



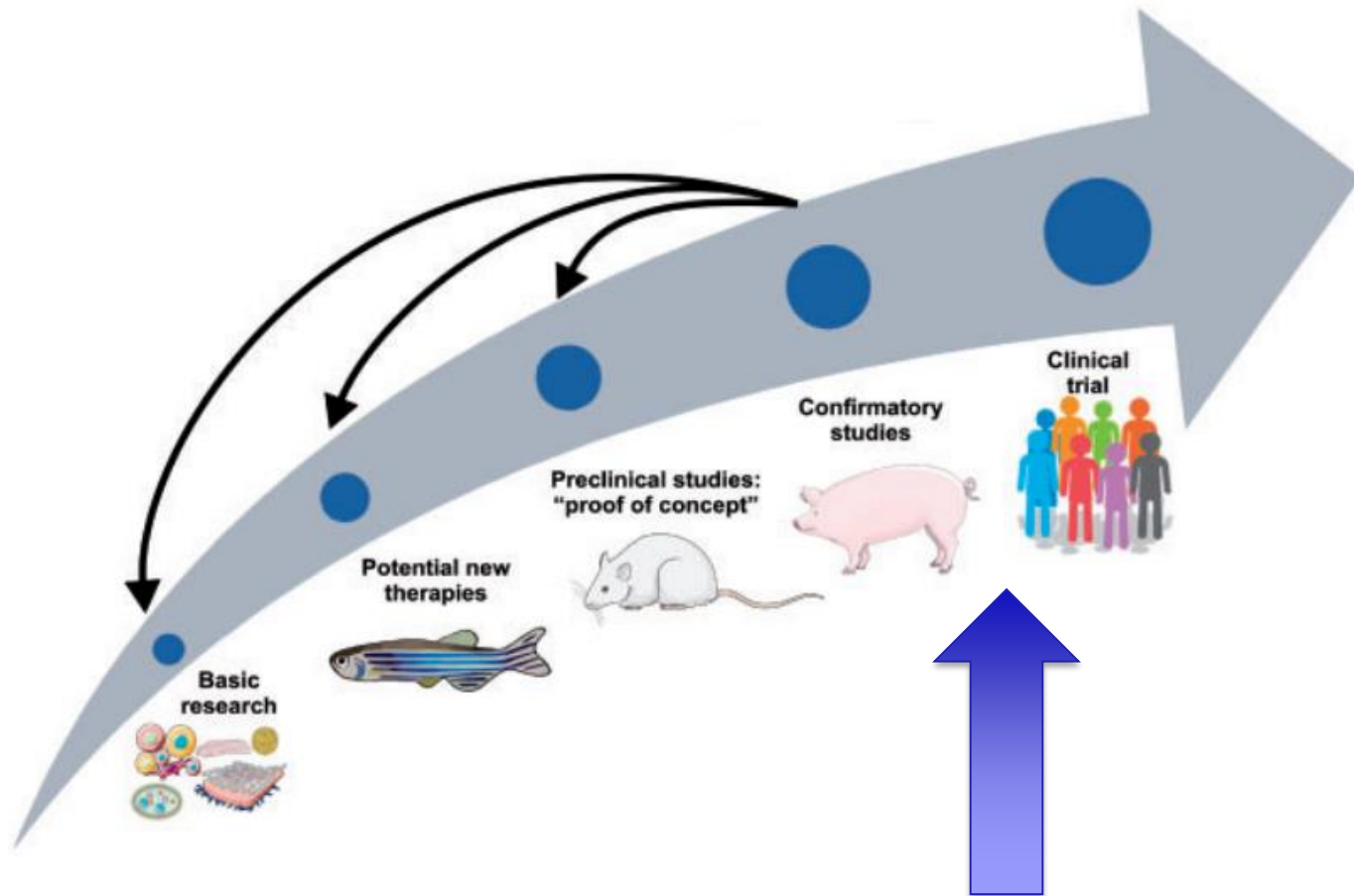
UMC Utrecht

# Promoting transparency in preclinical research:

preregistration of preclinical studies on  
[www.preclinicaltrials.eu](http://www.preclinicaltrials.eu)

