# evbres

## Evidence-Based Research

The project is supported by

## cost
### EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

Funded by the Horizon 2020 Framework Programme of the European Union

# What is research waste?

**Malcolm Macleod**
Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies and University of Edinburgh

Bergen Public Meeting. 6th February, 2019

**CAMARADES: Bringing evidence to translational medicine**

# What is research waste?

**Malcolm Macleod**

Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies

and

University of Edinburgh

# Neural Correlates of Interspecies Perspective Taking in the Post-Mortem Atlantic Salmon: An Argument For Proper Multiple Comparisons Correction

Craig M. Bennett[1*], Abigail A. Baird[2], Michael B. Miller[1] and George L. Wolford[3]

One mature Atlantic Salmon (Salmo salar) participated in the fMRI study. The salmon measured approximately 18 inches long, weighed 3.8 lbs, and was not alive at the time of scanning. It is not known if the salmon was male or female, but given the post-mortem state of the subject this was not thought to be a critical variable.
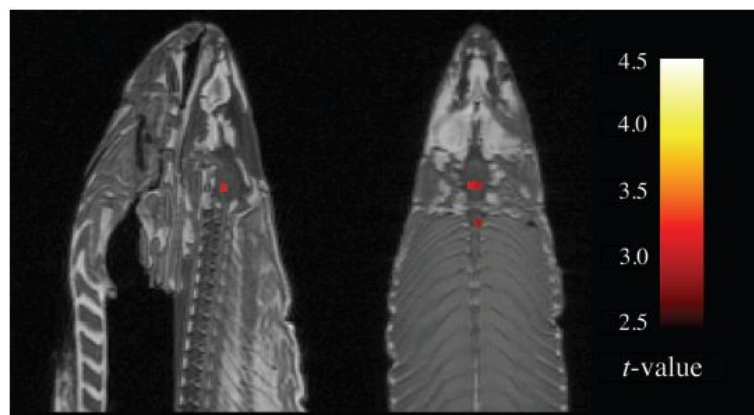
The task administered to the salmon involved completing an open-ended mentalizing task. The salmon was shown a series of photographs depicting human individuals in social situations with a specified emotional valence, either socially inclusive or socially exclusive. The salmon was asked to determine which emotion the individual in the photo must have been experiencing.



Several active voxels were observed in a cluster located within the salmon's brain cavity (see Fig. 1). The size of this cluster was $81 \text{ mm}^3$ with a cluster-level significance of $p = 0.001$.

Either we have stumbled onto a rather amazing discovery in terms of post-mortem ichthyological cognition, or there is something a bit off with regard to our uncorrected statistical approach.

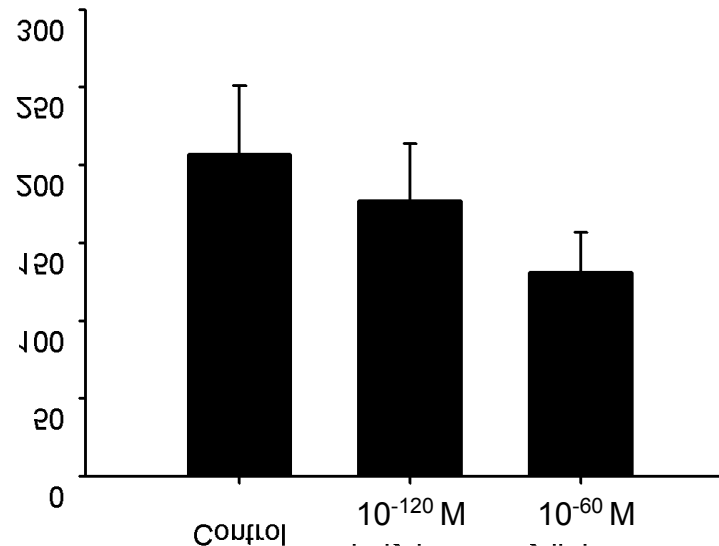Winner of the 2012 Ignoble Prize for Neuroscience

