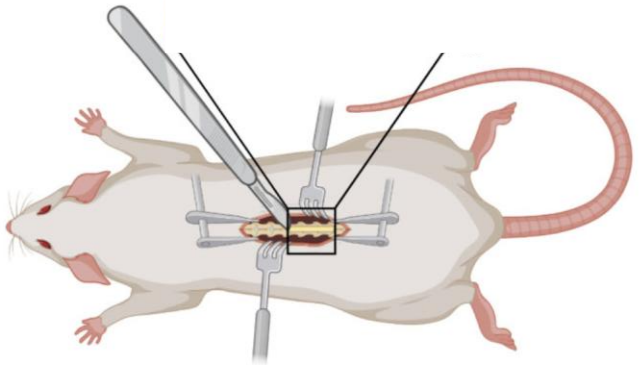
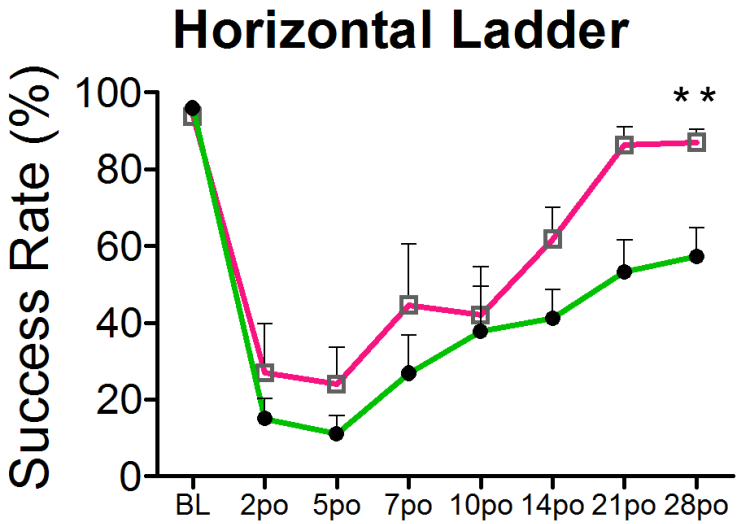
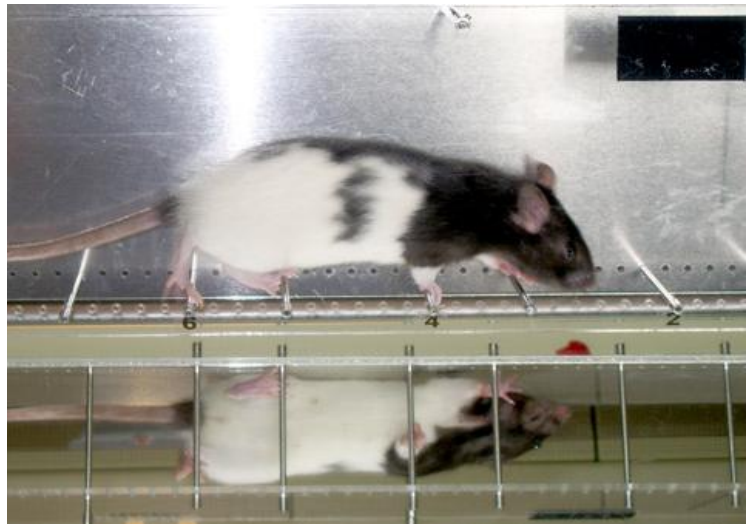






Liu et al., Front Immunol, 2023
Liebscher et al., Ann Neurol. 2005
Ineichen et al., Acta Neuropath. 2017
Weidner et al., Lancet Neurol, 2025

Safety and efficacy of intrathecal antibodies to Nogo-A in patients with acute cervical spinal cord injury: a randomised, double-blind, multicentre, placebo-controlled, phase 2b trial

*Norbert Weidner, Rainer Abel, Doris Maier, Klaus Röhl, Frank Röhrich, Michael Baumberger, Margret Hund-Georgiadis, Marion Saur, Jesús Benito-Penalva, Kerstin Rehahn, Mirko Aach, Andreas Badke, Jiri Kriz, Katalin Barkovits, Tim Killeen, Lynn Farner, Maryam Seif, Michèle Hubli, Katrin Marcus, Michael A Maurer, Bérénice Robert, Rüdiger Rupp, Paulina S Scheuren, Martin Schubert, Christian Schuld, Christina Sina, Bettina Steiner, Tanja Weis, Andreas Hug, Marc Bolliger, Nikolaus Weiskopf, Patrick Freund, Torsten Hothorn, Martin E Schwab, Armin Curt, for the Nogo Inhibition in Spinal Cord Injury Study Group**

Findings From May 20, 2019, to July 20, 2022, 463 patients with acute traumatic cervical spinal cord injury were screened, 334 were deemed ineligible and excluded, and 129 were randomly assigned to an intervention (80 patients in the NG101 group and 49 in the placebo group). The full analysis set comprised 78 patients from the NG101 group and 48 patients from the placebo group. 107 (85%) patients were male and 19 (15%) patients were female, with a median age of 51·5 years (IQR 30·0–60·0). Across all patients, the primary endpoint showed no significant difference between groups (with UEMS change at 6 months 1·37 [95% CI −1·44 to 4·18]; placebo group mean 19·20 [SD 11·78] at baseline and 30·91 [SD 15·49] at day 168; NG101 group mean 18·23 [SD 15·14] at baseline and 31·31 [19·54] at day 168). Treatment-related adverse events were similar between groups (nine in the NG101 group and six in the placebo group). 25 severe adverse events were reported: 18 in 11 (14%) patients in the NG101 group and seven in six (13%) patients in the placebo group. Although no treatment-related fatalities were reported in the NG101 group, one fatality not related to treatment occurred in the placebo group. Infections were the most common adverse event affecting 44 (92%) patients in the placebo group and 65 (83%) patients in the NG101 group.

Interpretation NG101 did not improve UEMS in patients with acute spinal cord injury. Post-hoc subgroup analyses assessing UEMS and Spinal Cord Independence Measure of self-care in patients with motor-incomplete injury indicated potential beneficial effects that require investigation in future studies.

Vom Code zum Heilmittel: Die Rolle der KI in der modernen Medikamentenentwicklung

Brain Week 2026

Prof. Dr. Dr. Benjamin V. Ineichen
Department of Clinical Research
Universität Bern
17. März 2026

The STRIDE-Lab

STRIDE-Lab

Natural language processing for drug development from animal studies to clinical trials to regulatory approval

Methods:

- Evidence synthesis
- Data pipelines with Natural language processing (NLP) and large language models

Impact:

1. Improve efficiency and safety of drug dev
2. Reduce unnecessary animal testing
3. Increase transparency and reproducibility

STRIDE-Lab webpage

What is medical data science?