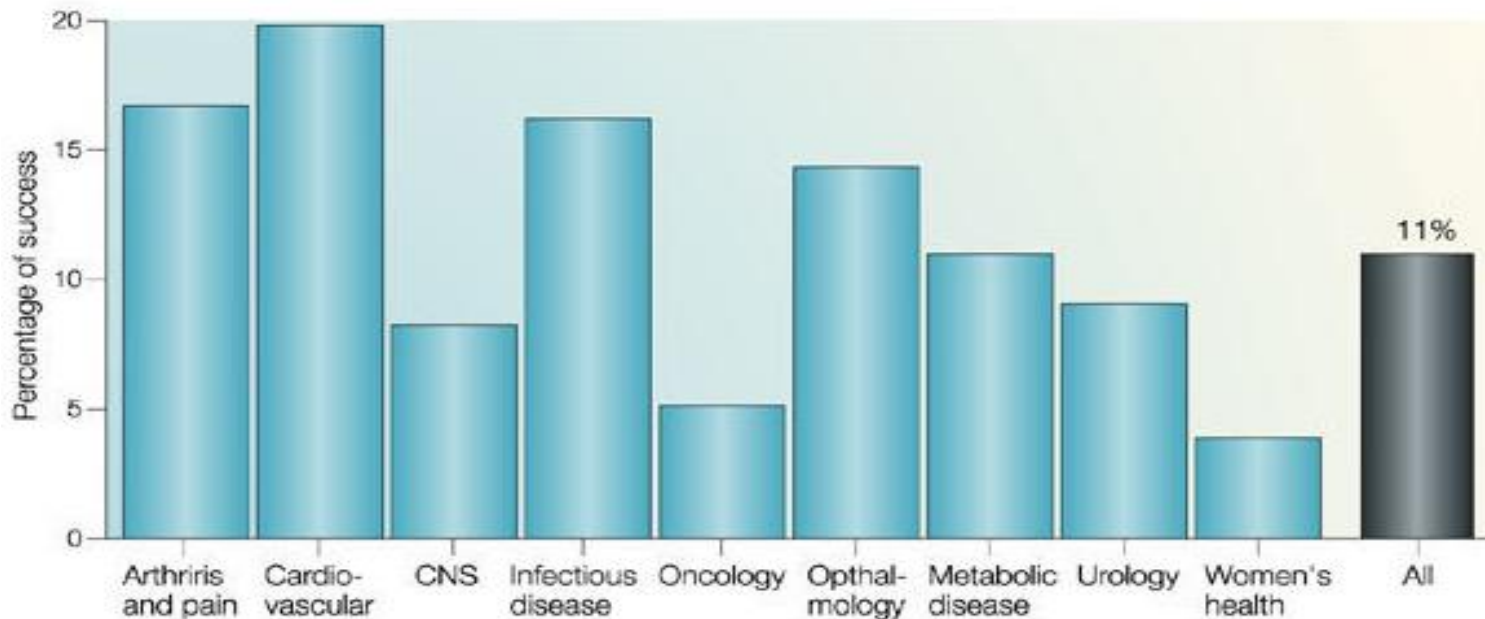


# Translational research axis



# Translational failure

Only 11% of compounds tested in first-in-man studies gets approved<sup>1</sup>



<sup>1</sup>Kola, Nature Reviews Drug Discovery, 2004

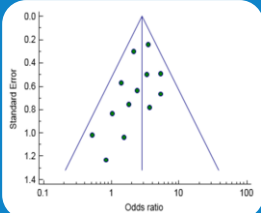
# Major biases in preclinical research



Internal study validity



Selective outcome reporting



Publication bias