# Treatment of experimental stroke with low-dose glutamate and homeopathic Arnica montana*

W. Jonas[1], Y. Lin[2], A. Williams[2], F. Tortella[2], R. Tuma[3]
[1] Uniformed Services University of the Health Sciences, Bethesda, Maryland
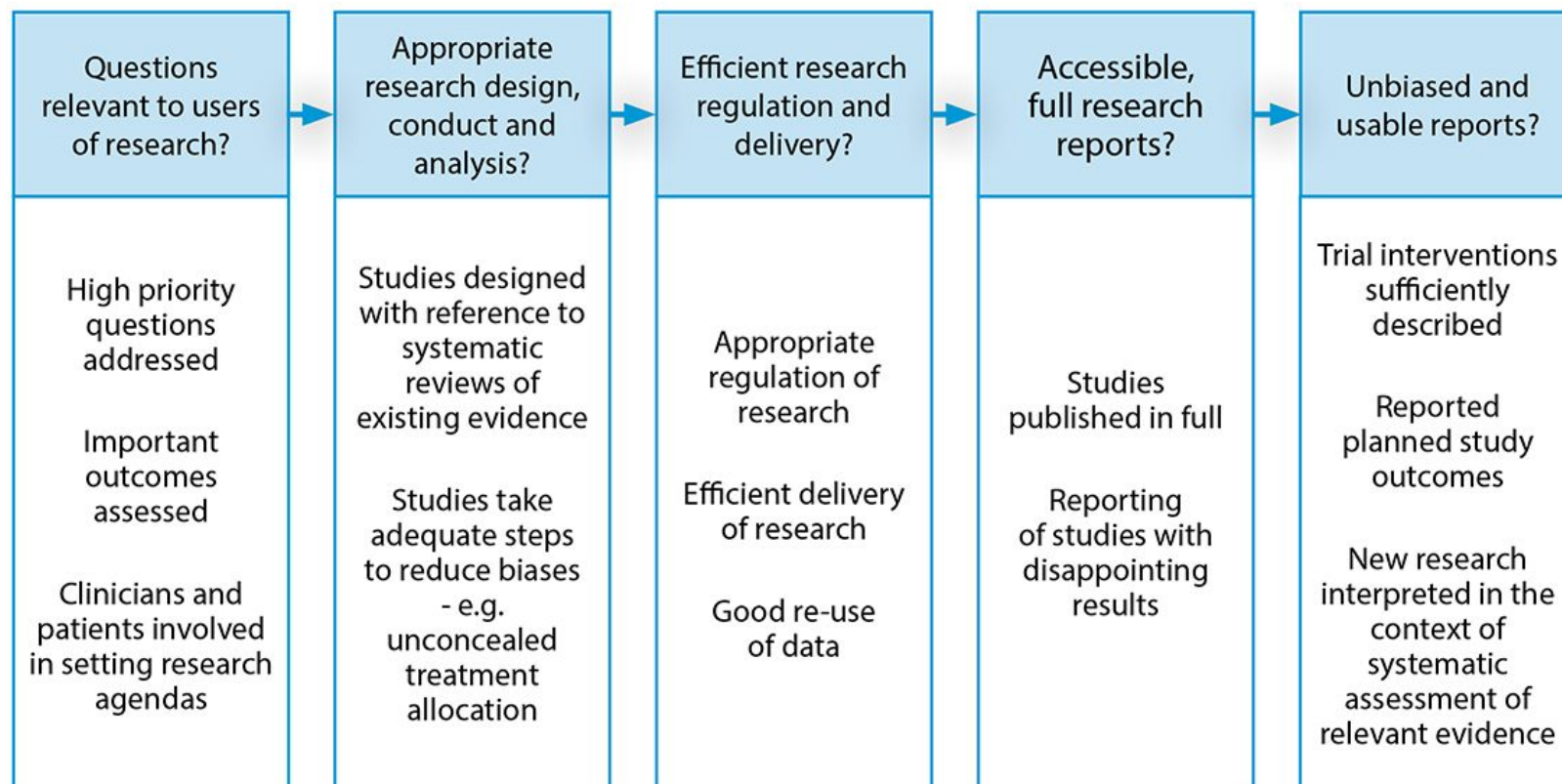[2] Walter Reed Army Institute of Research, Washington, D.C.
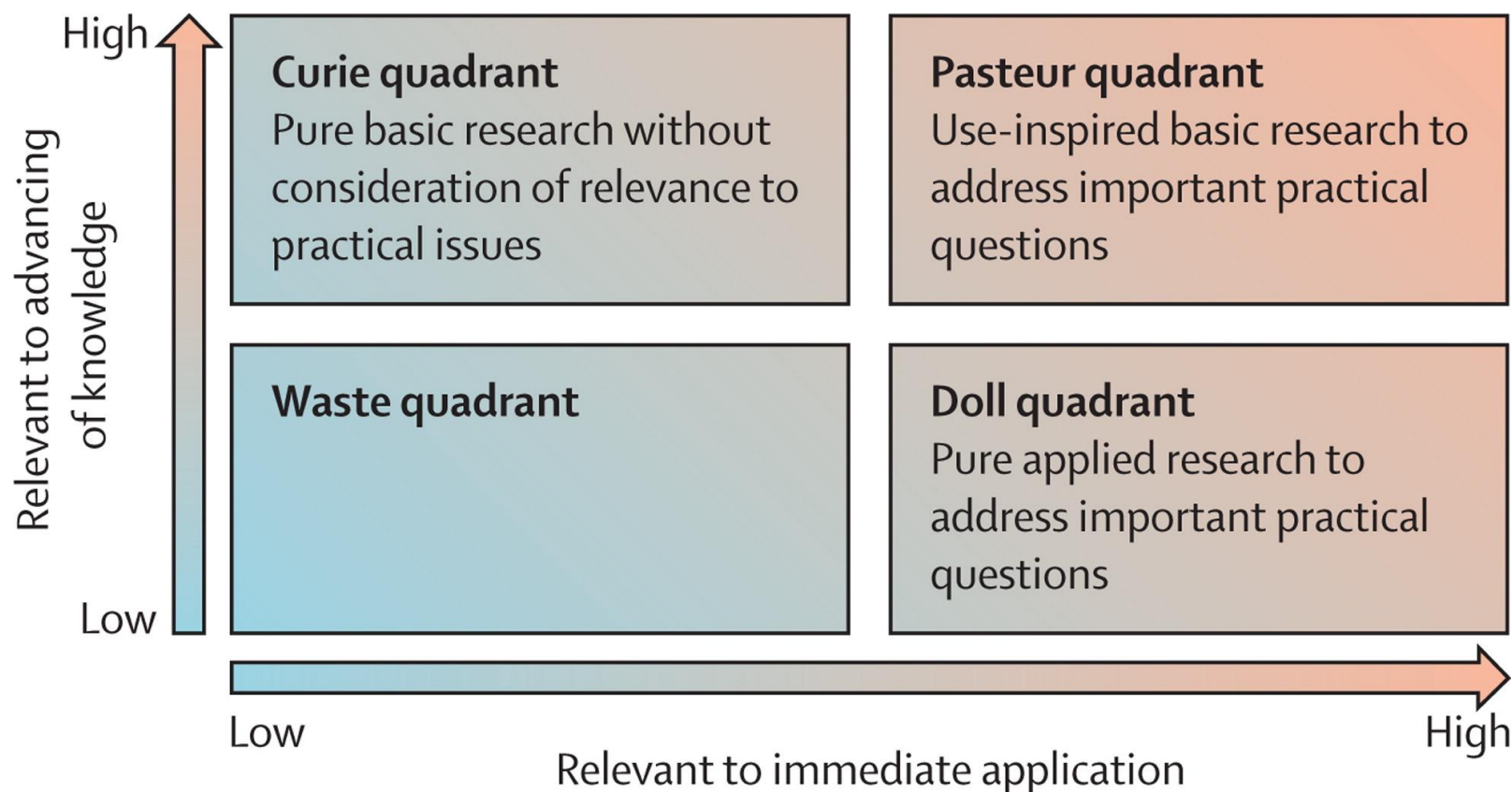[3] Temple University, Philadelphia, PA

# Biomedical research: Increasing value, reducing waste



| Questions relevant to users of research? | Appropriate research design, conduct and analysis? | Efficient research regulation and delivery? | Accessible, full research reports? | Unbiased and usable reports? |
|---|---|---|---|---|
| High priority questions addressed<br><br>Important outcomes assessed<br><br>Clinicians and patients involved in setting research agendas | Studies designed with reference to systematic reviews of existing evidence<br><br>Studies take adequate steps to reduce biases - e.g. unconcealed treatment allocation | Appropriate regulation of research<br><br>Efficient delivery of research<br><br>Good re-use of data | Studies published in full<br><br>Reporting of studies with disappointing results | Trial interventions sufficiently described<br><br>Reported planned study outcomes<br><br>New research interpreted in the context of systematic assessment of relevant evidence |

