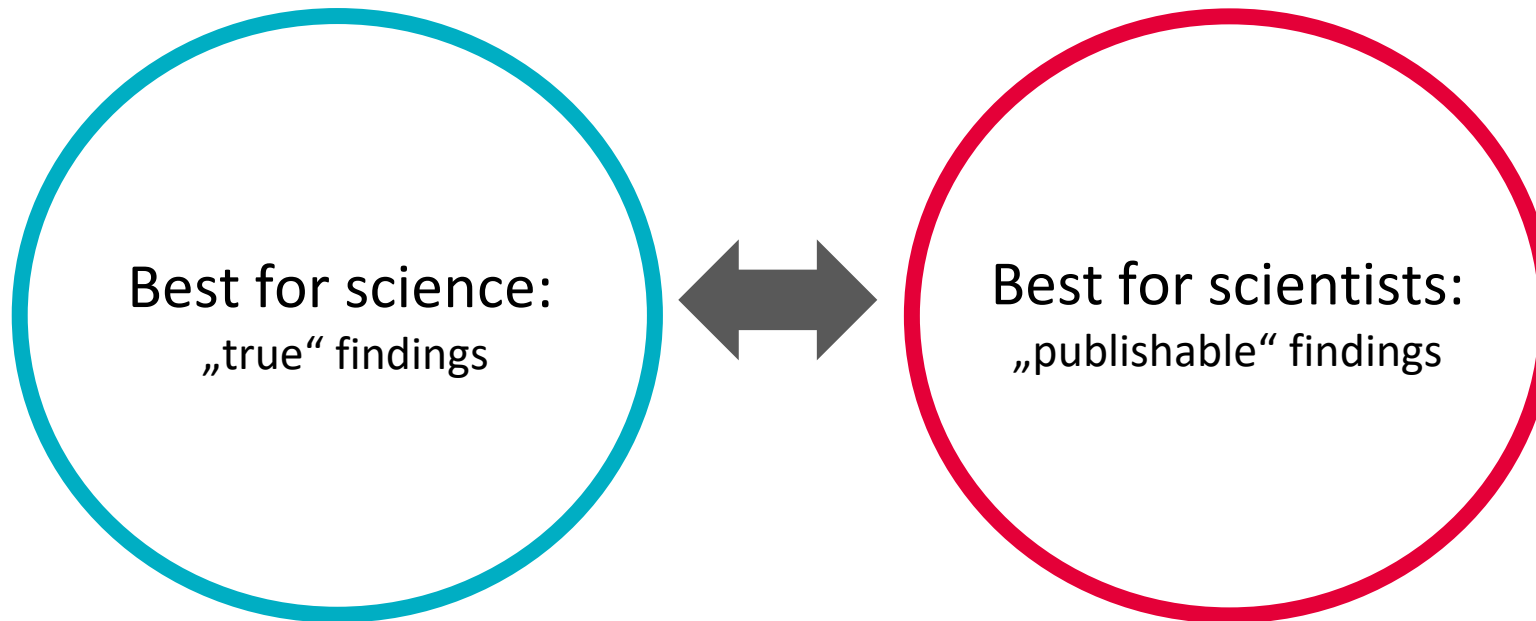


Preregistration in animal research – Animal welfare and scientific progress

23/02/2023, Joint meeting of the BfR and the Ethological Society

Céline Heintz

The paradox of the research system



The flood of positive results

Intervention	No. of Data Sources	No. of Experiments	No. of Animals	Reported Effect Size (95%CI)
Estrogens [10]	27	99	1,452	26.7% (20.4%–33.0%)
FK506 [12]	27	96	1,596	32.0% (27.8%–36.3%)
Growth factors	70	128	1,750	29.7% (25.9%–33.4%)