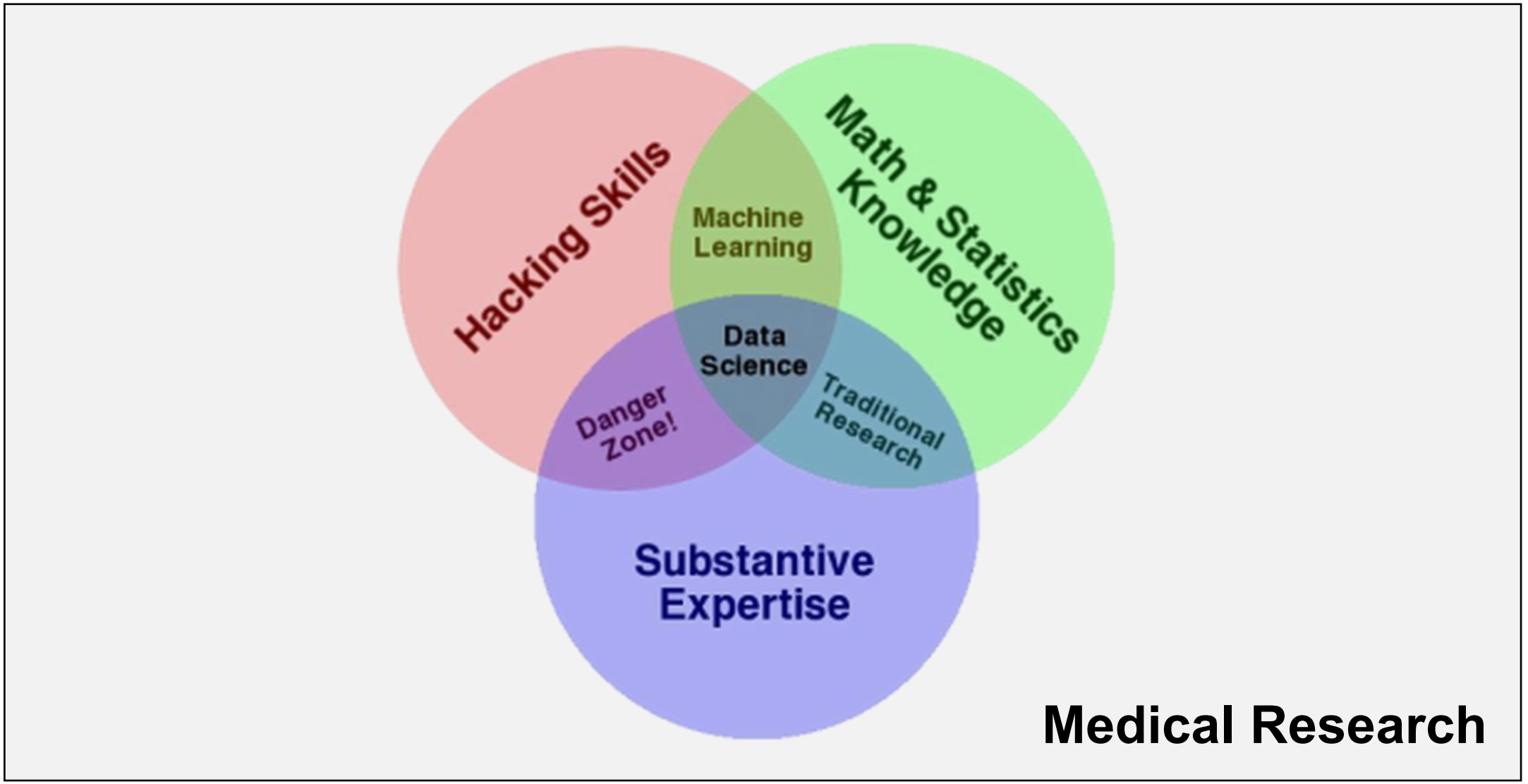
What medical data science is not

What is medical data science?

The discipline of making medical data useful

Subfield	Function
Descriptive analysis	Get inspired
Machine learning/AI	Make recipe (hypothesis-generating)
Statistics	Decide wisely (hypothesis-testing)

What is medical data science



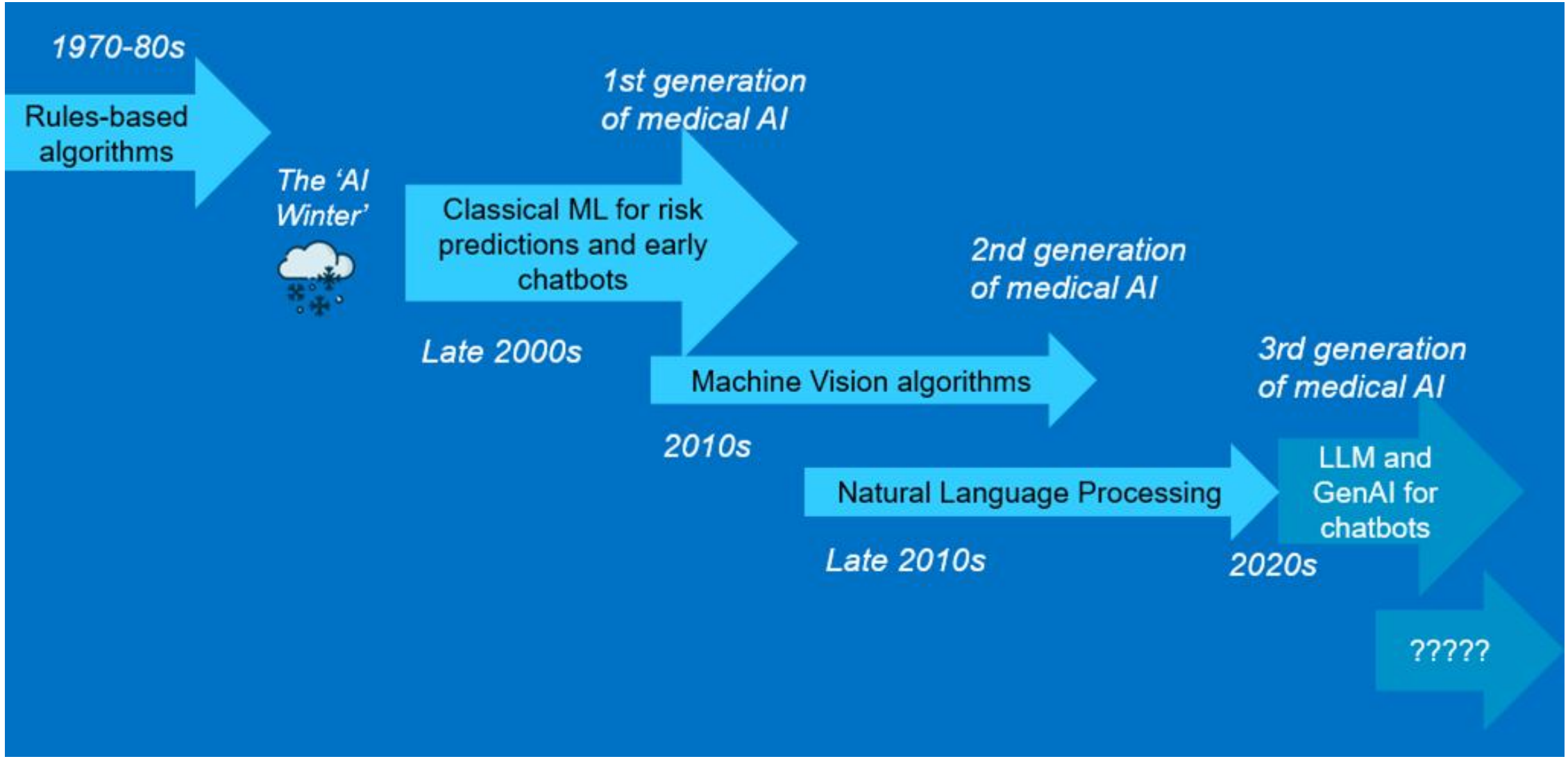
The AI hype


2015
SELF-DRIVING CARS IN 2 YEARS
CausalPython.io
imgflip.com
2016
RADIOLOGISTS OBSOLOLETE IN 5 YEARS
2024
RADIOLOGISTS IN REGULAR CARS DRIVING TO WORK

Die wie vielte KI-Welle reiten wir aktuell?