Macleod et al, Lancet 2014

# 1. Setting research priorities
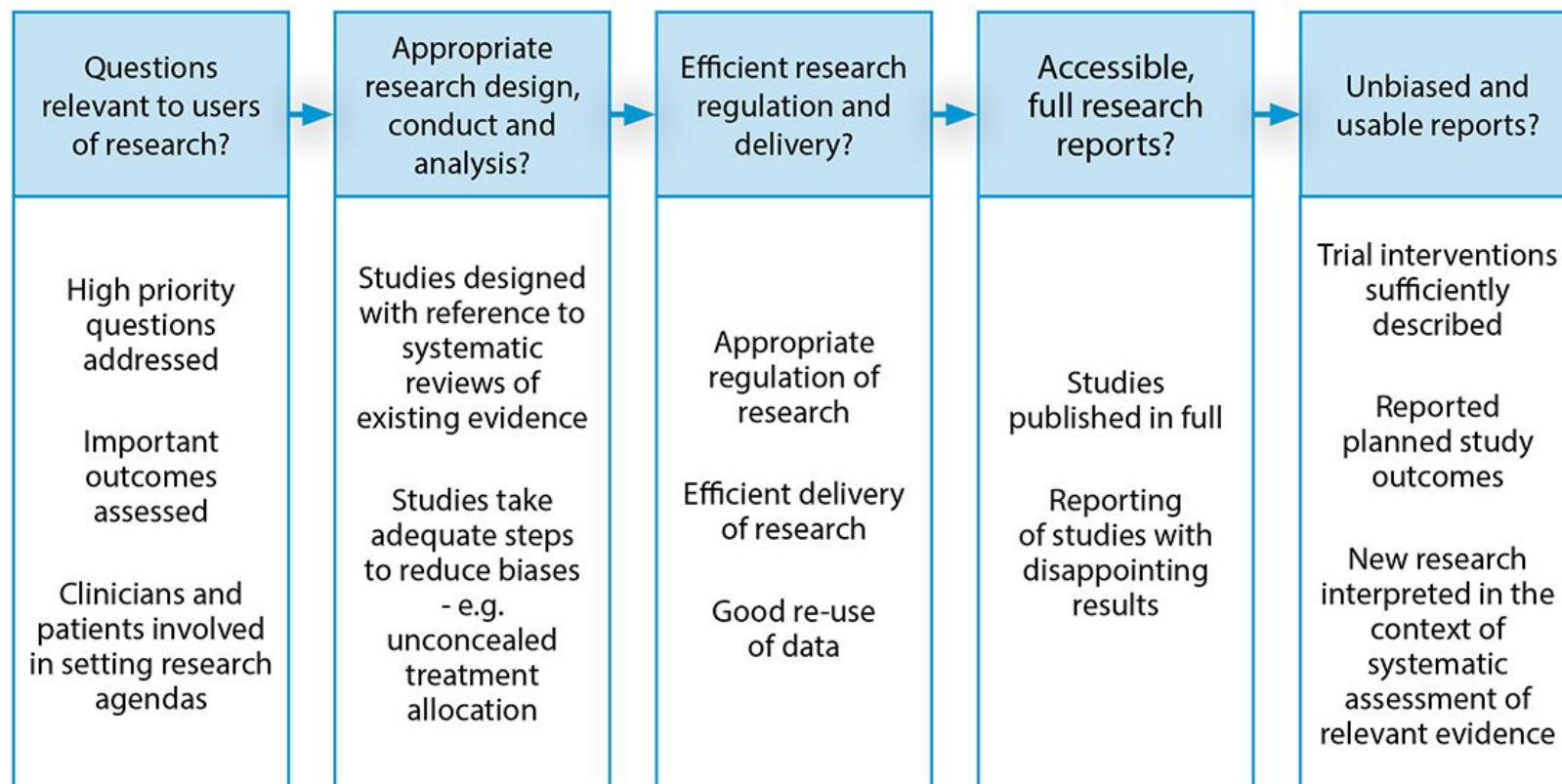
# 1. Setting research priorities
## *Whose priorities?*
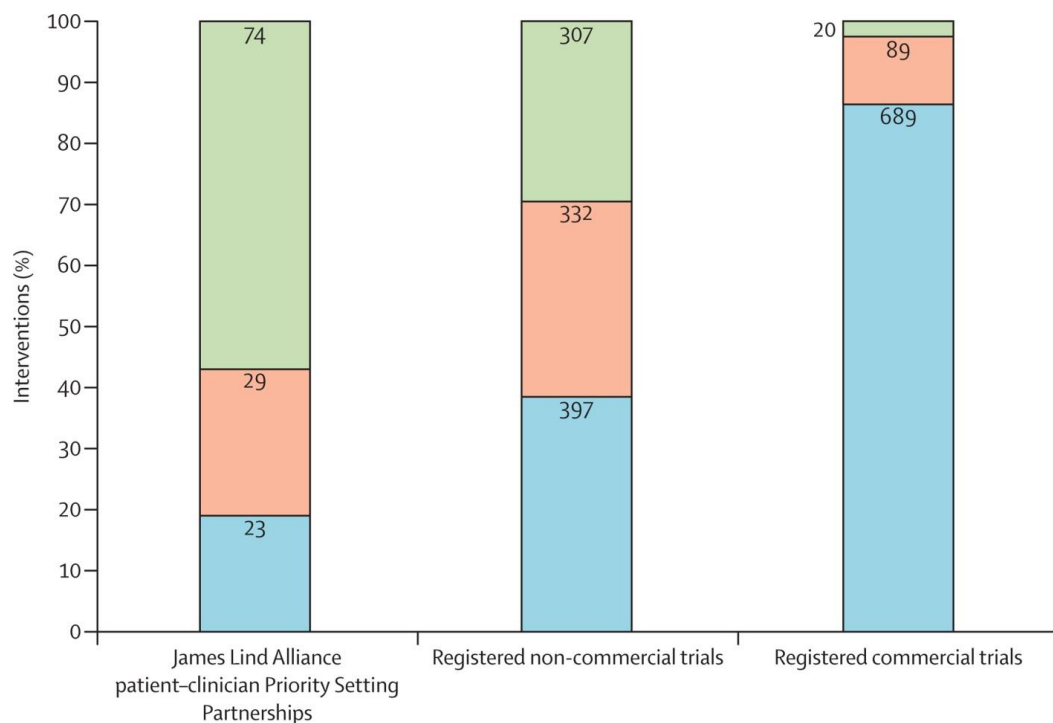


Legend:
- Education and training, service delivery, psychological interventions, physical interventions, excercise, complementary interventions, diet, and other
- Radiotherapy, surgery and perioperative interventions, devices, and diagnostic interventions
- Drugs, vaccines, and biologicals

# Biomedical research: Increasing value, reducing waste



| Questions relevant to users of research? | Appropriate research design, conduct and analysis? | Efficient research regulation and delivery? | Accessible, full research reports? | Unbiased and usable reports? |
|---|---|---|---|---|
| High priority questions addressed<br><br>Important outcomes assessed<br><br>Clinicians and patients involved in setting research agendas | Studies designed with reference to systematic reviews of existing evidence<br><br>Studies take adequate steps to reduce biases - e.g. unconcealed treatment allocation | Appropriate regulation of research<br><br>Efficient delivery of research<br><br>Good re-use of data | Studies published in full<br><br>Reporting of studies with disappointing results | Trial interventions sufficiently described<br><br>Reported planned study outcomes<br><br>New research interpreted in the context of systematic assessment of relevant evidence |