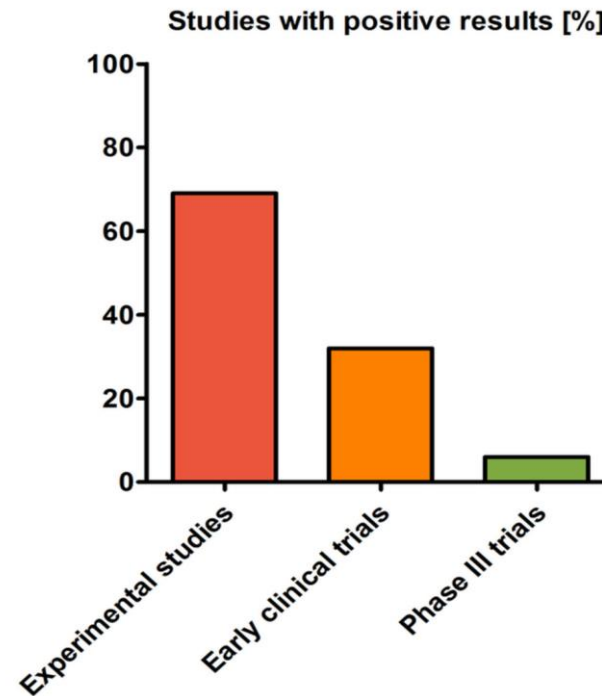
“In animal studies of acute ischaemic stroke involving 525 unique publications. **Only ten publications (2%) reported no significant effects** on infarct volume and only six (1.2%) did not report at least one significant finding.”

Piracetam and related compounds [18]	5	14	197	29.6% (16.1%–44.4%)
Stem cells	46	112	1,352	29.6% (23.7%–35.4%)
Tirilazad [16]	18	34	544	31.9% (23.1%–40.7%)
tPA [15]	105	256	4,029	22.5% (19.2%–25.9%)
Other thrombolytics	12	26	410	46.6% (35.7%–57.5%)
Pooled analysis	525*	1,359	19,956	31.3% (29.7%–32.8%)

*Fifteen data sources were represented in more than one review and are included only once in the pooled analysis.
doi:10.1371/journal.pbio.1000344.t001

Sena ES, van der Worp HB, Bath PMW, Howells DW, Macleod MR (2010). PLOS Biology 8(3): e1000344. <https://doi.org/10.1371/journal.pbio.1000344>

Too good to be true



Schmidt-Pogoda et al. (2019) *Annals of Neurology* 87(1): 40-51, DOI: (10.1002/ana.25643)

The *file drawer problem* and its ethical implications



RESEARCH ARTICLE

Publication rates in animal research. Extent and characteristics of published and non-published animal studies followed up at two German university medical centres

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The overall publication rate was **67%**. Excluding doctoral theses as result publications, the publication rate decreased to **58%**.

Open access

Original research

BMJ Open Science

Publication rate in preclinical research: a plea for preregistration

Mira van der Naald^{1,2}, Steven Wenker¹, Pieter A Doevendans^{1,3}, Kimberley E Wever⁴, Steven A J Chamuleau^{1,2}

To cite: van der Naald M, Wenker S, Doevendans PA, et al. Publication rate in preclinical research: a plea for preregistration. *BMJ Open Science* 2020;4:e100051. doi:10.1136/bmjos-2019-100051

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjos-2019-100051>).

Received 04 November 2019
Revised 15 February 2020
Accepted 27 April 2020

ABSTRACT

Objectives The ultimate goal of biomedical research is the development of new treatment options for patients. Animal models are used if questions cannot be addressed otherwise. Currently, it is widely believed that a large fraction of performed studies are never published, but there are no data that directly address this question.

Methods We have tracked a selection of animal study protocols approved in the University Medical Center Utrecht in the Netherlands, to assess whether these have led to a publication with a follow-up period of 7 years.

Results We found that 60% of all animal study protocols led to at least one publication (full text or abstract). A total of 5590 animals were used in these studies, of which 26% was reported in the resulting publications.

Conclusions The data presented here underline the

Strengths and limitations of this study

- This study directly traces animal study protocols to potential publications and is the first study to assess the number of animals used and the number of animals published.
- We had full access to all documents submitted to the animal experiment committee of the University Medical Center Utrecht from the selected protocols.
- There is a sufficient follow-up period for researchers to publish their animal study.
- Due to privacy reasons, we are not able to publish the exact search terms used.
- A delay has occurred between the start of this project and time of publishing, this is related to the political sensitivity of this subject.

60% of all animal study protocols led to at least one publication (full text or abstract). A total of 5590 animals were used, of which **26%** was reported in the resulting publications.