A. Die Erste.
B. Die Dritte.
C. Die Fünfte.
D. Die Siebte.

The current Data science/AI wave is part of a 30-year tide



Slide adjusted from James Teo

Vera
Data scientist

Amelia
MD candidate

Simona
PhD student

Marianna
Postdoc

Johann
MD candidate

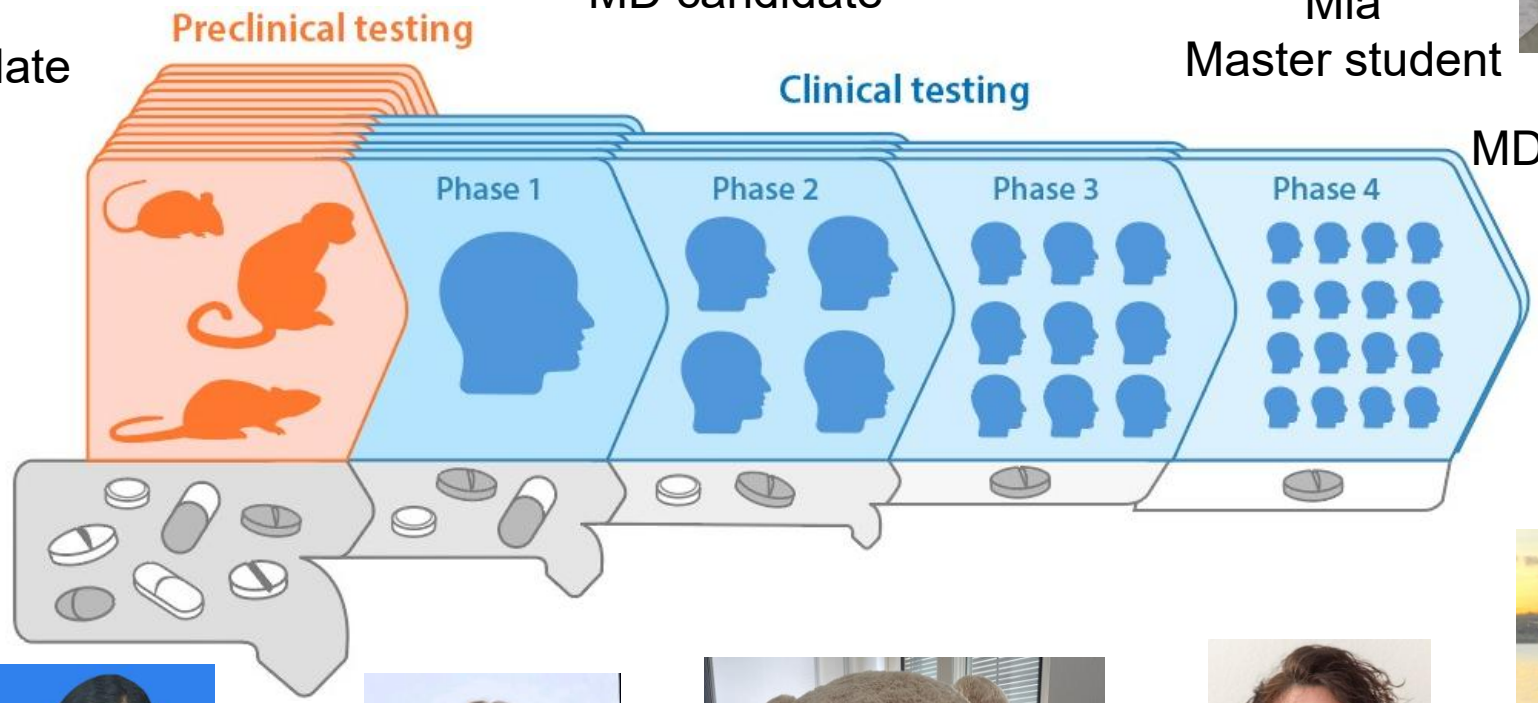
David
MD candidate

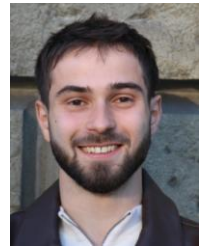
Mia
Master student

Brian
MD candidate

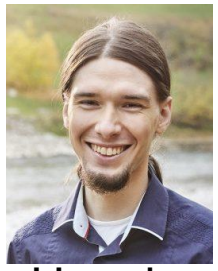
Wolfgang
Researcher

Jacqueline
Master student





Enrico
Master student



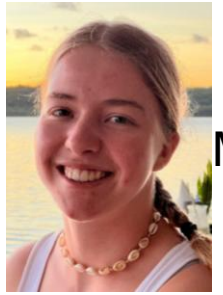
Henning
Data scientist

Rosni
Postdoc

Miriam
PhD student

Bernie
Hug scientist

Hanna
Data scientist



Dora
Master student

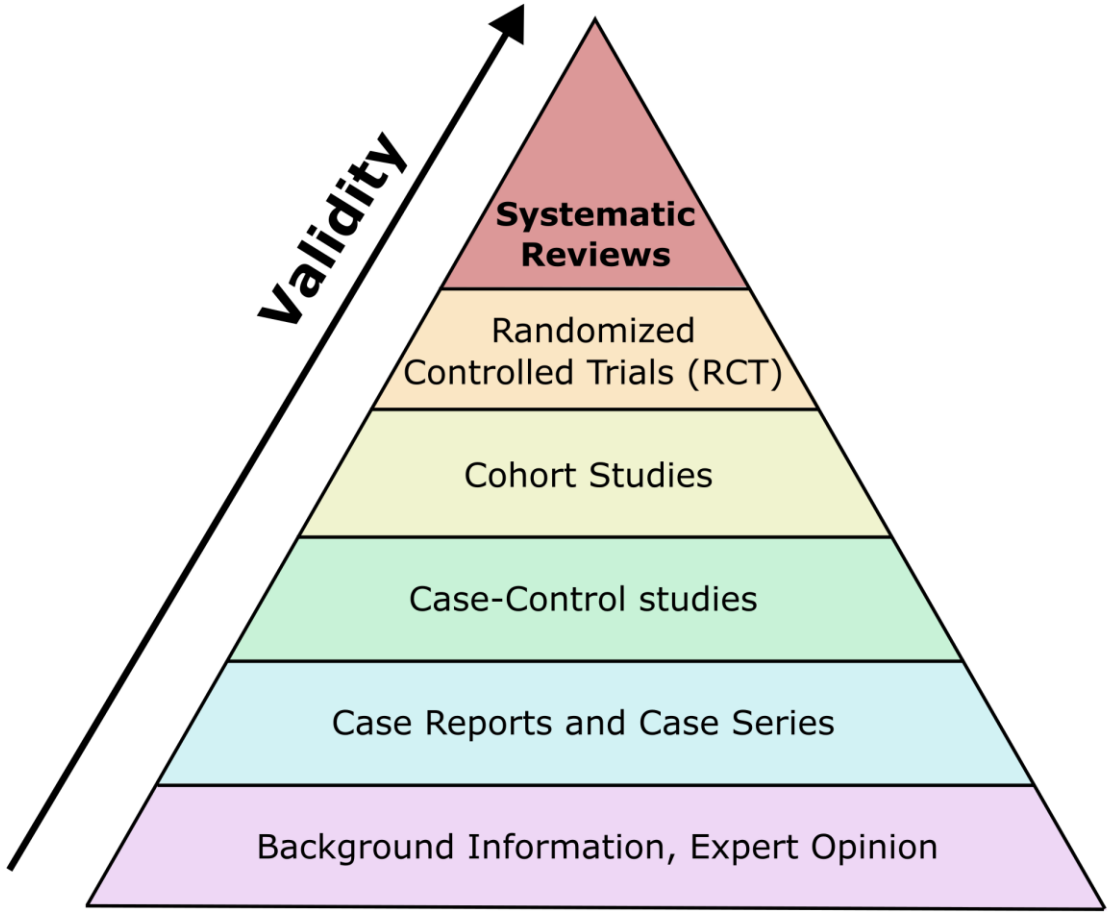
1. Systematic Review

What is a systematic review?

A systematic review is a research summary that addresses a focused question using **explicit methods**.