Macleod et al, Lancet 2014

**CAMARADES: Bringing evidence to translational medicine**

# 2. Design, conduct and analysis

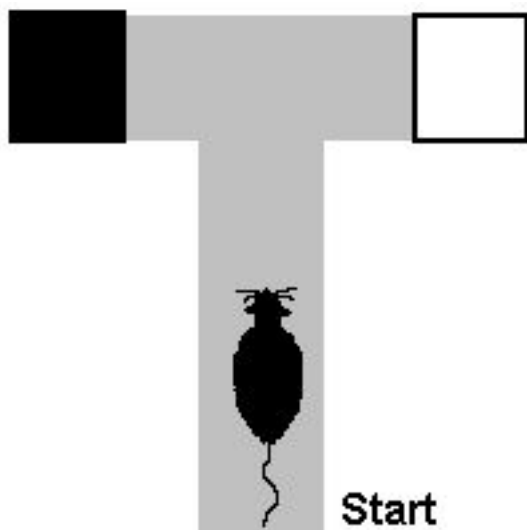*Failure to replicate published pre-clinical academic results*
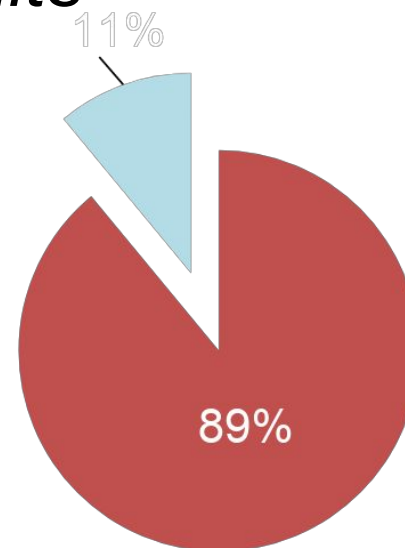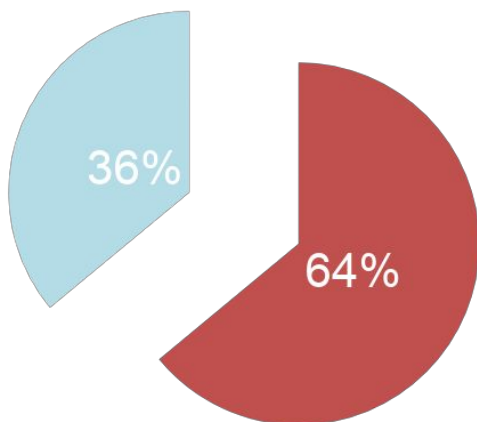
# You can usually find what you're looking for …

- 12 graduate psychology students
- 5 day experiment: rats in T maze with dark arm alternating at random, and the dark arm always reinforced
- 2 groups – "Maze Bright" and "Maze dull"



Start

| Group | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 |
|-------|-------|-------|-------|-------|-------|
| "Maze bright" | 1.33 | 1.60 | 2.60 | 2.83 | 3.26 |
| "Maze dull" | 0.72 | 1.10 | 2.23 | 1.83 | 1.83 |
| Δ | +0.60 | +0.50 | +0.37 | +1.00 | +1.43 |

Rosenthal and Fode (1963), Behav Sci 8, 183-9

# The scale of the problem
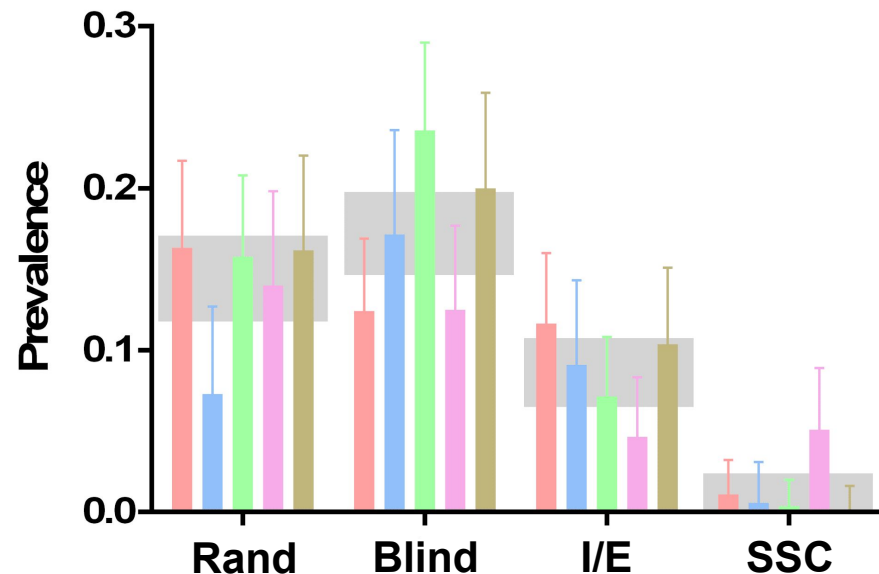## RAE 1173

"an outstanding contribution to the internationally excellent position of the UK in biomedical science and clinical/translational research."
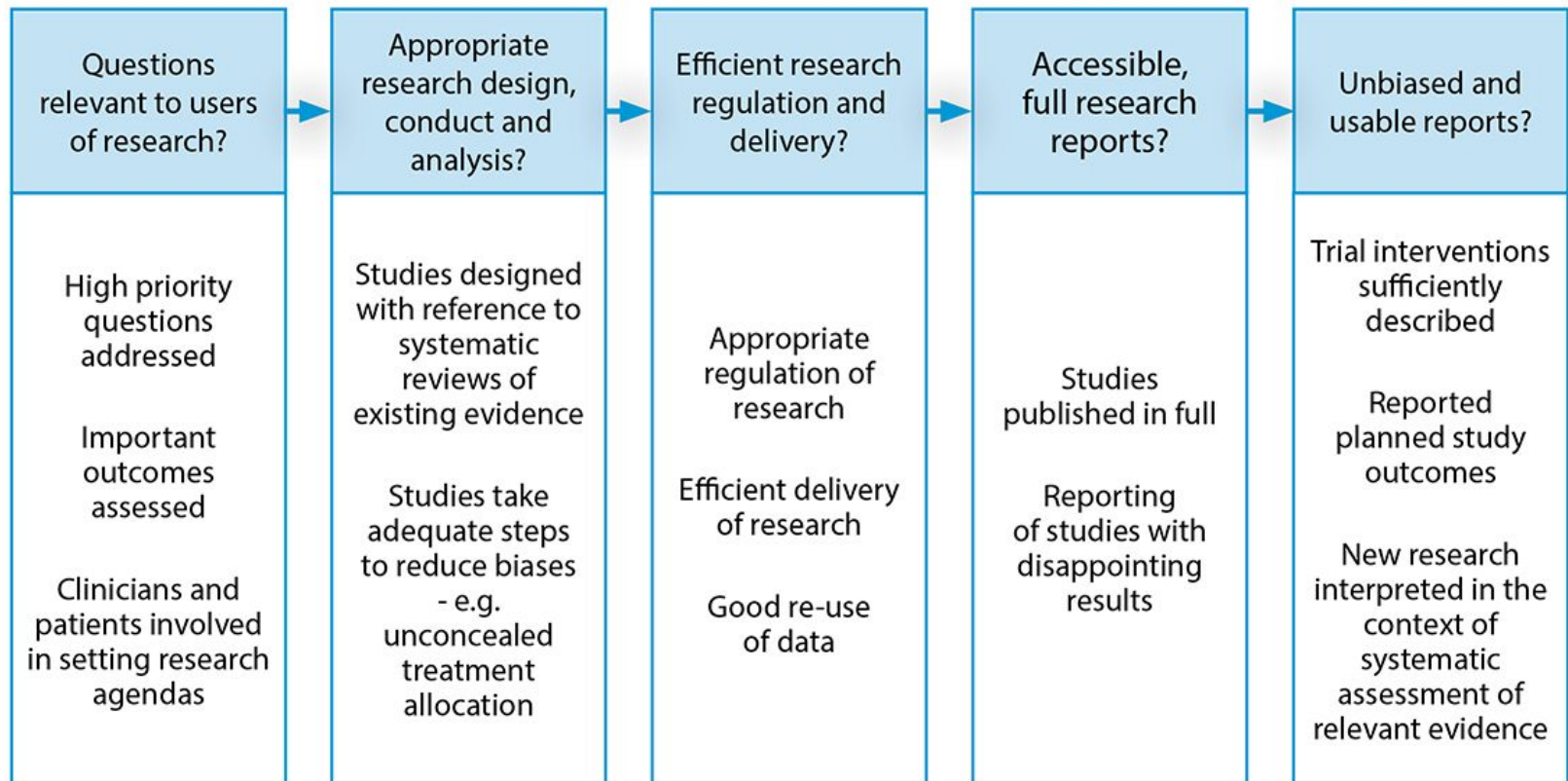
"impressed by the strength within the basic neurosciences that were returned …particular in the areas of behavioural, cellular and molecular neuroscience"

