

# Research Waste: Why we need to rethink meta-analysis



Judith ter Schure  
Peter Grünwald

**Safe Statistics**

**CWI**

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The Netherlands

COMMENT • 20 MARCH 2019

# Scientists rise up against statistical significance

*Valentin Amrhein, Sander Greenland, Blake McShane and more than 800 signatories*

## Analysis

### Towards evidence based research

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To avoid waste of research, no new studies should be done without a systematic review of existing evidence, argue **Hans Lund and colleagues**

# Statistical Significance is not up to the job

thebmj

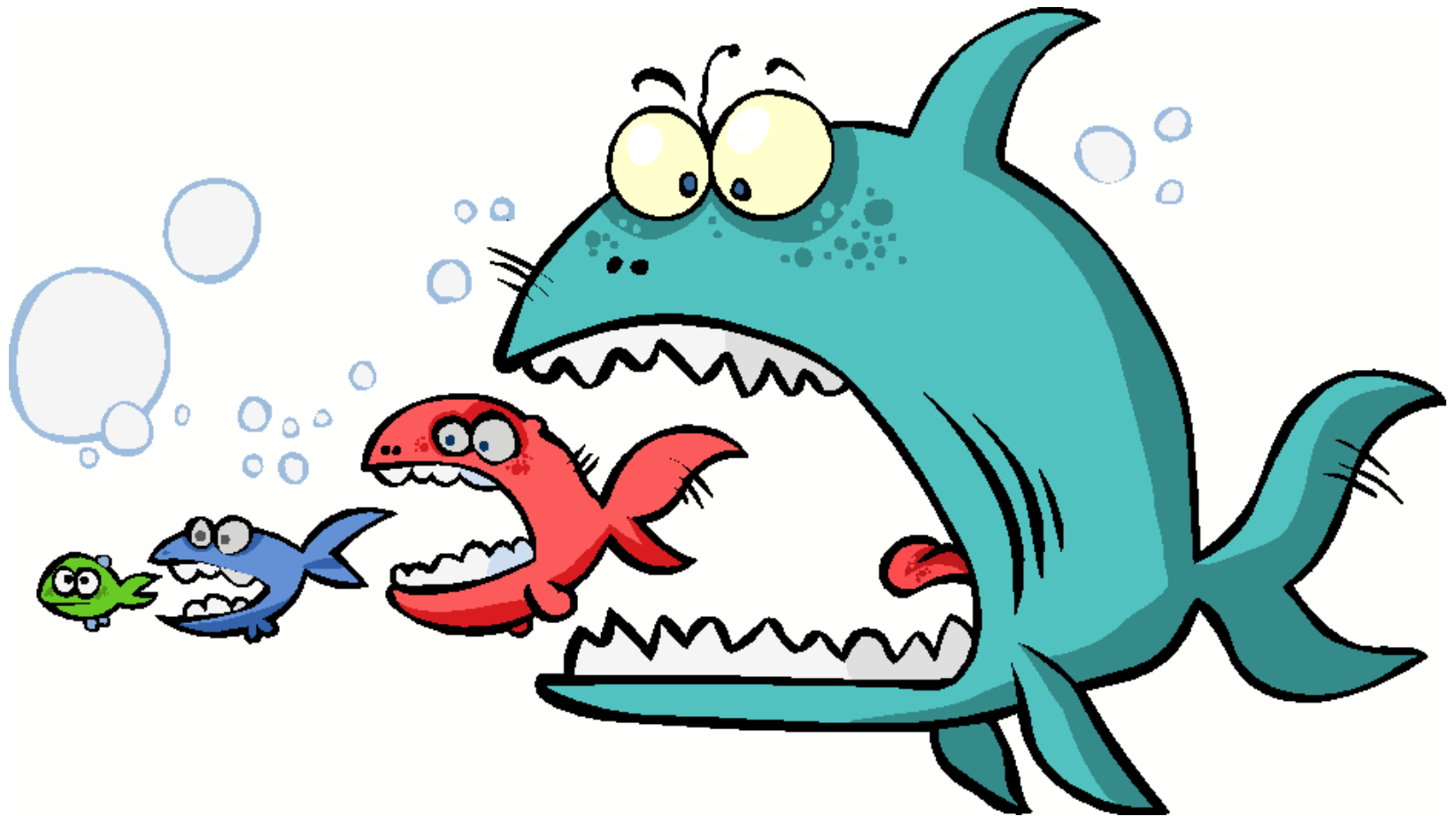
## Analysis

### Towards evidence based research

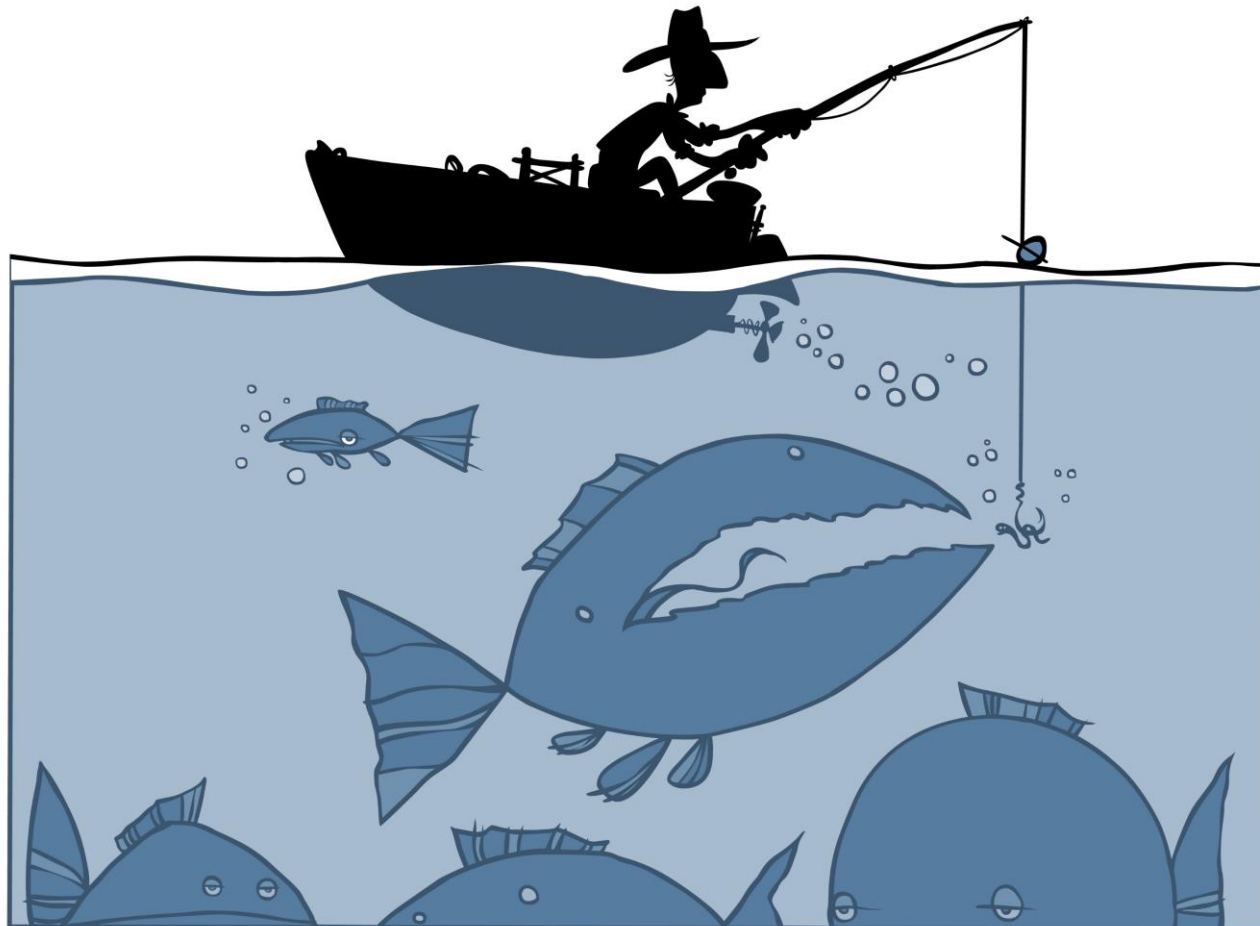
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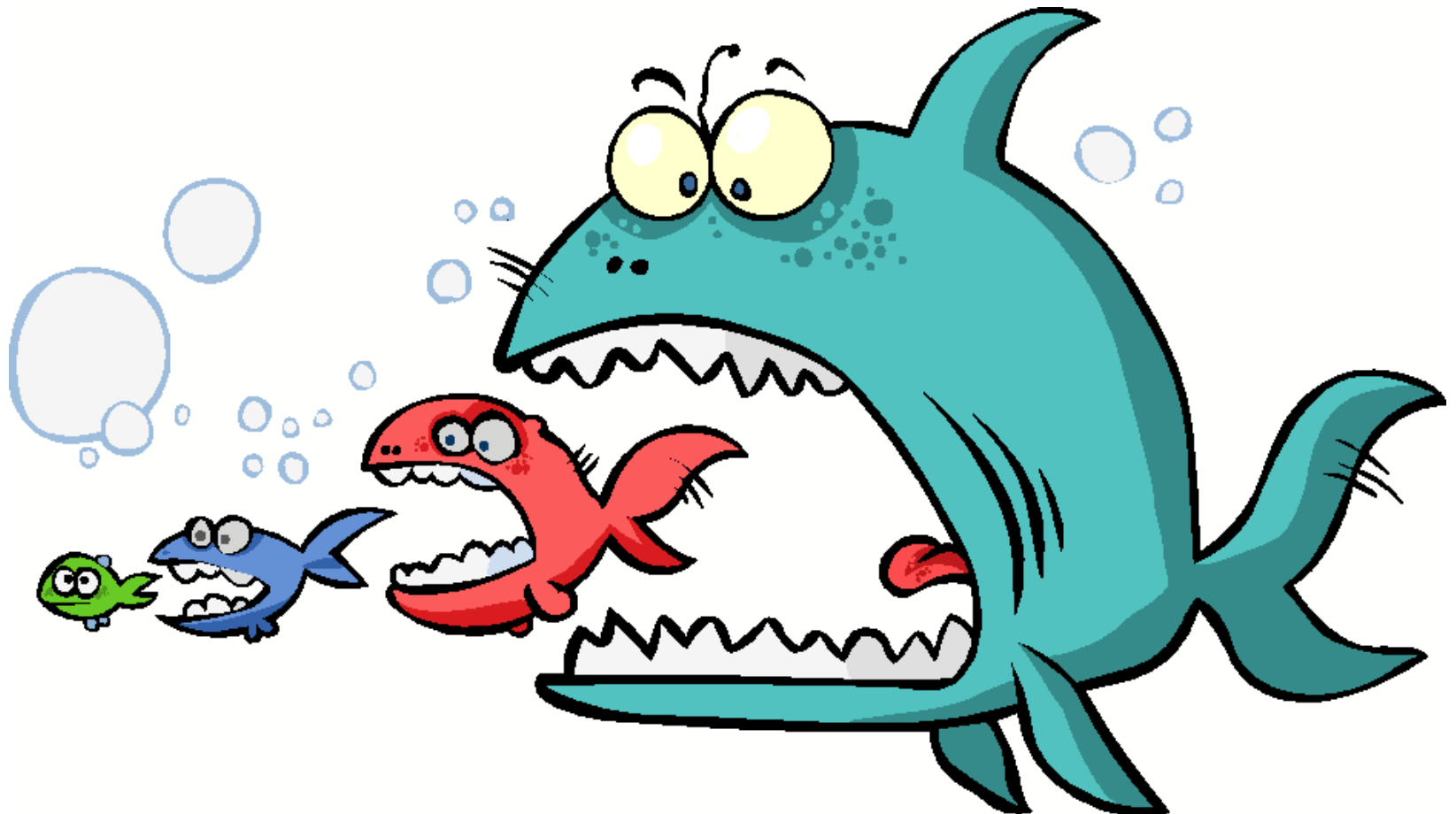
# Science