<https://doi.org/10.1371/journal.pone.0223758>

<http://dx.doi.org/10.1136/bmjos-2019-100051>

Questionable research practices



Good scientific practice

Questionable research practices

Fraud

- P-hacking
 - Using the flexibility of analysis to obtain a p-value under 0.05
- HARKing: **H**ypothesizing **A**fter **R**esults are **K**nown
 - Screening through collected data to find something significant and presenting it as predefined hypothesis

Clinical trial registration can increase null results



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 All studies

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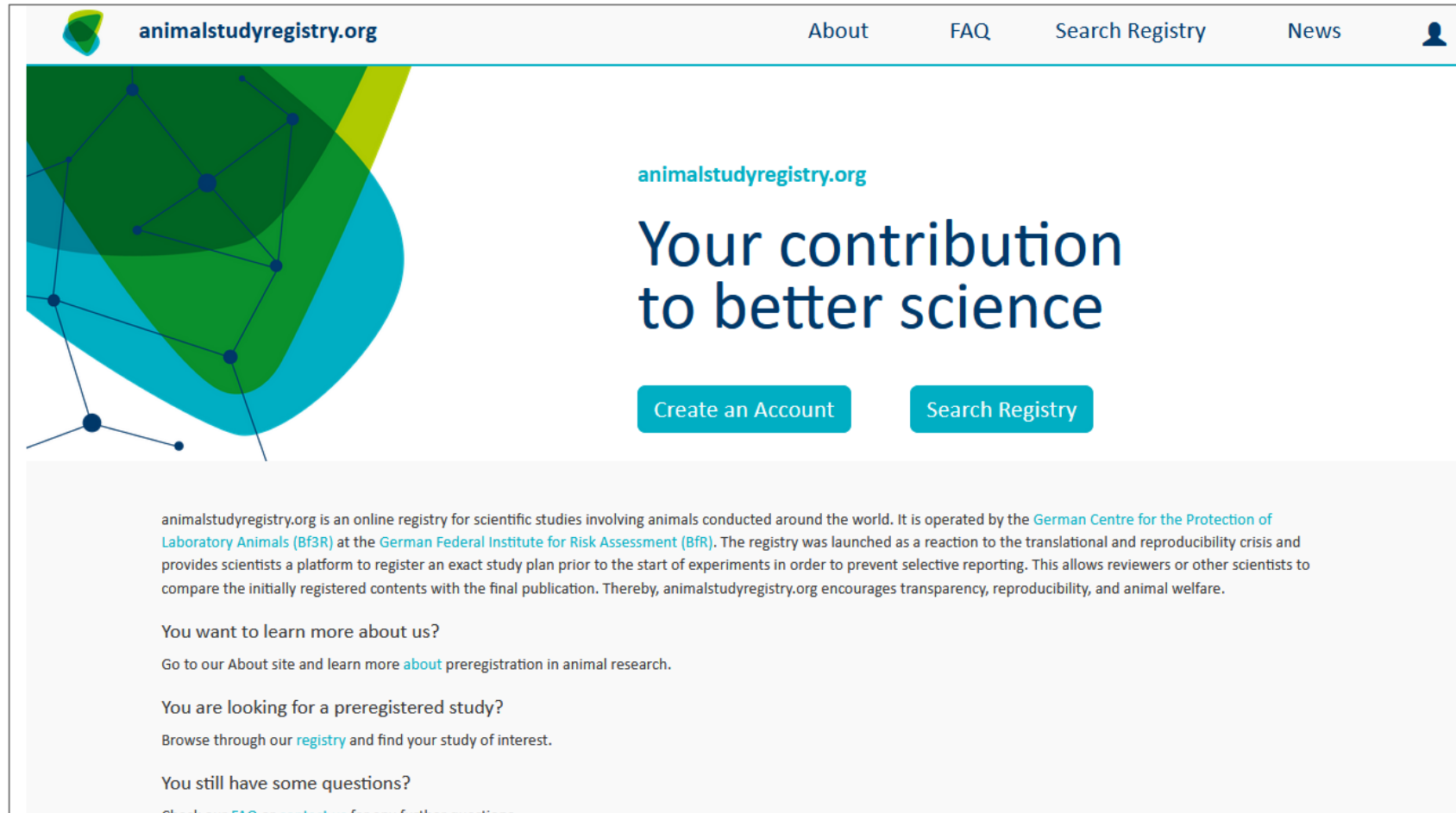
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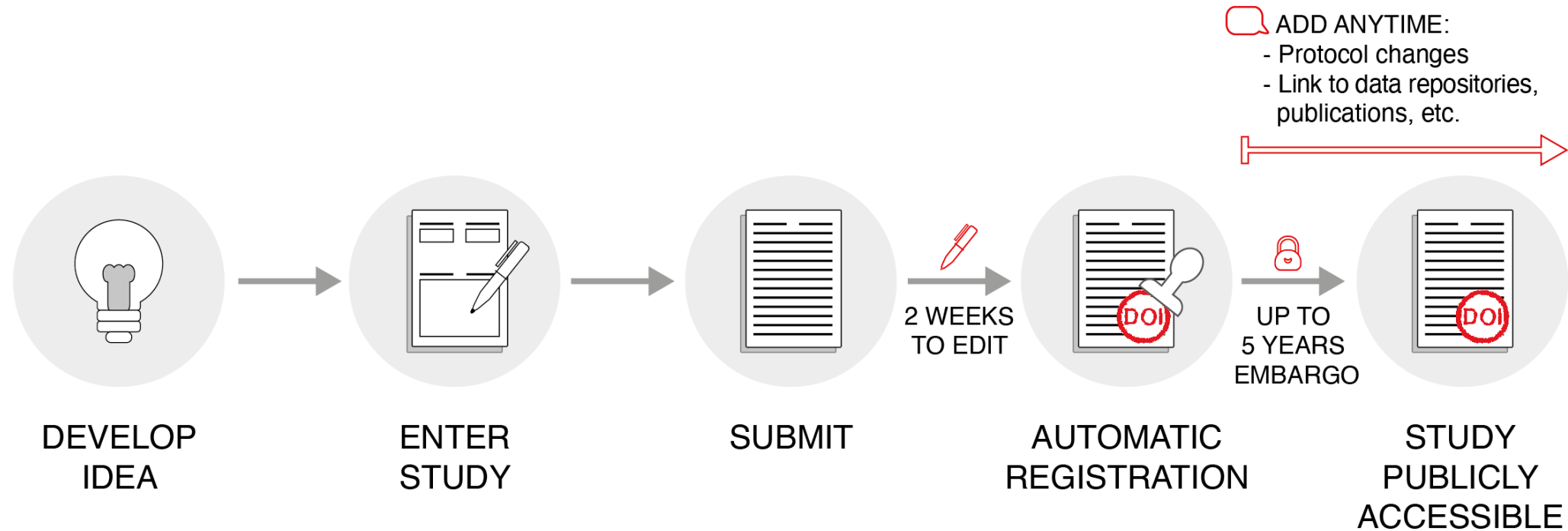
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animalstudyregistry.org – online since January 2019