1173 publications using non human animals, published in 2009 or 2010, from 5 leading UK universities

# Biomedical research: Increasing value, reducing waste



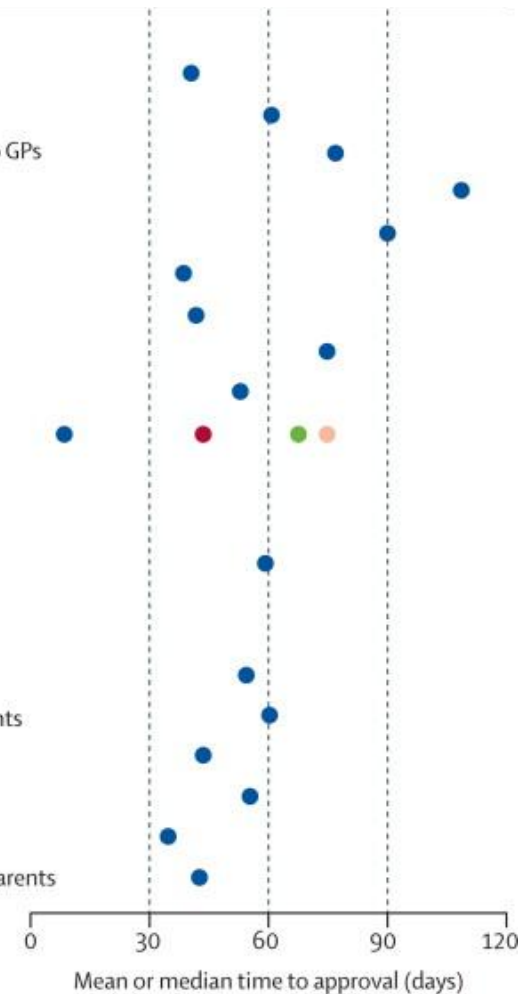| Questions relevant to users of research? | Appropriate research design, conduct and analysis? | Efficient research regulation and delivery? | Accessible, full research reports? | Unbiased and usable reports? |
|---|---|---|---|---|
| High priority questions addressed<br><br>Important outcomes assessed<br><br>Clinicians and patients involved in setting research agendas | Studies designed with reference to systematic reviews of existing evidence<br><br>Studies take adequate steps to reduce biases - e.g. unconcealed treatment allocation | Appropriate regulation of research<br><br>Efficient delivery of research<br><br>Good re-use of data | Studies published in full<br><br>Reporting of studies with disappointing results | Trial interventions sufficiently described<br><br>Reported planned study outcomes<br><br>New research interpreted in the context of systematic assessment of relevant evidence |

Macleod et al, Lancet 2014

# Delays and inconsistency in ethics and governance

# Biomedical research: Increasing value, reducing waste



| Questions relevant to users of research? | Appropriate research design, conduct and analysis? | Efficient research regulation and delivery? | Accessible, full research reports? | Unbiased and usable reports? |
|---|---|---|---|---|
| High priority questions addressed<br><br>Important outcomes assessed<br><br>Clinicians and patients involved in setting research agendas | Studies designed with reference to systematic reviews of existing evidence<br><br>Studies take adequate steps to reduce biases - e.g. unconcealed treatment allocation | Appropriate regulation of research<br><br>Efficient delivery of research<br><br>Good re-use of data | Studies published in full<br><br>Reporting of studies with disappointing results | Trial interventions sufficiently described<br><br>Reported planned study outcomes<br><br>New research interpreted in the context of systematic assessment of relevant evidence |