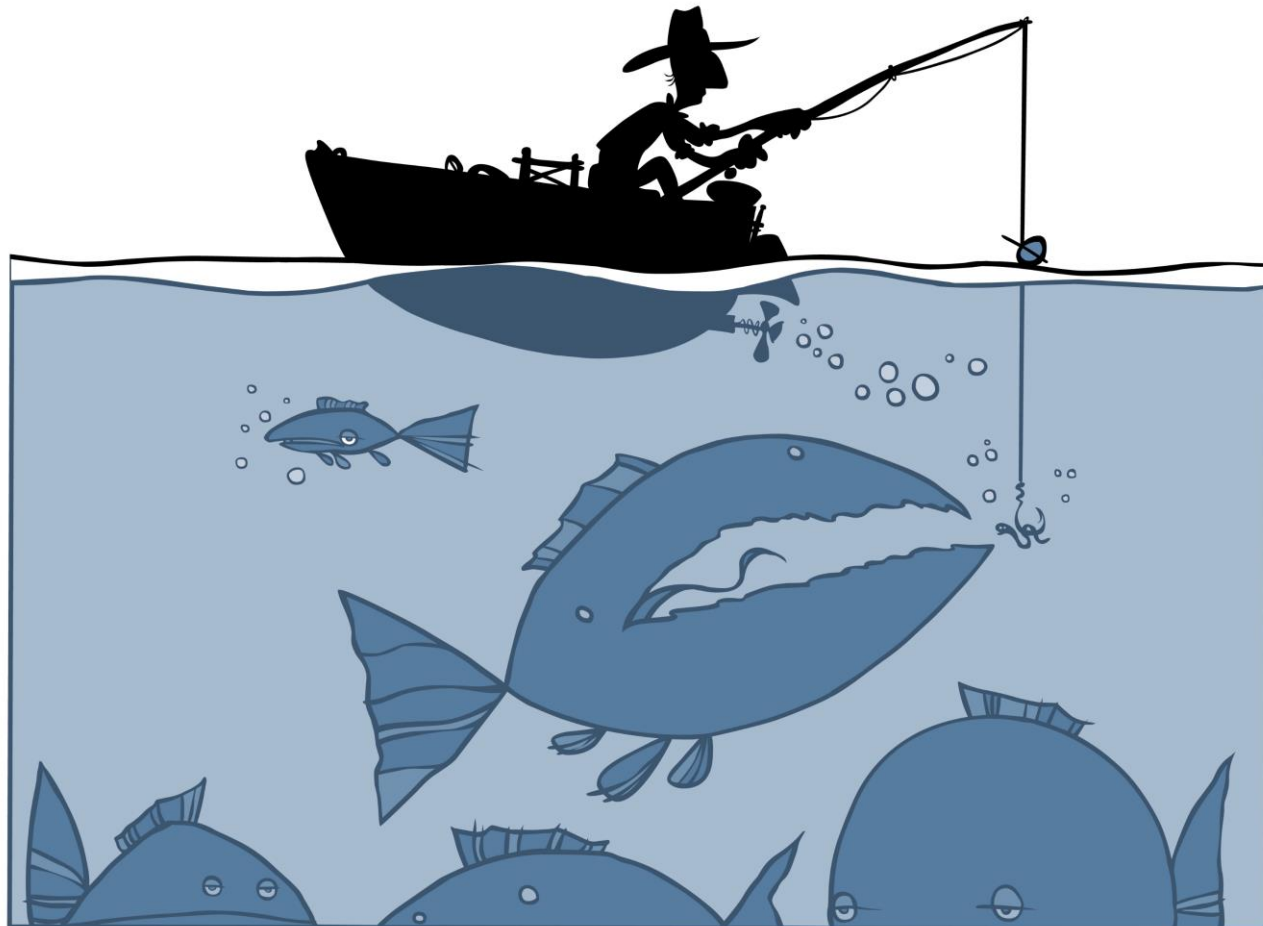
# Meta-analysis



# Size is dependent on intermediate results



# Timing is dependent on intermediate results