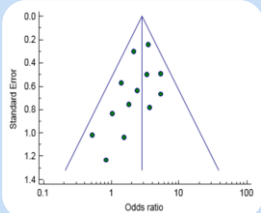
# Major biases in preclinical research



**Internal study validity**



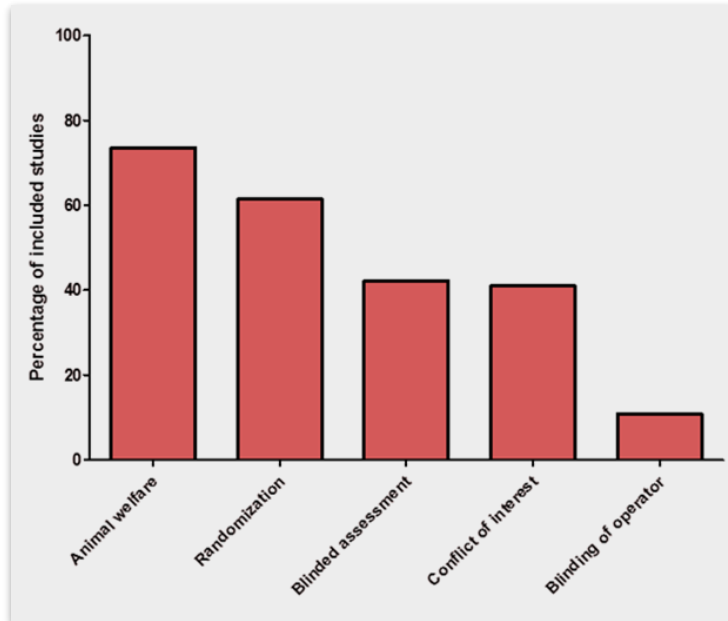
Selective outcome reporting



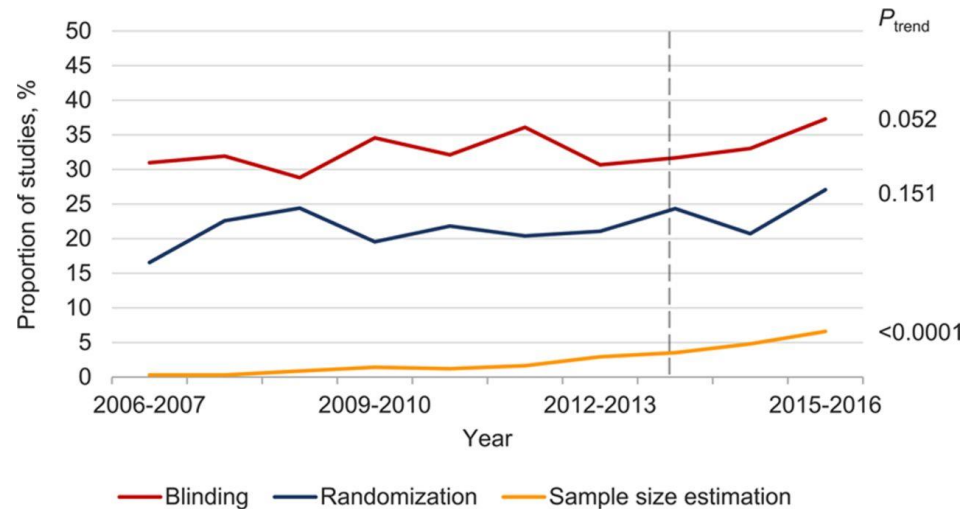
Publication bias



# Poor internal validity of preclinical research



Cardiac regenerative therapy<sup>1</sup>  
(large animal models)



Cardiovascular studies<sup>2</sup>  
(small & large animal studies)