Macleod et al, Lancet 2014

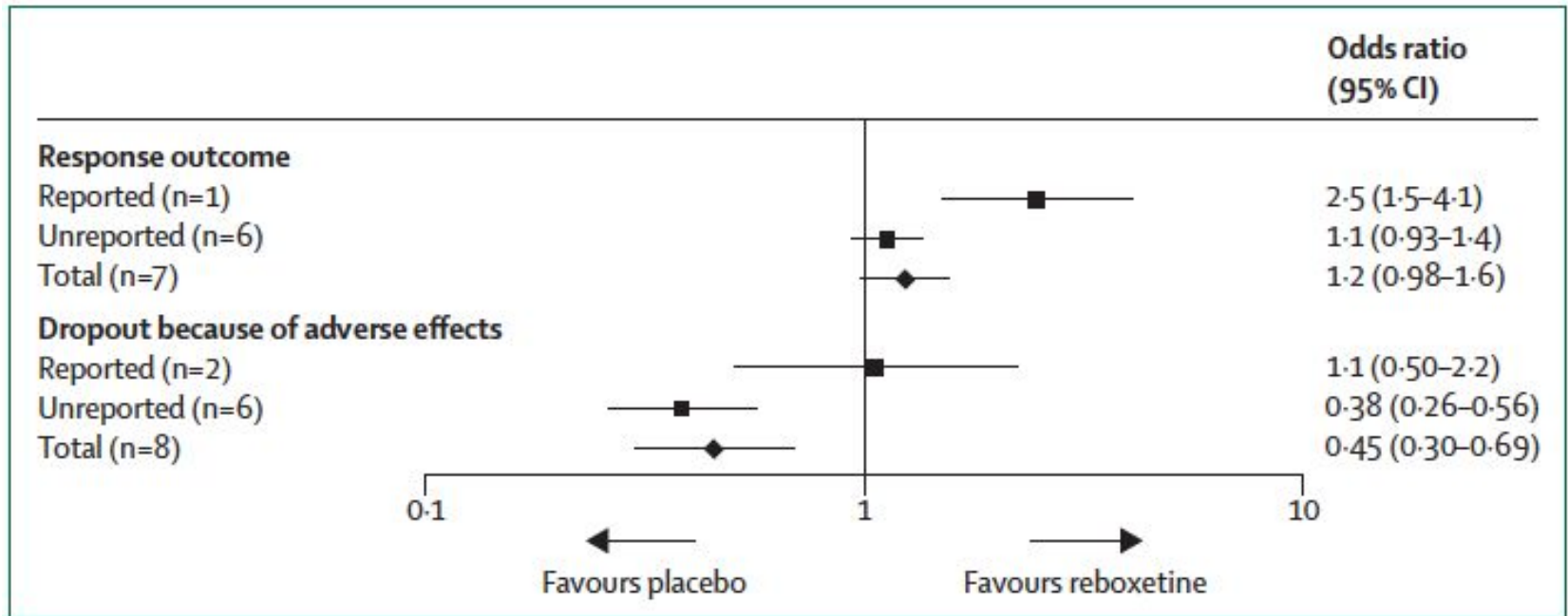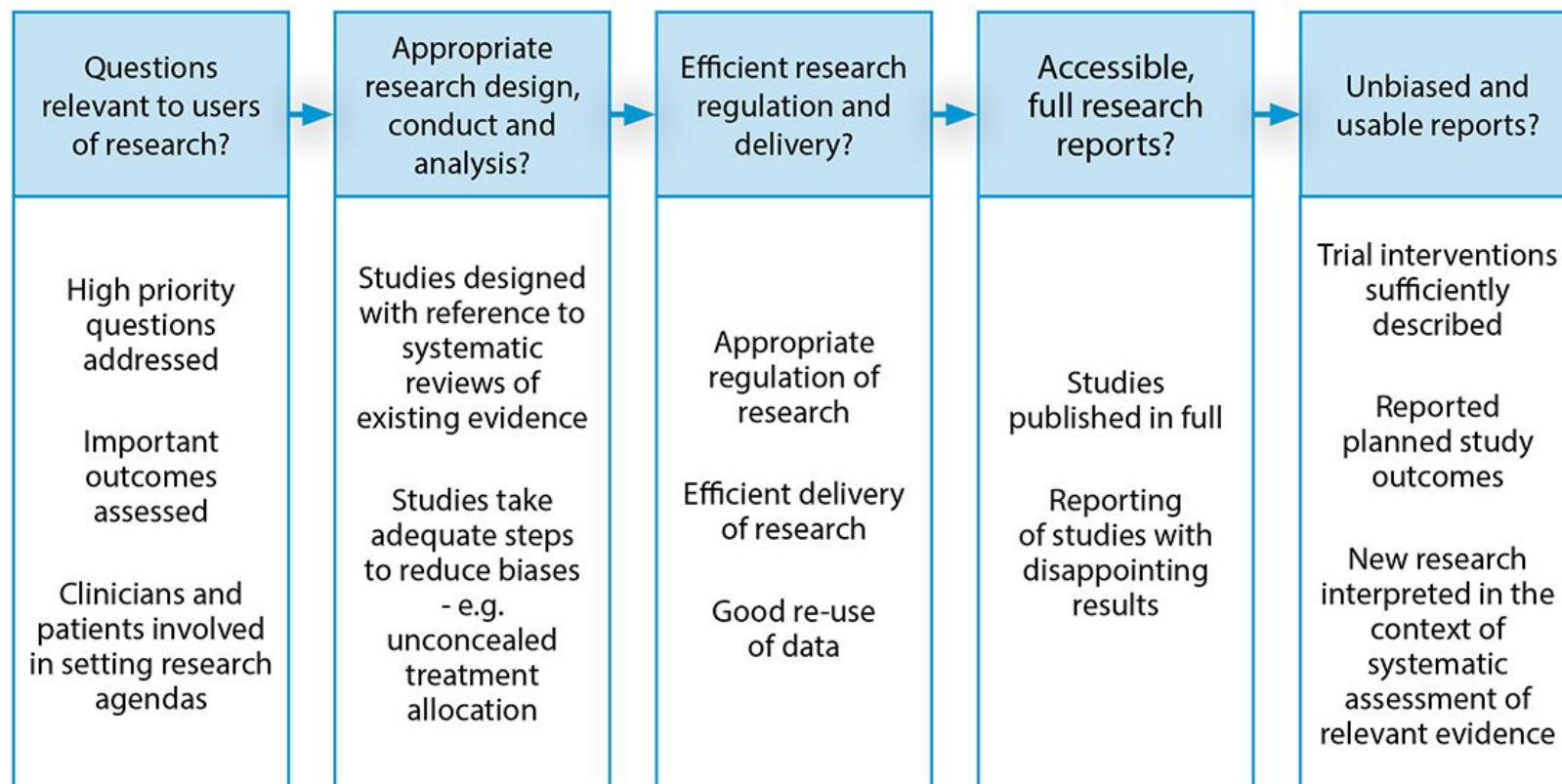CAMARADES: Bringing evidence to translational medicine