# Statistical Significance is not up to the job

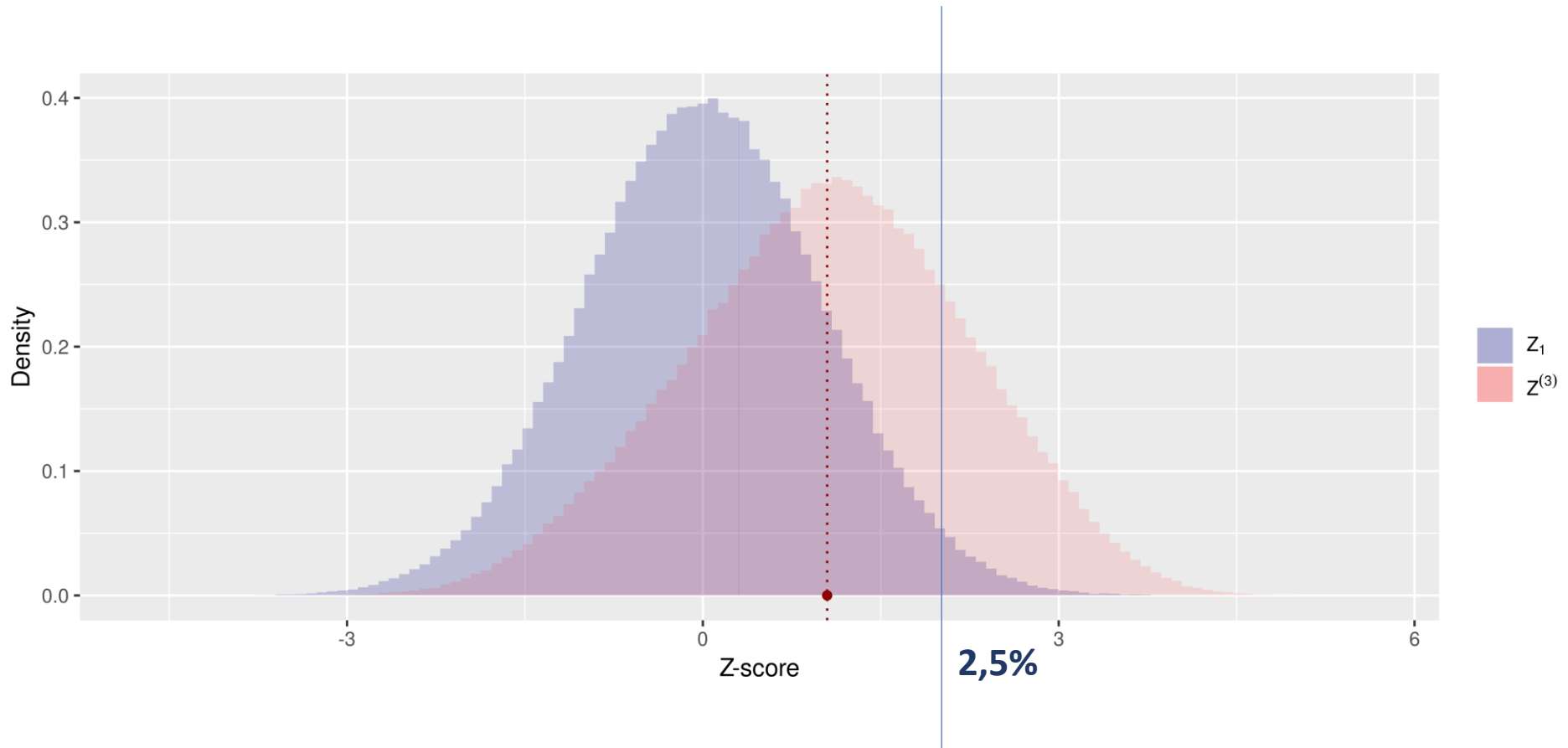
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## Analysis

