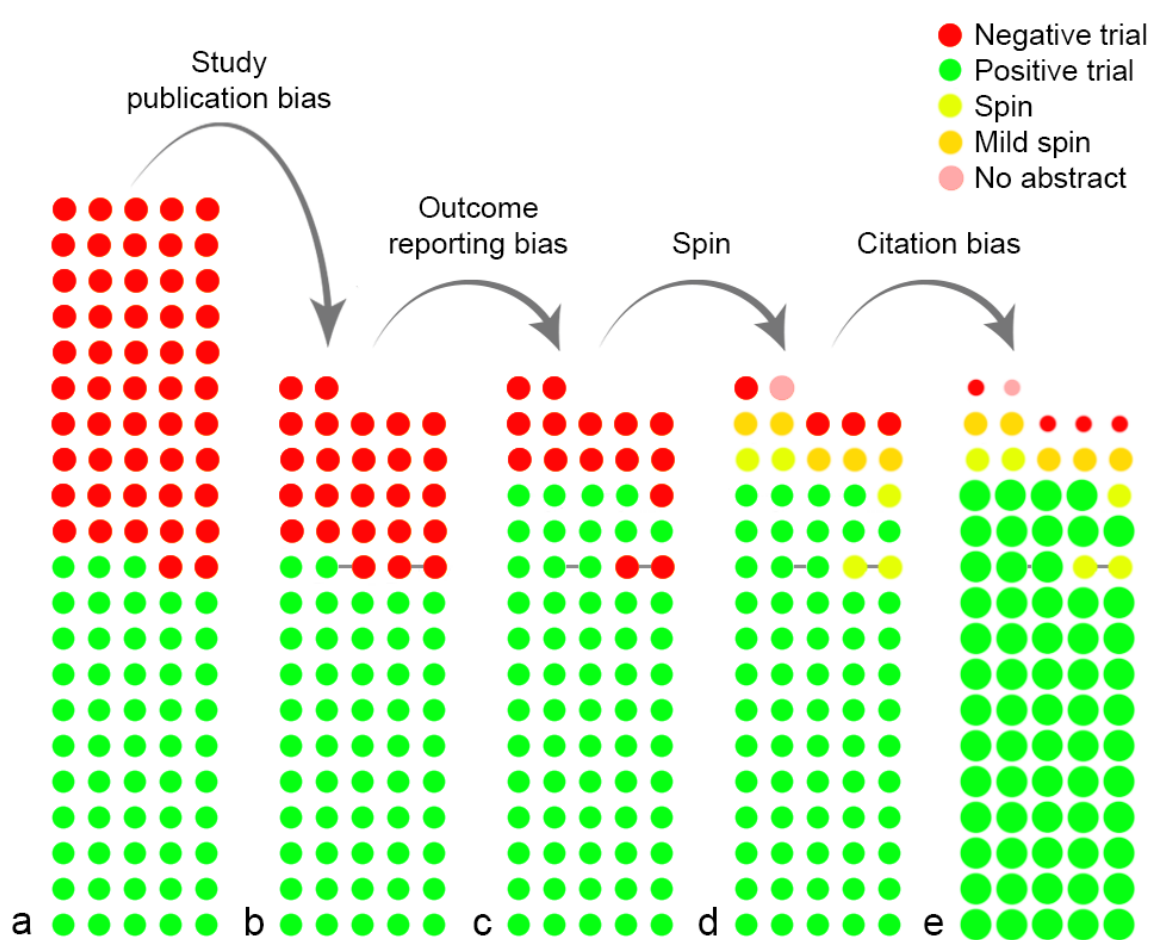
**c) Outcome reporting bias:** 10/25 negative trials were published with positive primary outcomes

- positive-negative trial ratio 81/19

**d) Spin:** abstracts of 5/15 remaining negative trials contained spin (“treatment was effective”), and 5 contained mild spin (“treatment was numerically better”, “trial failed”)



# Cumulative effect of biases



## a) Original cohort (n=105)

- positive-negative trial ratio is 50/50

## b) Publication bias: 98% of the positive and 48% of the negative trials were published

- positive-negative trial ratio of the 77 published trials is 68/32

## c) Outcome reporting bias: 10/25 negative trials were published with positive primary outcomes

- positive-negative trial ratio 81/19

## d) Spin: abstracts of 5/15 remaining negative trials contained spin (“treatment was effective”), and 5 contained mild spin (“treatment was numerically better”, “trial failed”)

## e) Citation bias: positive trials are cited more (92 citations) than negative trials (32 citations)

# Conclusions



- ❑ Within the antidepressant literature, 50% of all trials are negative, but the cumulative impact of these biases is such that only 5% of published trials unambiguously report that the treatment was not effective, and these trials are cited less frequently than trials reporting positive results.
- ❑ The effects of publication bias, outcome reporting bias, spin, and citation bias accumulate to hide negative results from view.
- ❑ These biases are not unique to antidepressant trials.

# Conclusions



- ❑ Mandatory universal registration, in combination with openness to negative results and vigilance on the part of peer reviewers, journal editors, and readers, may help to prevent and uncover bias.

# Acknowledgements



University Medical Center Groningen

Ymkje Anna de Vries

Annelieke Roest

Peter de Jonge

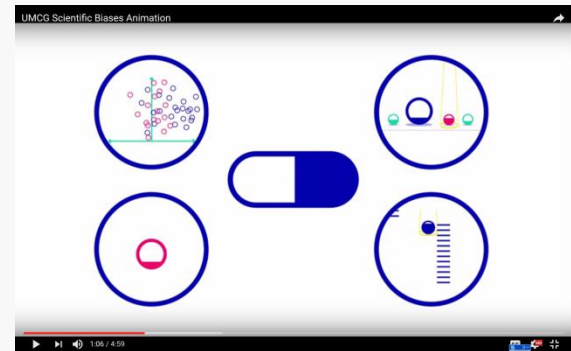
University of Bristol

Marcus Munafò

VU University

Pim Cuijpers

UMCG Biases Animation



[goo.gl/dsvSzu](https://goo.gl/dsvSzu)



[j.bastiaansen@umcg.nl](mailto:j.bastiaansen@umcg.nl)

# Questions



# Psychotherapy



- **Dataset:** 142 papers from meta-analysis on psychotherapy
- **Publication bias & outcome reporting bias:** no standardized registry of trials available
- **Spin:** 49 (35%) of 142 papers were considered negative by Flint et al. (2015), but only 12 (8%) abstracts concluded that psychotherapy was not more effective than a control condition.
- **Citation bias:** negative trials without spin are cited less (26 citations) than negative trials with (mild) spin (73 citations) and positive trials (111 citations)