01	DEFINE A SPECIFIC RESEARCH QUESTION	06	SCREEN FULL TEXTS FOR RELEVANCE
02	DEFINE YOUR TEAM	07	EXTRACT DATA FROM STUDIES
03	CONDUCT A LITERATURE SEARCH	08	ASSESS THE RISK OF BIAS
04	WRITE AND REGISTER A PROTOCOL	09	DRAW CONCLUSIONS FROM YOUR DATA
05	SCREEN ABSTRACTS FOR RELEVANCE	10	MAKE YOUR SR PUBLICLY AVAILABLE

Why perform a systematic review?



Stroke
Volume 27, Issue 9, September 1996; Pages 1453-1458
https://doi.org/10.1161/01.STR.27.9.1453

ARTICLE

A Randomized Trial of Tirilazad Mesylate in Patients With Acute Stroke (RANTTAS)

on behalf of The RANTTAS Investigators

ABSTRACT: *Background and Purpose* Tirilazad mesylate, a nonglucocorticoid 21-aminosteroid lipid peroxidation inhibitor, has shown promise as a neuroprotectant in experimental models of focal cerebral ischemia.*Methods* To test whether early treatment with tirilazad, 6 mg/kg per day for 3 days, would improve functional outcome after acute human stroke, 27 North American centers conducted a prospective, randomized, double-blinded, vehicle-controlled trial in patients with acute stroke treated within 6 hours of onset. The primary outcome measures were disability as measured by the Glasgow Outcome Scale and activities of daily living by the Barthel Index determined 3 months after stroke.*Results* From May 1993 through December 1994, 660 patients were randomized. The trial was prematurely terminated on the advice of an independent monitoring committee after review of outcome data at a preplanned interim analysis. In 556 fully eligible patients (276 tirilazad, 280 vehicle), the odds ratio of a favorable outcome in favor of tirilazad was 0.87 (95% confidence interval [CI], 0.60 to 1.25) for the Glasgow Outcome Scale and 0.87 (95% CI, 0.60 to 1.25) for the Barthel Index, after adjustment for imbalances between the groups in preexisting disability, prior stroke, and diabetes.*Conclusions* These observations suggest that tirilazad, 6 mg/kg per day for 3 days administered beginning at a median of 4.3 hours after stroke, does not improve overall functional outcome.

TABLE 1. Study Characteristics

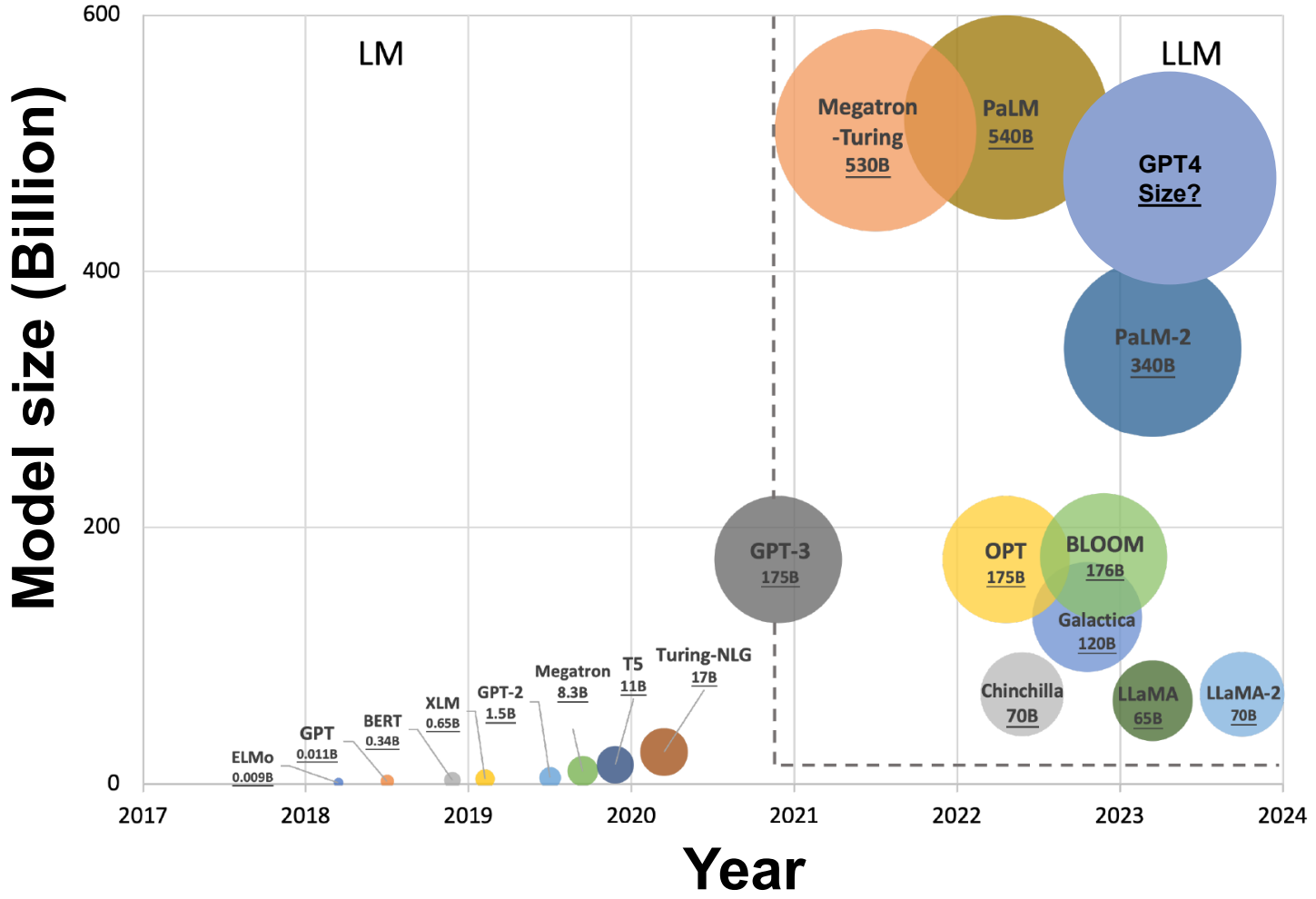
Author	Year	Drug	Species	Sex	N (C)	N (Rx)	Dose Range	Time of Admin, min	Anaesthetic	Type of Ischemia	Route of Delivery	Outcome Measure(s)
Alessandri	2000	Tirilazad	Rat	Male	6	6	29 mg/kg	15	Halothane	Permanent	IV	Infarct Volume
Beck	1991	Tirilazad	Rat	Unknown	12	10	4–40 mg/kg	−30	Halothane	Permanent	IP	Infarct Volume
Gross	1997	Tirilazad	Rabbit	Both	8	8	3 mg/kg	210	Ketamine	Thrombotic	IV	Infarct Volume
Hellström	1994	Tirilazad	Rat	Male	8	10	6 mg/kg	10	Halothane	Permanent	IV	Infarct Volume Neurological Score
Lythgoe	1990	Tirilazad	Rat	Male	7	7	26 mg/kg	10	Pentobarbital	Permanent	IV	Infarct Volume
Öktem	2000	Tirilazad	Rabbit	Unknown	6	6	6 mg/kg	15	Ketamine	Permanent	IV	Infarct Volume Neurological Score
Orozco	1995	Tirilazad	Rabbit	Unknown	10	10	3 mg/kg	120	Acepromazine	Thrombotic		Infarct Volume
Park	1994	Tirilazad	Rat	Male	7	7	1.89–18.9 mg/kg	15	Halothane	Permanent	IV	Infarct Volume Neurological Score
Schmid-Elaesser	1998	Tirilazad	Rat	Male	10	10	6 mg/kg	−15	Halothane	Reversible	IV	Infarct Volume
Schmid-Elaesser	1999b	Tirilazad	Rat	Male	10	10	6 mg/kg	−20	Halothane	Reversible	IV	Infarct Volume Neurological Score
Schmid-Elaesser	1999a	Tirilazad	Rat	Male	10	10	6 mg/kg	−15	Halothane	Reversible	IV	Infarct Volume Neurological Score

Sena et al., Stroke, 2007

2. Large Language Models (LLMs)

What are (Large) language models (LLMs)?