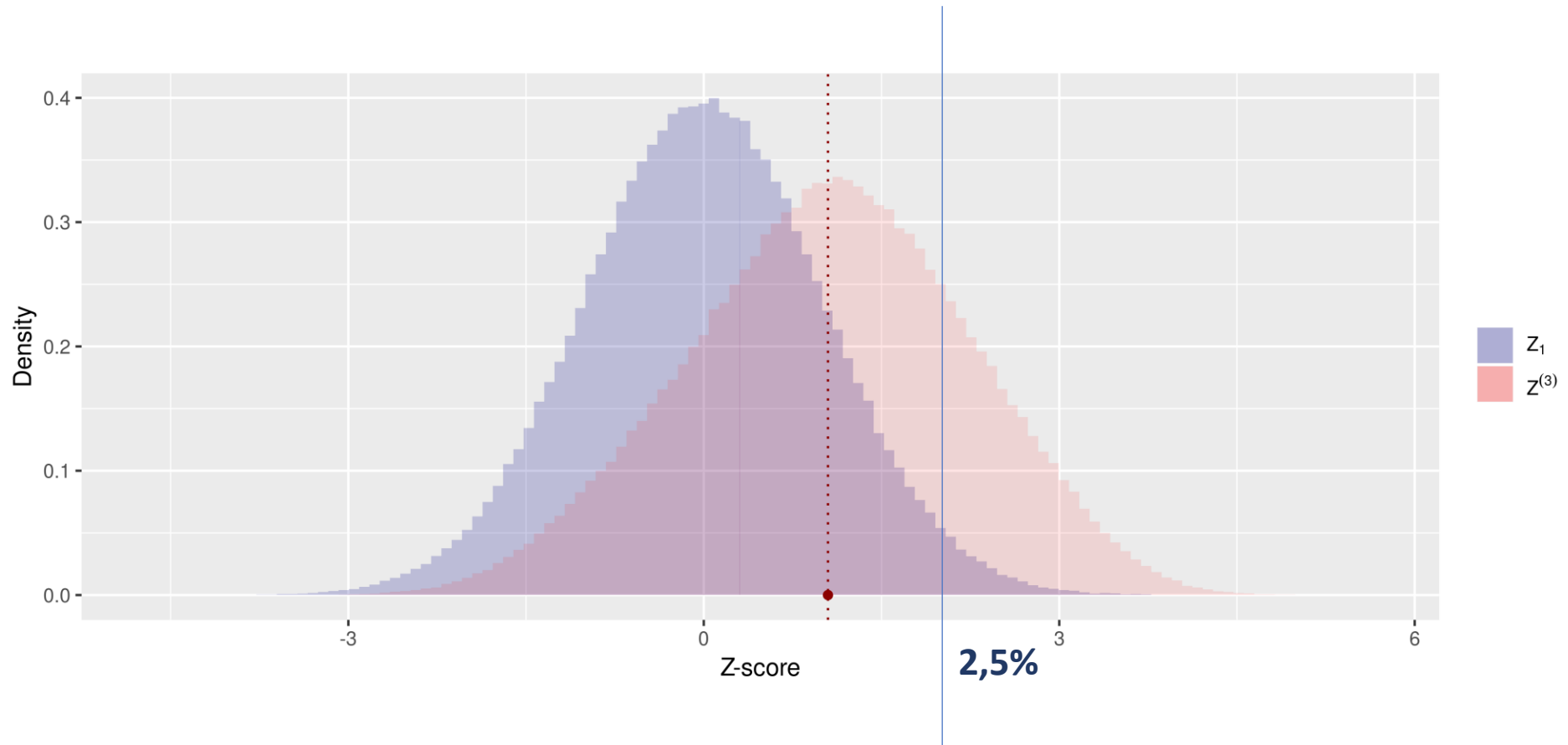
### Towards evidence based research

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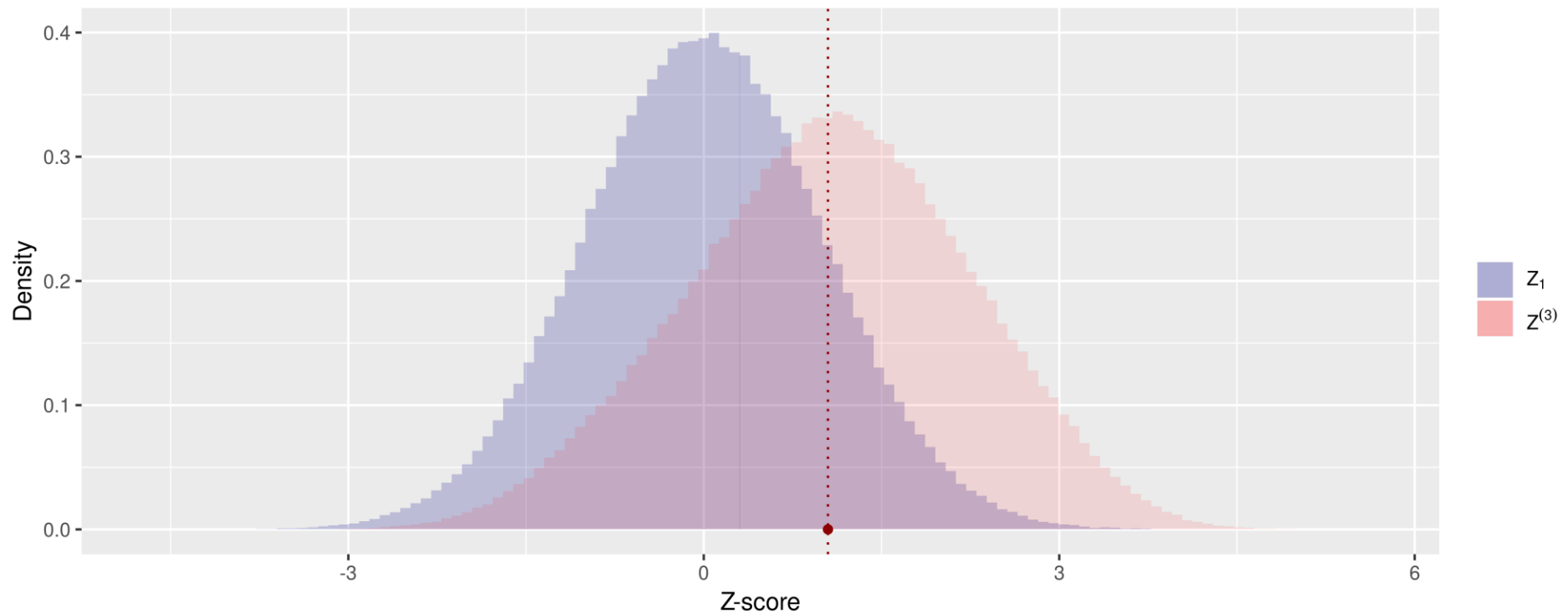
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# Inflated error rates