Figure 3: Results of a meta-analysis of reported and unreported randomised trials of reboxetine versus placebo for acute treatment of major depression
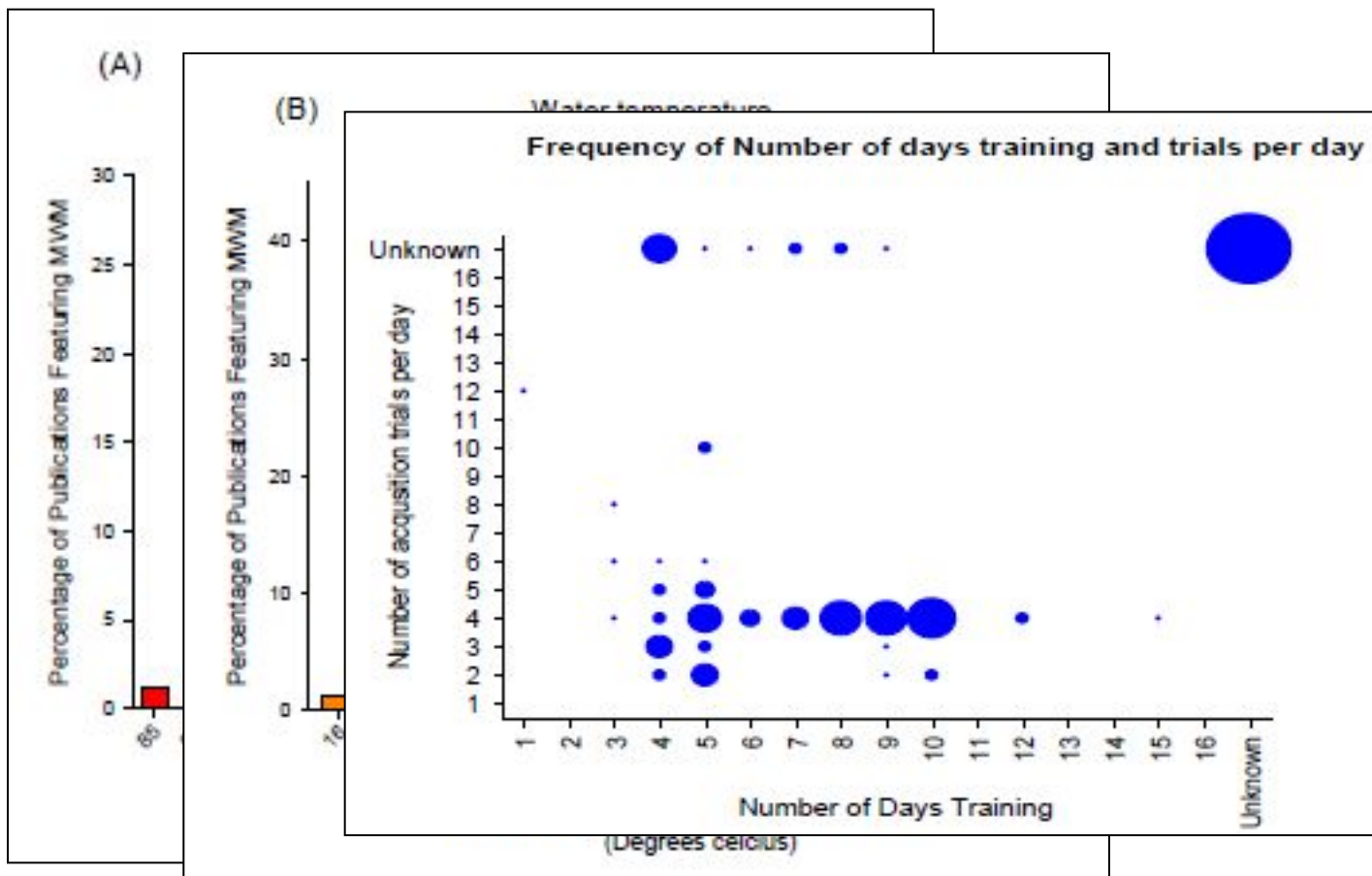Data used to create this figure from Eyding et al.[18]

# Biomedical research: Increasing value, reducing waste



| Questions relevant to users of research? | Appropriate research design, conduct and analysis? | Efficient research regulation and delivery? | Accessible, full research reports? | Unbiased and usable reports? |
|---|---|---|---|---|
| High priority questions addressed<br><br>Important outcomes assessed<br><br>Clinicians and patients involved in setting research agendas | Studies designed with reference to systematic reviews of existing evidence<br><br>Studies take adequate steps to reduce biases - e.g. unconcealed treatment allocation | Appropriate regulation of research<br><br>Efficient delivery of research<br><br>Good re-use of data | Studies published in full<br><br>Reporting of studies with disappointing results | Trial interventions sufficiently described<br><br>Reported planned study outcomes<br><br>New research interpreted in the context of systematic assessment of relevant evidence |

Macleod et al, Lancet 2014

# Use of the Morris Water Maze



(A)

Percentage of Publications Featuring MWM

(B)

Water temperature

Percentage of Publications Featuring MWM

(Degrees celcius)