A computational model capable of “understanding” and generating human language, performing tasks like text generation, translation, summarization, and classification.



He et al., Arxiv, 2024
(L)LM = (Large) language model

How successful is drug development from animals to humans?

Wie viele Medikamente, die am Tierversuch erfolgsversprechend wirken, erhalten letztlich die Zulassung für den Menschen?

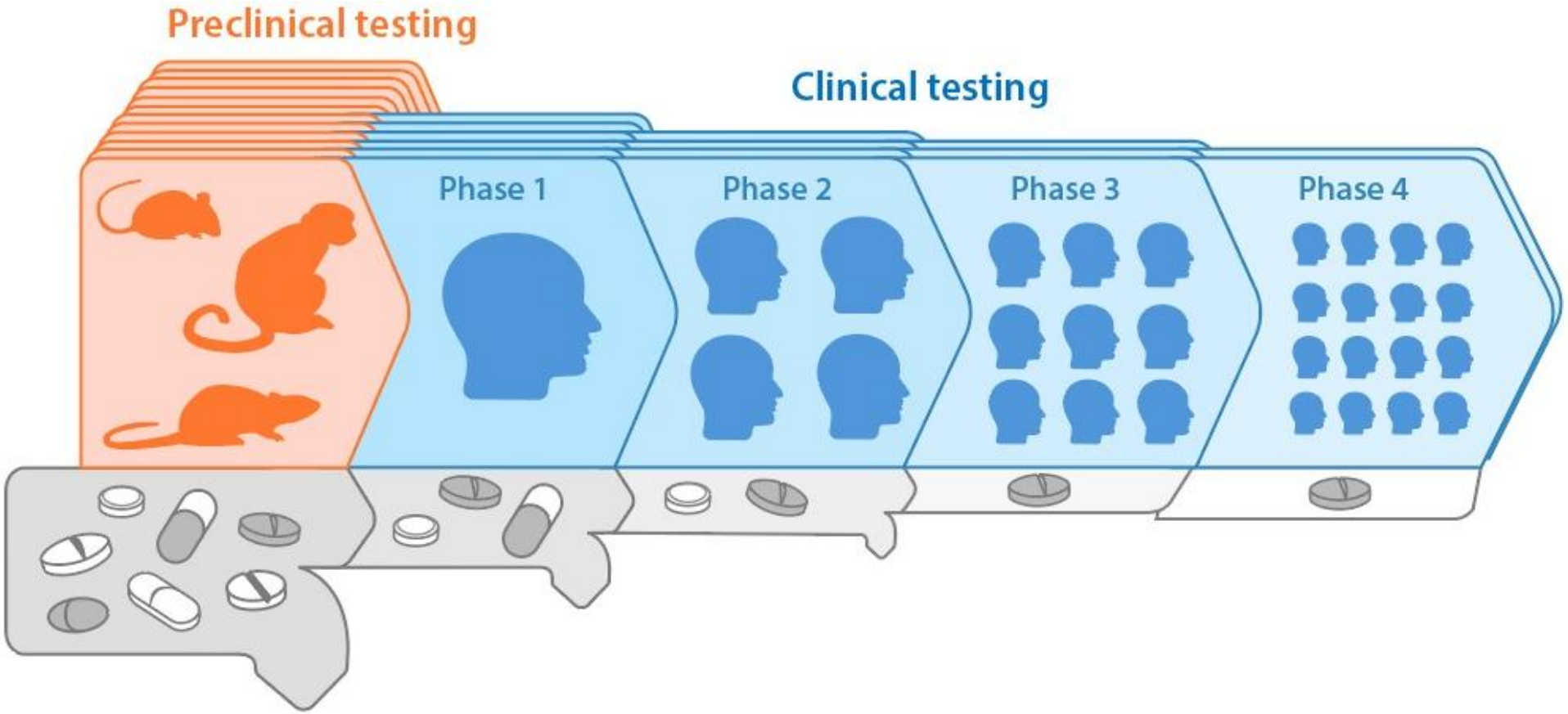
A. 1%

B. 5%

C. 10%

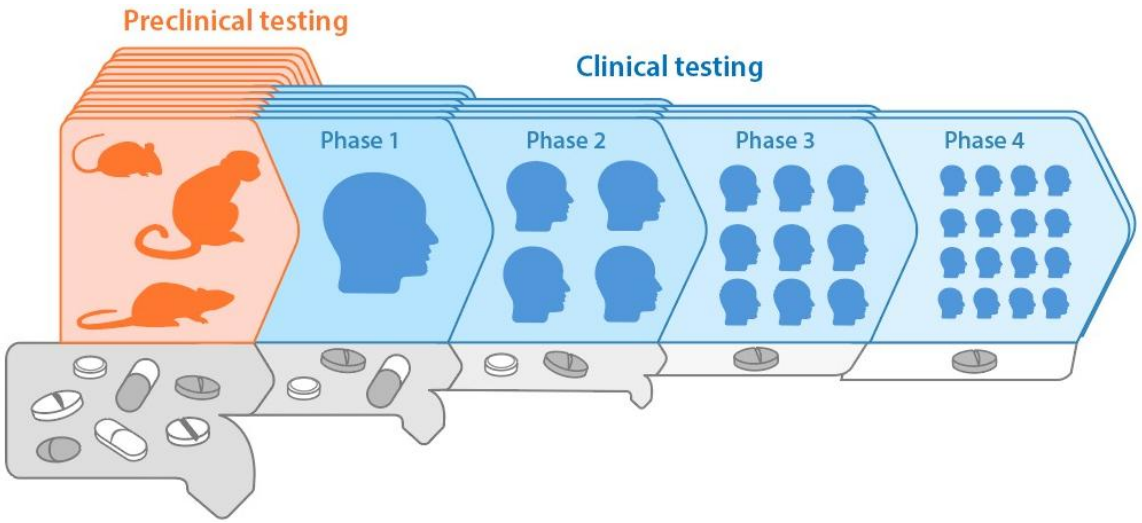
D. 20%

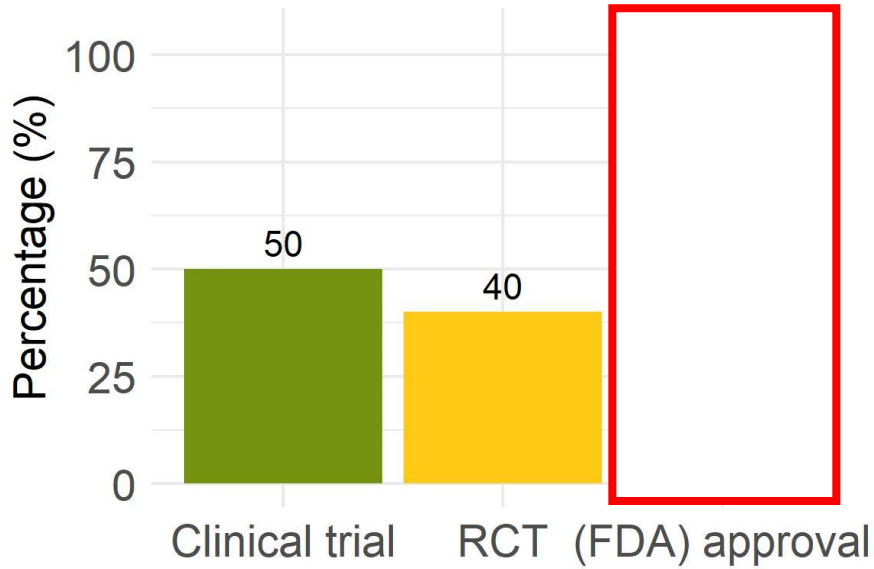
Animal-to-human translation



Proportion of successful translation

367 therapies
54 unique diseases
6736 observation years

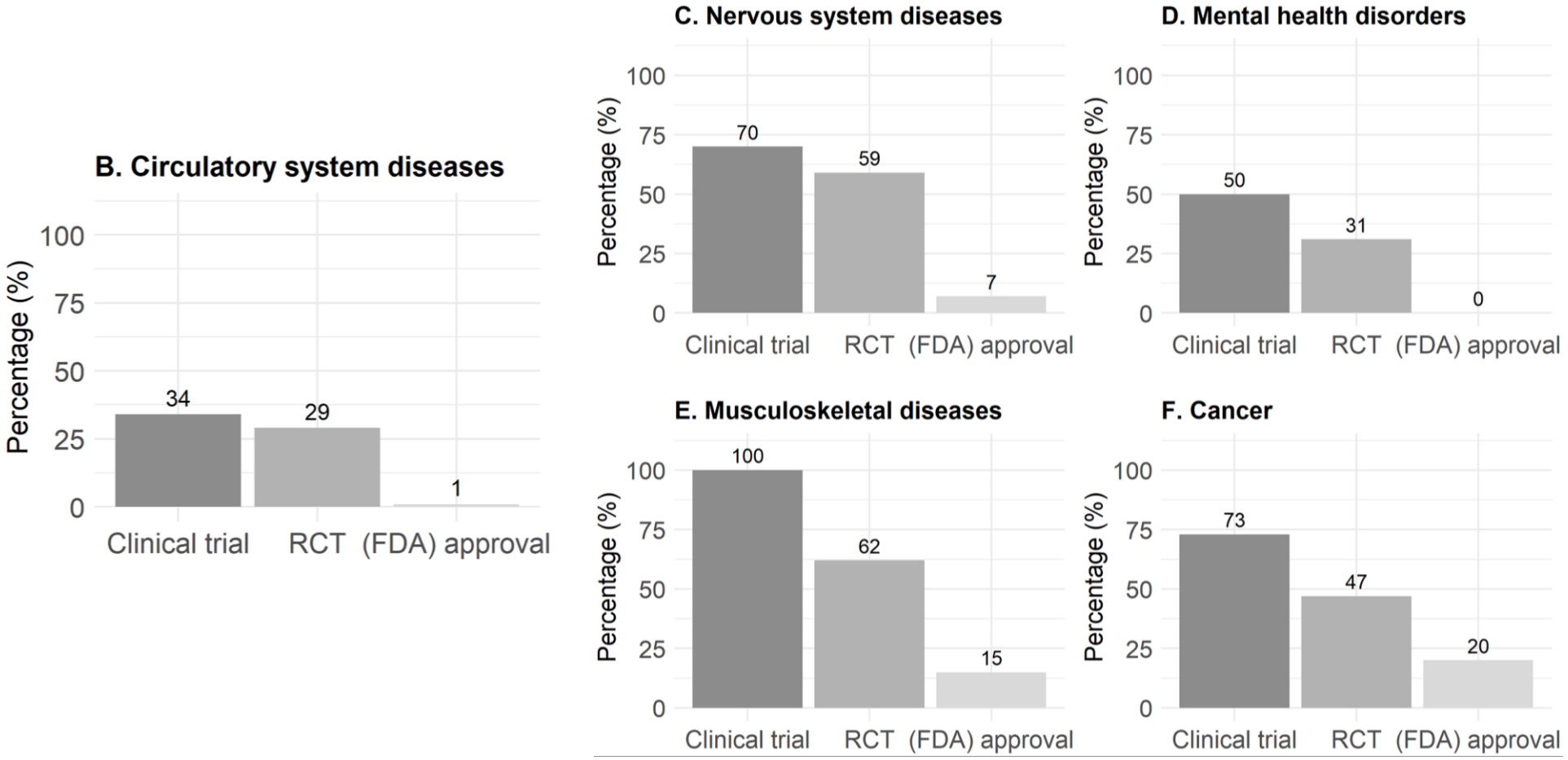