# Accumulation Bias



# Accumulation Bias

# BMC Medical Research Methodology



Research article

**Open Access**

The **fading** of reported effectiveness. A meta-analysis of randomised controlled trials

Bernhard T Gehr<sup>1</sup>, Christel Weiss<sup>2</sup> and Franz Porzsolt\*<sup>3</sup>

**CWI**

**fading**

## How systematic reviews cause research waste

fading

Systematic reviews of small trials increase waste by advertising to the scientific community **inflated**, often significant treatment effects that become smaller or absent when large, high-quality trials are done. Effect estimates from systematic reviews often inform sample size calculations.<sup>4</sup> However, because most reviews provide **exaggerated estimates** of treatment effects due to inclusion

We declare no competing interests.

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fading

inflated,

exaggerated estimates

Perspective

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**Why do Phase III Trials of Promising Heart Failure Drugs Often Fail? The Contribution of 'Regression to the Truth'**

HENRY KRUM, MBBS, PhD, FRACP, ANDREW TONKIN, MD, FRACP

*Victoria, Australia*

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fading

inflated,

exaggerated estimates

Regression to the Truth

fading

inflated,

exaggerated estimates



## REVIEW ARTICLES

Early extreme contradictory estimates may appear in published research: **The Proteus phenomenon** in molecular genetics research and randomized trials

John P.A. Ioannidis<sup>a,b,c,\*</sup>, Thomas A. Trikalinos<sup>a,b</sup>

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## Systematic reviews and research waste

We share Ian Roberts' and Katharine Ker's frustration with the poor quality of much research (Oct 17,

their suggestion scientifically flawed, it is also unrealistic. Funders and regulators cannot be expected to support and endorse large studies without some reassurance from the results of smaller existing studies that the substantial investment needed is justified. We hope that, instead of promoting their

*\*Iain Chalmers, Paul Glasziou  
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## Correspondence

Early extreme contradictory estimates

The Proteus phenomenon

Regression to the Truth

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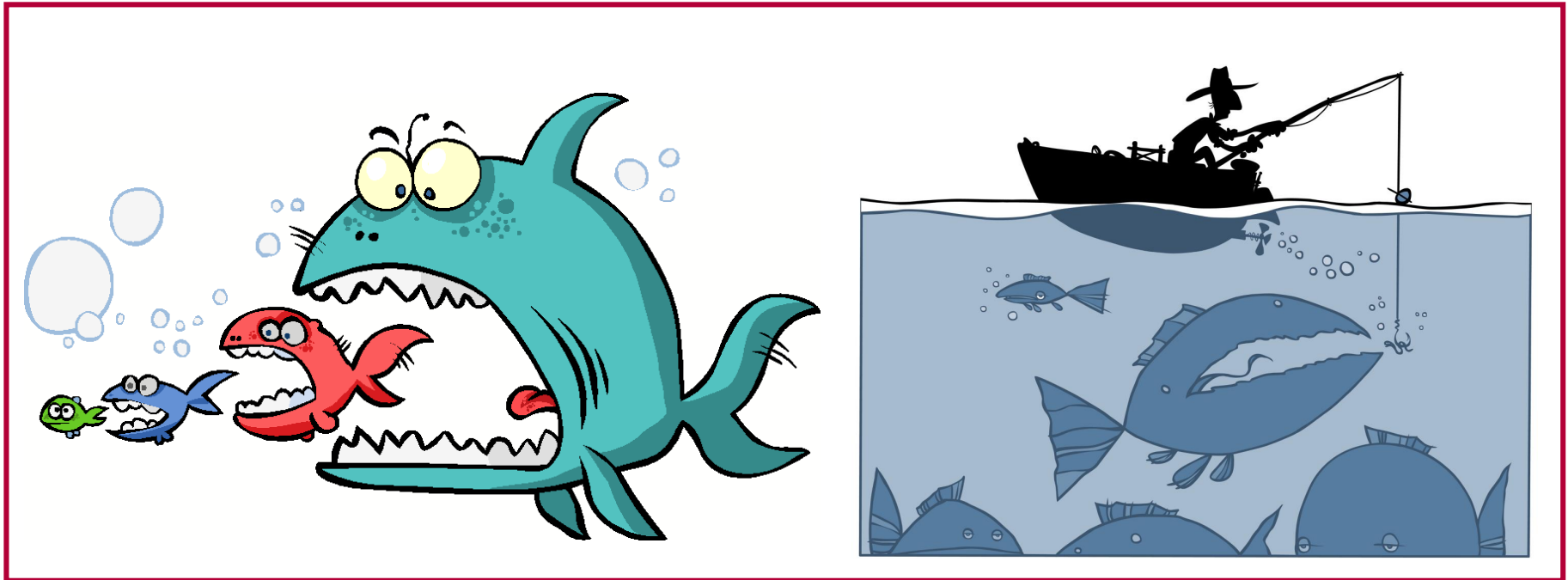
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# Accumulation Bias Framework