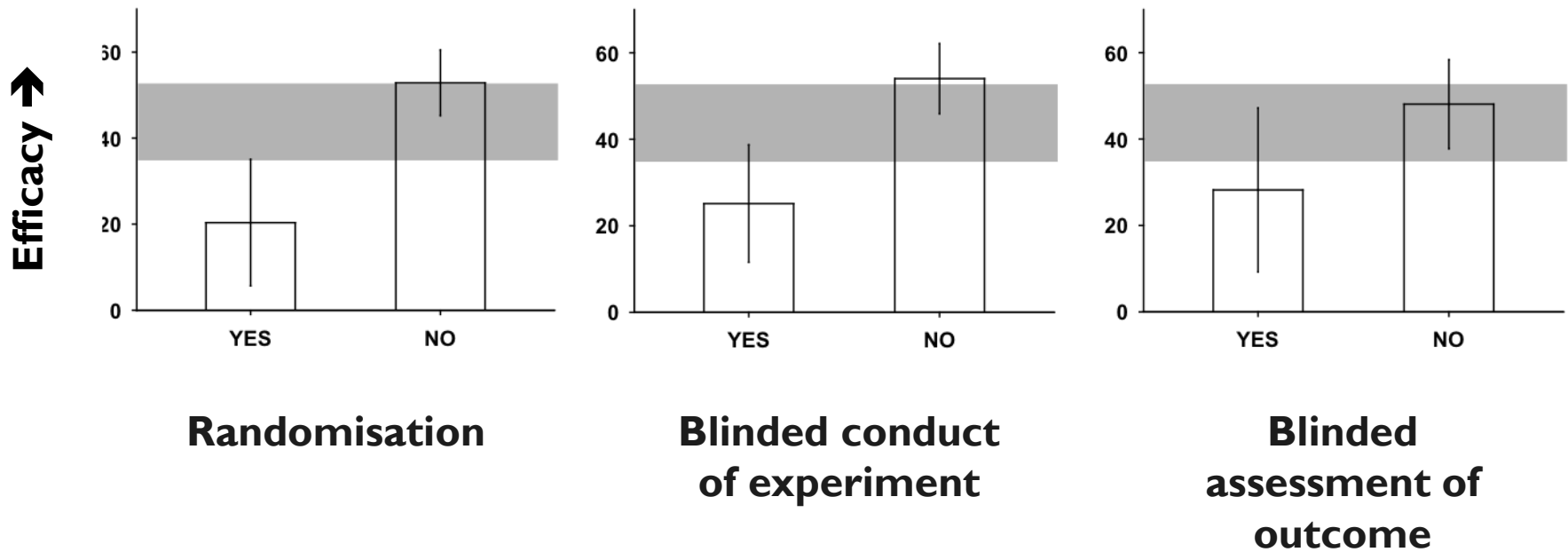
**Blinding <40%**

**Randomisation <60%**



<sup>1</sup>Jansen of Lorkeers, *Circ Res*, 2015, <sup>2</sup>Ramirez, *Circ Res*, 2017

# Why this is an issue



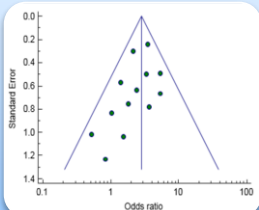
# Major biases in preclinical research



Internal study validity



**Selective outcome reporting**



Publication bias





# Outcome switching

67 trials in NEJM/JAMA/Lancet/Ann In Med/BMJ

- 9 trials were perfect
- On average (per trial)
  - 58% specified outcomes reported
  - 5.3 new outcomes silently added



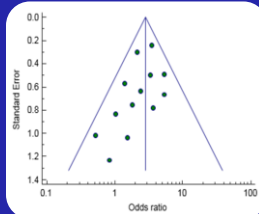
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# Publication bias

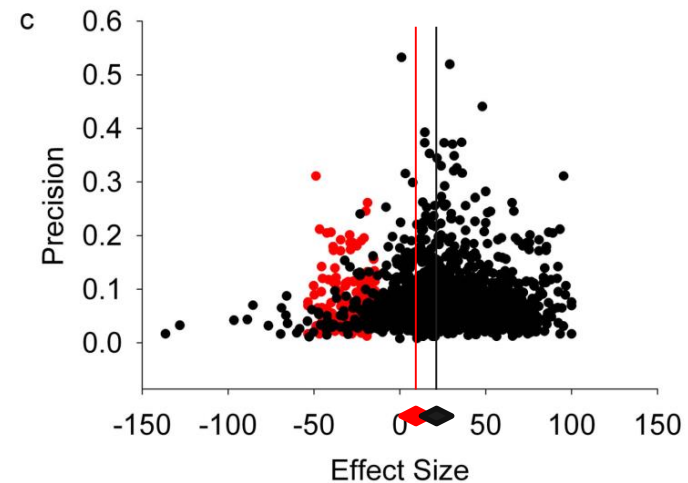
## Clinical research

- Ca. 50% registered clinical trials published
- Higher probability getting positive or sign. results published