<u>After 10 years</u>: Only 1 in 20 drugs reaches approval for human use

Ineichen et al., PLoS Biol, 2024

Results: proportion of translation per category



Translational proportions are different in different biomedical fields

Ineichen et al., PLoS Biol, 2024

abc NEWS

SRF

Blick

ORF

U.S.News & WORLD REPORT

Frankfurter Allgemeine
ZEITUNG FÜR DEUTSCHLAND

The Economist

Science & technology

Only 5% of therapies tested on animals are approved for human use

More rigorous experiments could improve those odds

After 10 years: Only 1 in 20 drugs reaches approval for human use

Ineichen et al., PLoS Biol, 2024

Solo 20% dei nuovi farmaci raggiunge approvazione per uso umano

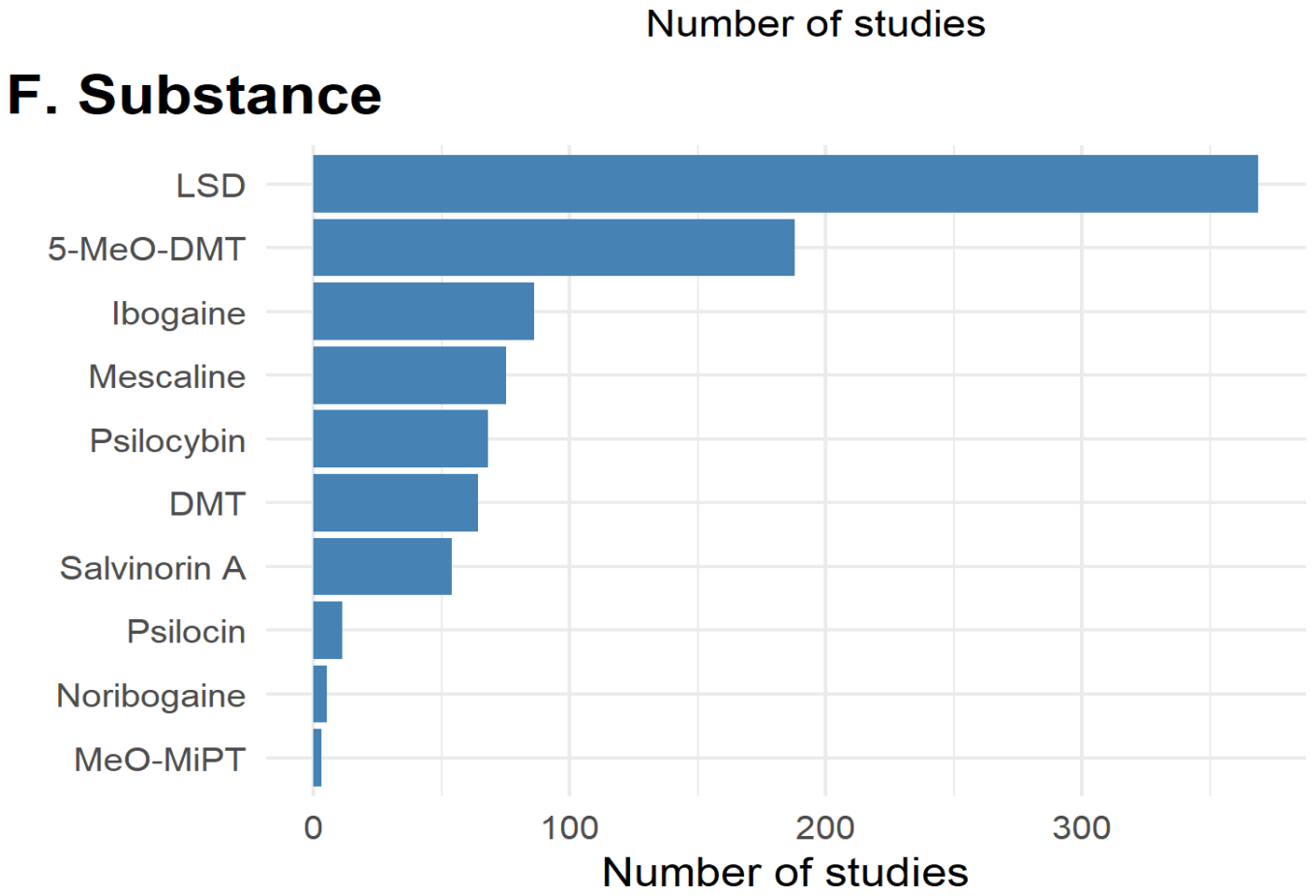
Studio pubblicato sulla rivista Plos Biology

Why is that?