# Accumulation Bias Framework

$$A(t)$$

$A(t)$

Early extreme contradictory estimates

The Proteus phenomenon

$A(t)$

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fading

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$\text{LR}_{10}^{(t)}$

$$\mathbf{LR}_{10}^{(t)} = \frac{f_1(z_1, \dots, z_t) \cdot A(t | z_1, \dots, z_t)}{f_0(z_1, \dots, z_t) \cdot A(t | z_1, \dots, z_t)}$$

$$\begin{aligned}\mathbf{LR}_{10}^{(t)} &= \frac{f_1(z_1, \dots, z_t) \cdot A(t | z_1, \dots, z_t)}{f_0(z_1, \dots, z_t) \cdot A(t | z_1, \dots, z_t)} \\ &= \frac{f_1(z_1, \dots, z_t)}{f_0(z_1, \dots, z_t)} \\ &= \mathbf{LR}_{10}(z_1, \dots, z_t).\end{aligned}$$

# Decision Making with Accumulation Bias



# Safe Tests: Accumulating Tests for Accumulating Science





**“Standing on the shoulders of giants”  
introduces**

**Accumulation Bias**

**and inflated error rates**

**in meta-analysis significance tests**

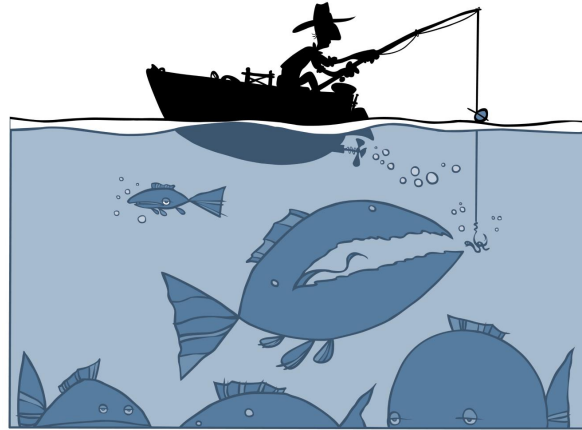
**Reducing Research Waste**

**by tests that control errors**

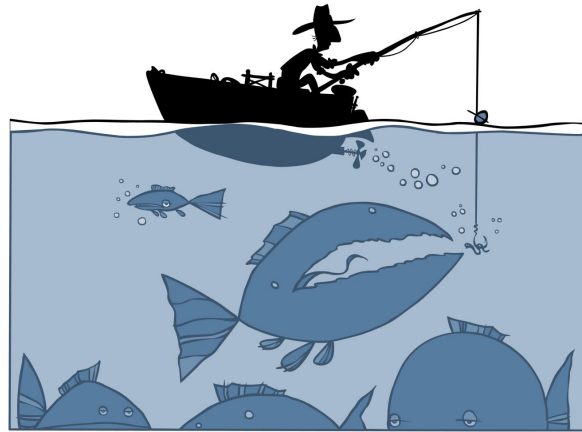
**is still possible**

**with Safe Tests**

Ter Schure & Grünwald (2019)  
Accumulation Bias in Meta-Analysis:  
The Need to Consider *Time* in Error Control



Ter Schure & Grünwald (2019)  
Accumulation Bias in Meta-Analysis:  
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**Thank you!**

Contact me at: [schure@cwi.nl](mailto:schure@cwi.nl)

CWI

## Accumulation Bias

$A(t)$

Random ~~X~~ sampling

Likelihood Ratios/  
Safe Tests

Reducing Research Waste  
with meta-analysis  
"Evidence-Based Research"

Statistical ~~X~~ Significance

Yes/No