The screenshot shows the homepage of animalstudyregistry.org. At the top, there is a navigation bar with the site logo, the URL "animalstudyregistry.org", and links for "About", "FAQ", "Search Registry", and "News". A user profile icon is also present. The main content area features a large graphic on the left with overlapping green and blue shapes and a network diagram. To the right, the text "animalstudyregistry.org" is followed by the headline "Your contribution to better science". Below this are two buttons: "Create an Account" and "Search Registry". A text block below explains the registry's purpose: "animalstudyregistry.org is an online registry for scientific studies involving animals conducted around the world. It is operated by the German Centre for the Protection of Laboratory Animals (Bf3R) at the German Federal Institute for Risk Assessment (BfR). The registry was launched as a reaction to the translational and reproducibility crisis and provides scientists a platform to register an exact study plan prior to the start of experiments in order to prevent selective reporting. This allows reviewers or other scientists to compare the initially registered contents with the final publication. Thereby, animalstudyregistry.org encourages transparency, reproducibility, and animal welfare." Below this are three sections: "You want to learn more about us?" with a link to "about" preregistration; "You are looking for a preregistered study?" with a link to "registry"; and "You still have some questions?" with a link to "FAQ" or "contact us".

Preregistration in animalstudyregistry.org



Olevska A, Bert B, Ebrahimi L, Schoenfelder G, Heidl C (2021). Science Editor 44:4-7. <https://doi.org/10.36591/SE-D-4401-4>

animalstudyregistry.org - content

hypothesis or
research question



Transparency

methodological
details



Reproducibility

study design and a
statistical plan



Reliability

Publication
Bias

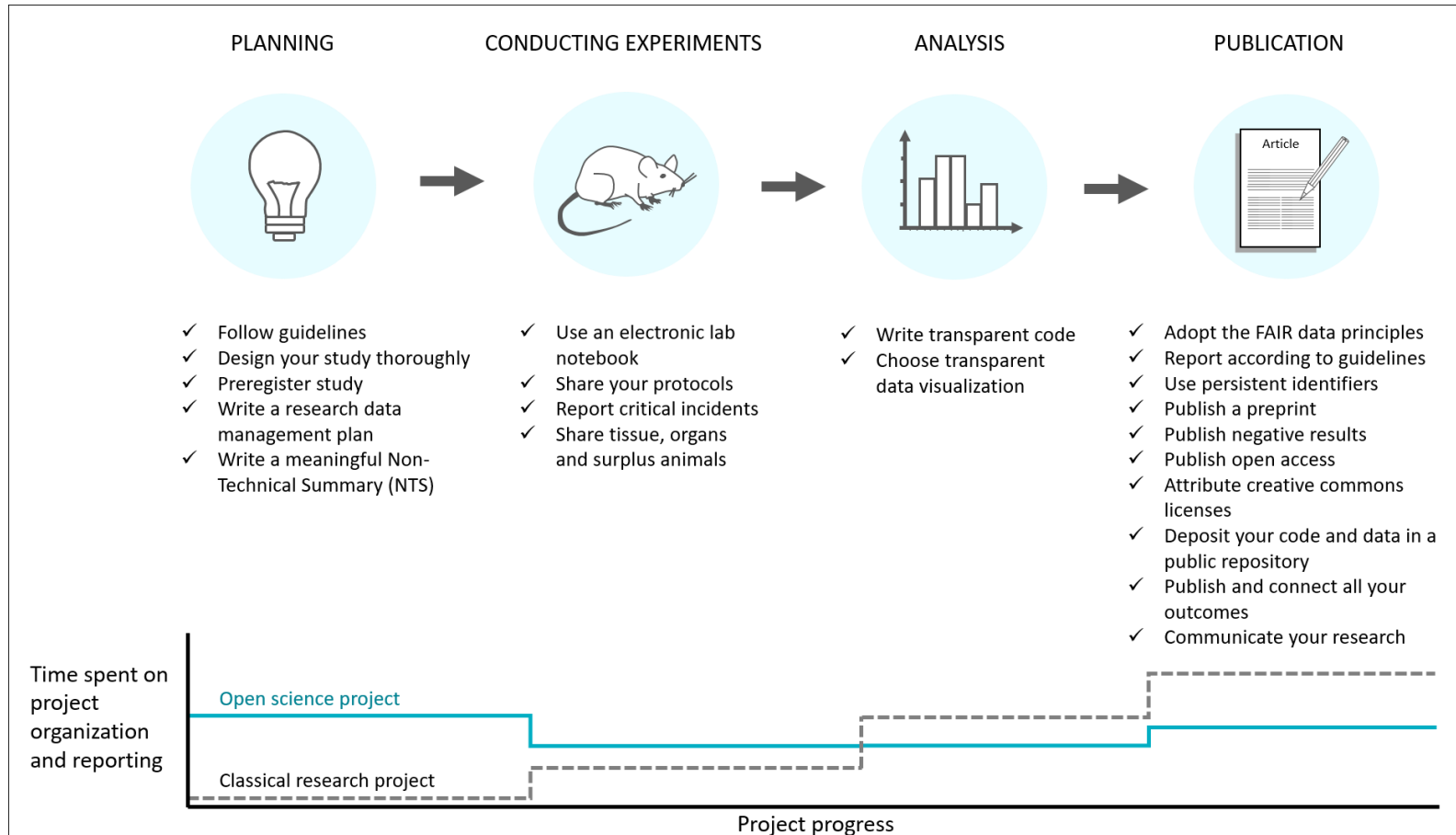
Loss of
experimental
knowledge

Questionable
research
practices

The „selfish“ benefits of preregistration

- ✓ Assists you planning your experiments thoroughly
- ✓ Raises the awareness for common mistakes
- ✓ Facilitates the reporting according to guidelines
- ✓ Identifier and embargo protect your study idea
- ✓ Proofs your commitment to open science practices

Maximize the gain of knowledge with open science



Diederich K, Schmitt K, Schwedhelm P, Bert B, Heintz C (2022). PLOS Biology 20(9): e3001810. <https://doi.org/10.1371/journal.pbio.3001810>


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