Use case 1: Identifying systemic problems in psychedelic animal research

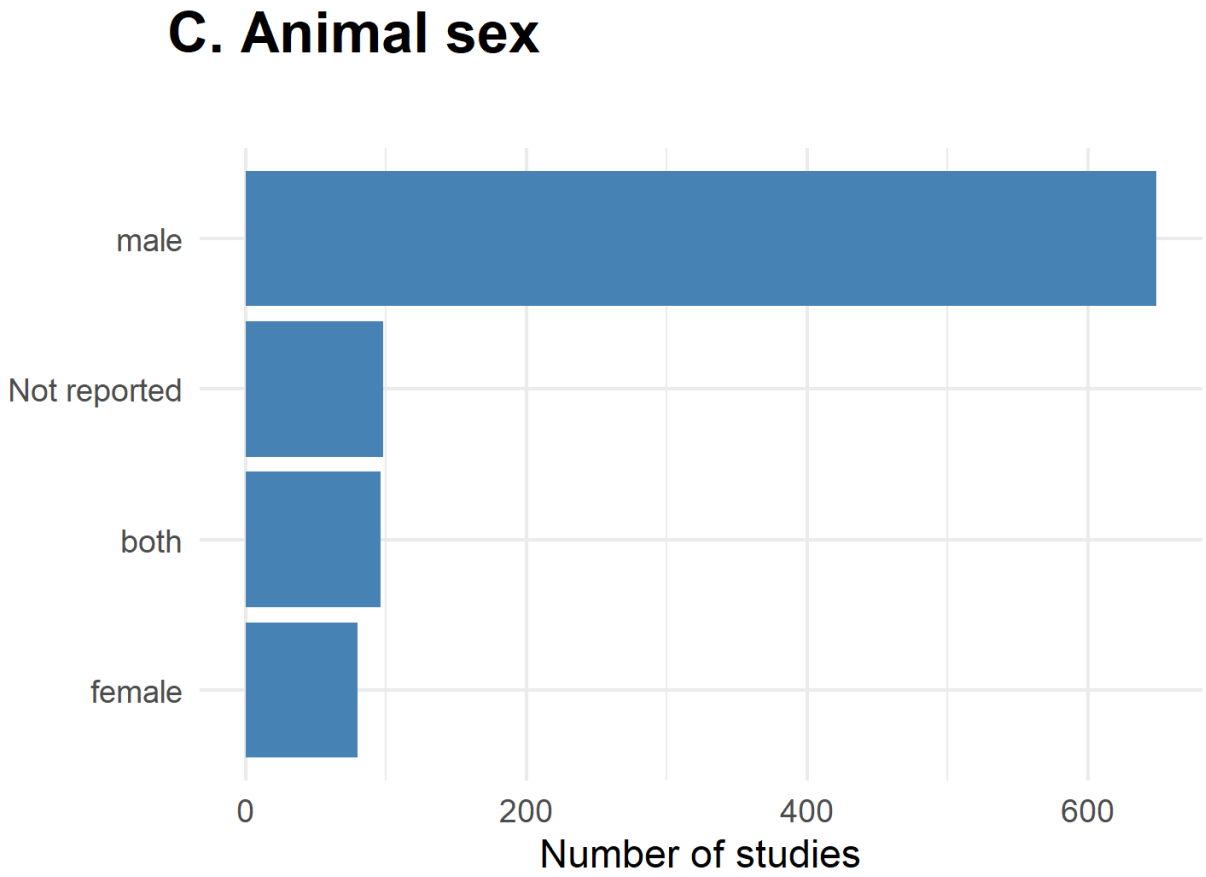
Brian Allen

Challenges in animal research testing psychedelic substances



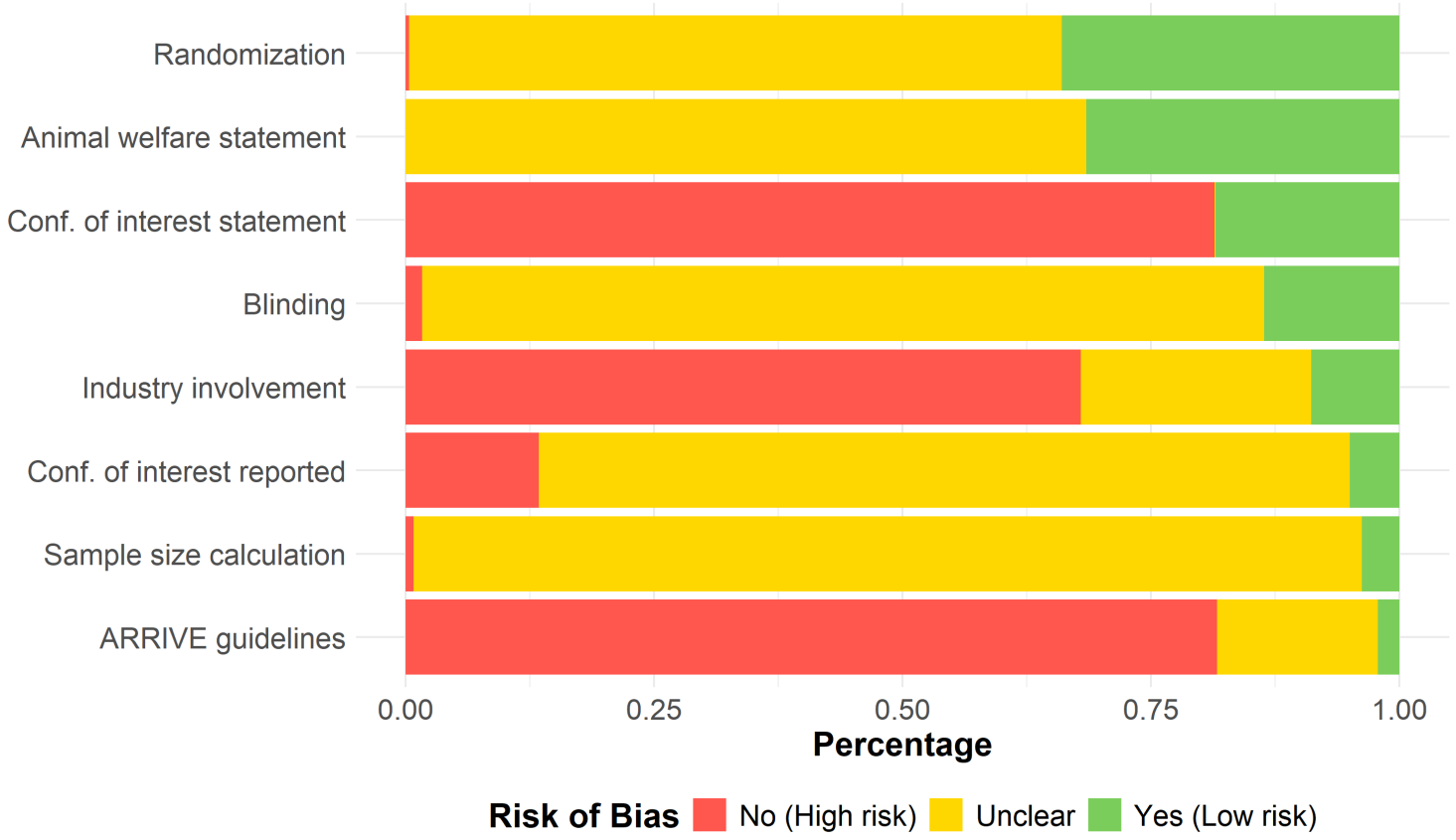
Allen et al., manuscript submitted