**Frequency of Number of days training and trials per day**
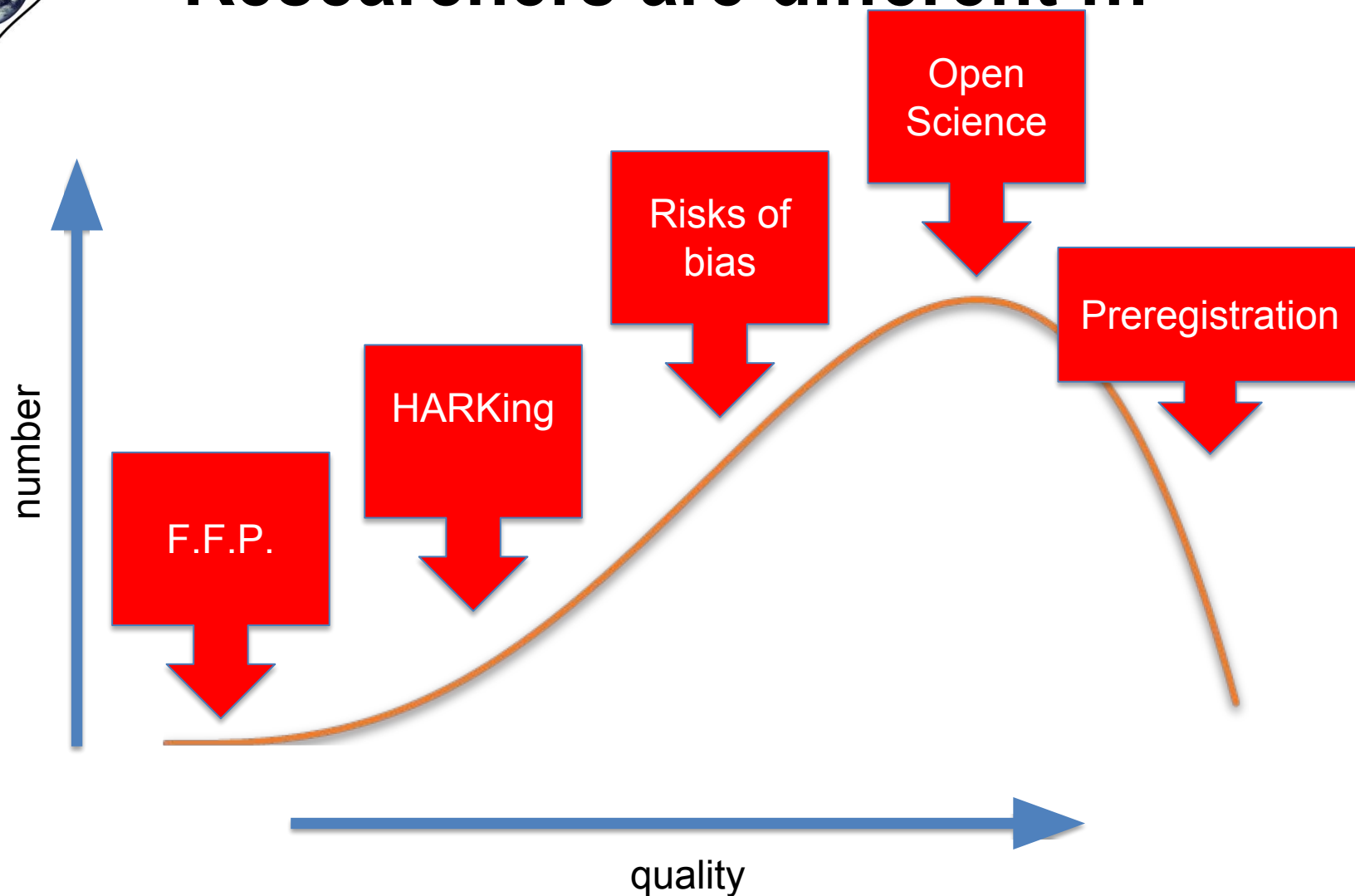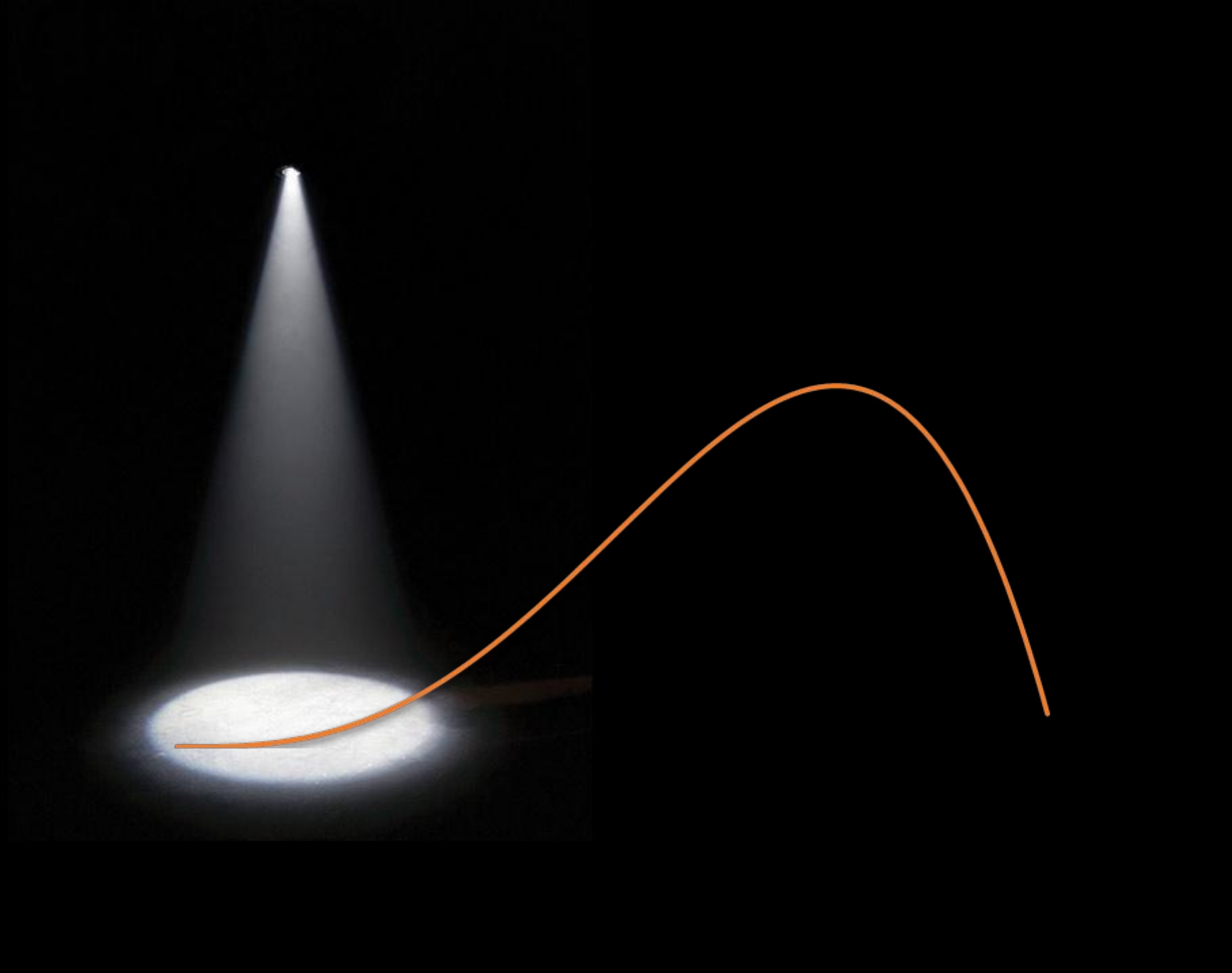
Number of acqusition trials per day
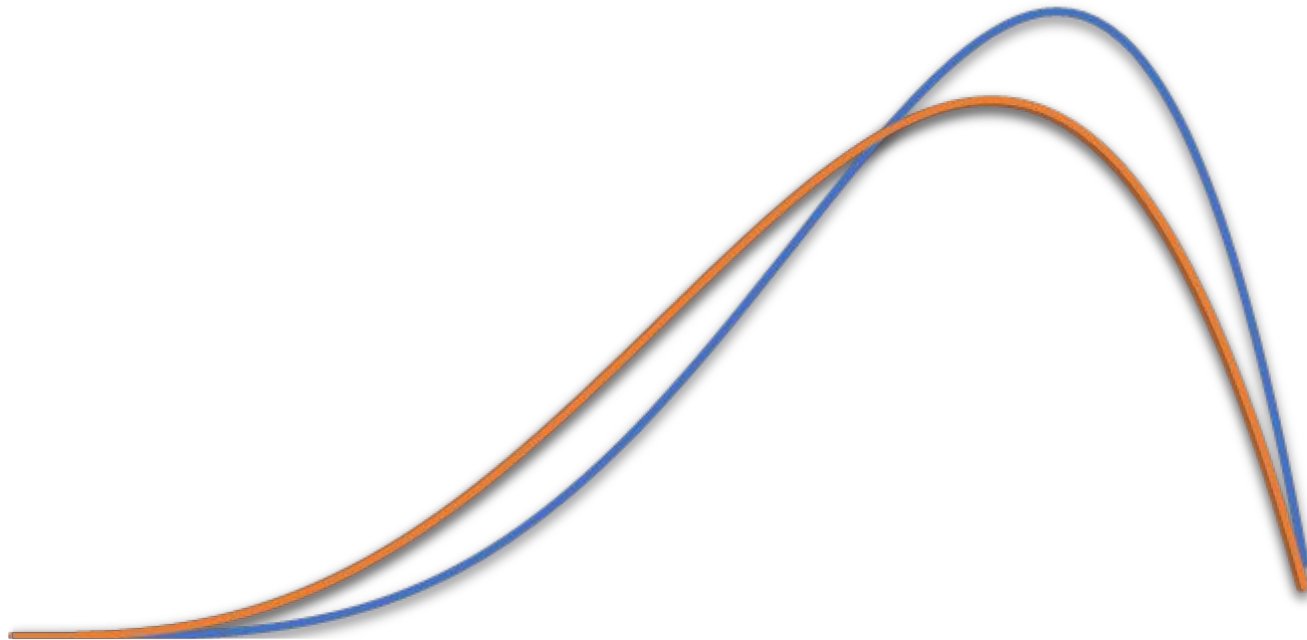
Number of Days Training

# Researchers are different …

# Research Improvement Strategy

If you are planning a systematic review or meta-analysis of animal data, CAMARADES are here to help: malcolm.macleod@ed.ac.uk

**CAMARADES: Bringing evidence to translational medicine**