# Publication bias

- Publication bias leads to an overestimation of the effect size (stroke)
  - Based on published results: 31,3%
  - Corrected result: 23,8%



# PRECLINICALTRIALS.EU

International register of preclinical trial protocols



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Join  
to create a user account

**Preclinicaltrials** aims to provide a comprehensive listing of preclinical animal study protocols.

Preferably registered at inception in order to **increase transparency**, help **avoid duplication**, and **reduce the risk of reporting bias** by enabling comparison of the completed study with what was planned in the protocol.

**Registration** of your study requires you to create an account that is

- Anonymous
- Free of charge
- Has an optional embargo period

This register is web-based, open to all types of animal studies and freely accessible and searchable to all with a preclinicaltrials.eu account.

The **[registration form](#)** is designed by experts on preclinical animal studies and preclinical evidence synthesis.

Please **[join](#)** us and create an user account, this will provide access to the database and enables you to register your preclinical trial.

Contact us at [info@preclinicaltrials.eu](mailto:info@preclinicaltrials.eu).

Promoting transparency in preclinical research

# PRECLINICALTRIALS.EU

International register of preclinical trial protocols

- Increase awareness
  - Blinding
  - Randomisation
  - Sample size calculation
- Decrease reporting bias
- Increase access to study related data (publications, data repositories)
- Increase transparency



# PRECLINICALTRIALS.EU

International register of preclinical trial protocols

## Steering Committee

Mira van der Naald

Dr Kim Wever

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Prof Dirk Jan Duncker

## Advisory board

Prof John Ioannidis

Prof Jonathan Kimmelman

Prof Paul Glasziou

Prof Annelien Bredenoord

Prof Lina Badimon

Prof Thomas Eschenhagen



## Data management

Netherlands Heart Institute

## Website development

Metaxis Ltd



# Official Launch April 2018

Supported by:

- ESC working groups
  - Cardiovascular regenerative and reparative medicine
  - Cellular biology of the heart
  - Coronary pathophysiology and microcirculation
- TACTICS alliance





# Motion Dutch Parliament

Accepted unanimously

## 32 336 Dierproeven

### Nr. 78 MOTIE VAN HET LID DE GROOT C.S.

Voorgesteld 28 juni 2018

De Kamer,

gehoord de beraadslaging,

constaterende dat er de komende jaren dierproeven zullen worden uitgevoerd om belangrijke medische wetenschappelijke inzichten te verkrijgen en nieuwe therapeutische opties te testen;

constaterende dat niet alle dierproeven, en met name de resultaten en onderzoeksdata van die individuele proeven, geregistreerd en achteraf openbaar worden gemaakt;

overwegende dat de regering ernaar streeft om in 2025 koploper proefdiervrij onderzoek te zijn;

verzoekt de regering, in samenspraak met onderzoekers en kennisinstellingen te bezien of alle individuele dierproeven en de resultaten daarvan kunnen worden geregistreerd en achteraf openbaar gemaakt, om zo onnodige duplicatie van dierproeven tegen te gaan,

en gaat over tot de orde van de dag.

De Groot

Dik-Faber

Von Martels

# Concerns of preregistration

- Sharing confidential ideas/plans
  - Embargo
- Patents
  - Embargo + Claim the field!
- Workload
  - Link to current digital systems
- Limited flexibility for creativity of researchers
  - Exactly the purpose for confirmatory studies!
- Costs
  - Registration is free (and anonymous)



# PRECLINICALTRIALS.EU

International register of preclinical trial protocols

Go to [www.preclinicaltrials.eu](http://www.preclinicaltrials.eu) to

- Register your animal study
- Search the database

Questions?

Contact us at [info@preclinicaltrials.eu](mailto:info@preclinicaltrials.eu)