Challenges in animal research testing psychedelic substances



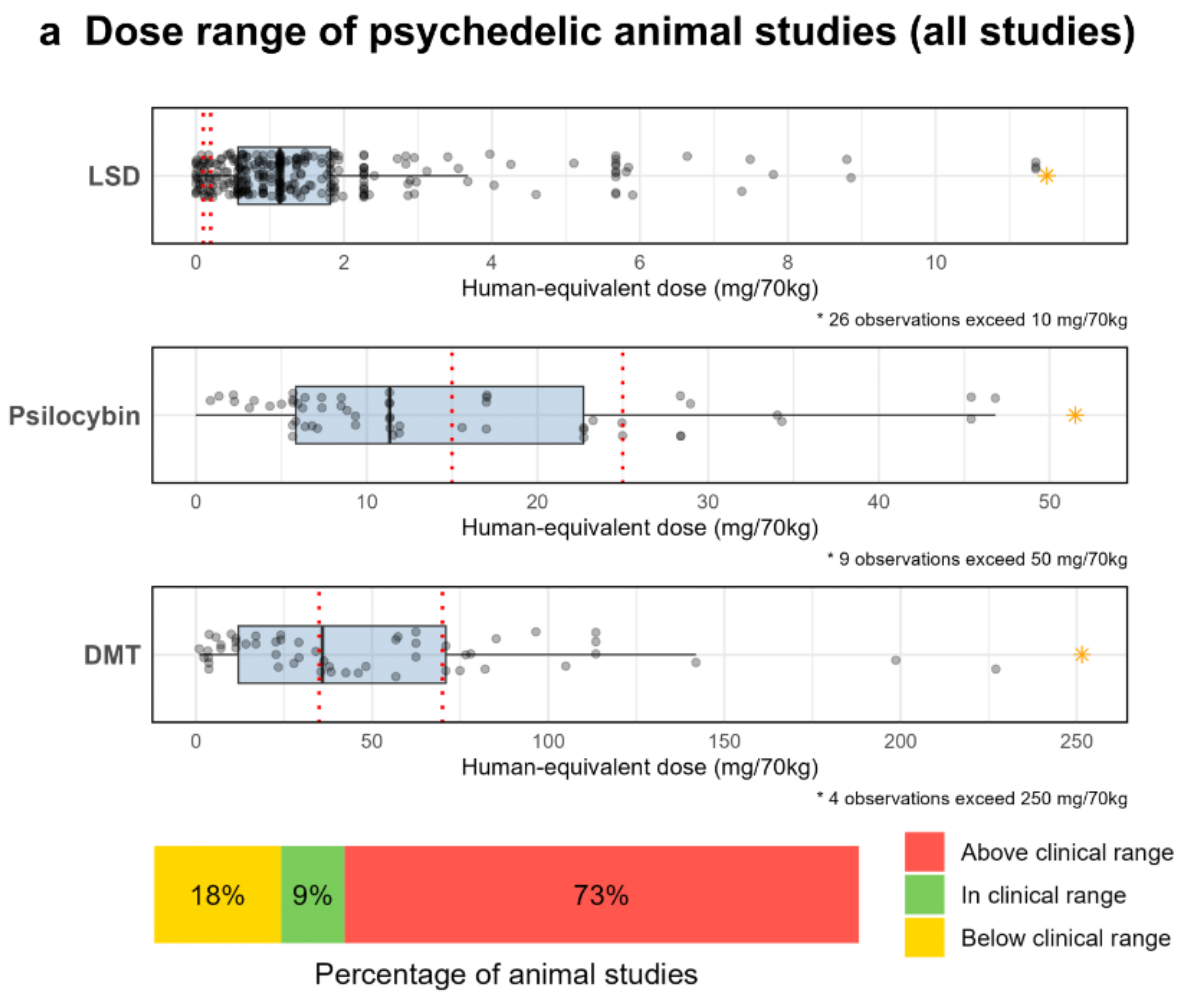
Allen et al., manuscript submitted

Low rigour of animal studies testing psychedelic substances



Allen et al., manuscript submitted

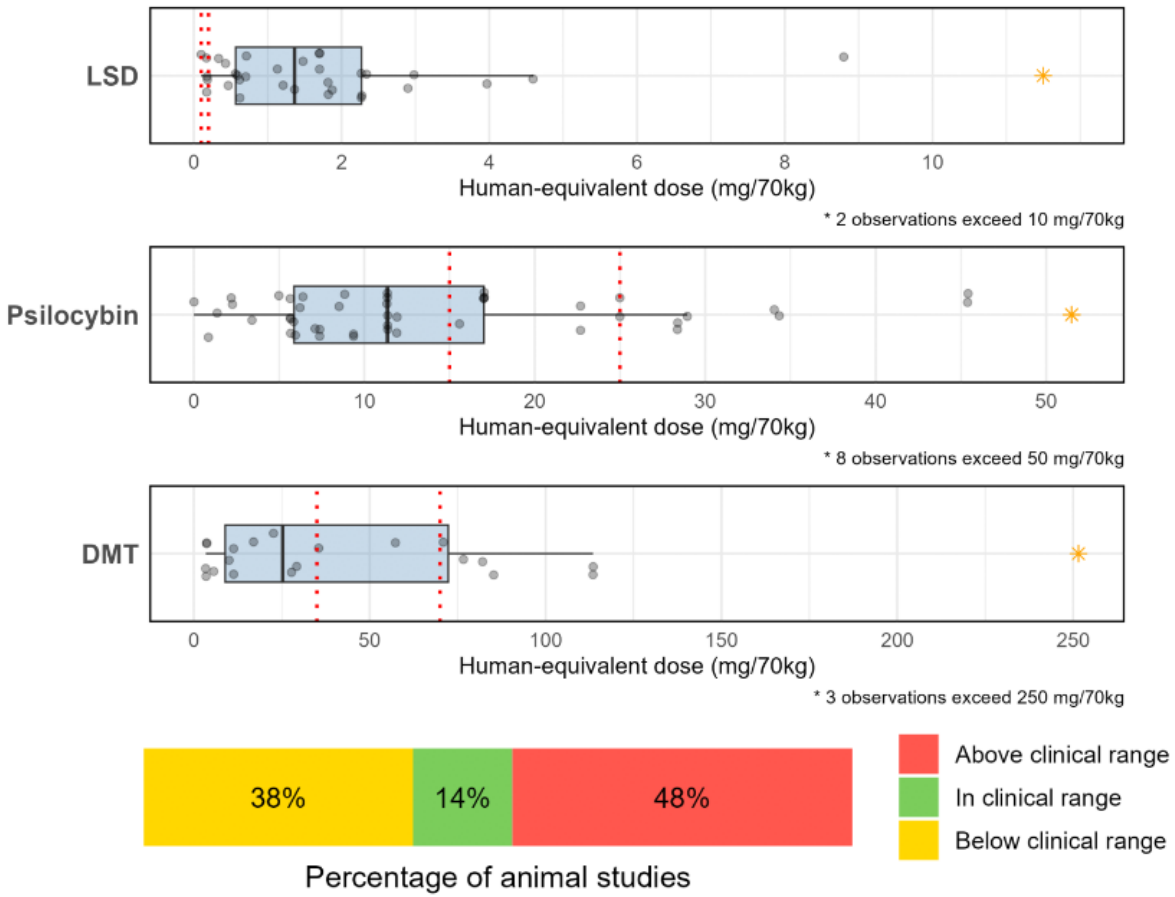
Questionable dosing of psychedelic substances



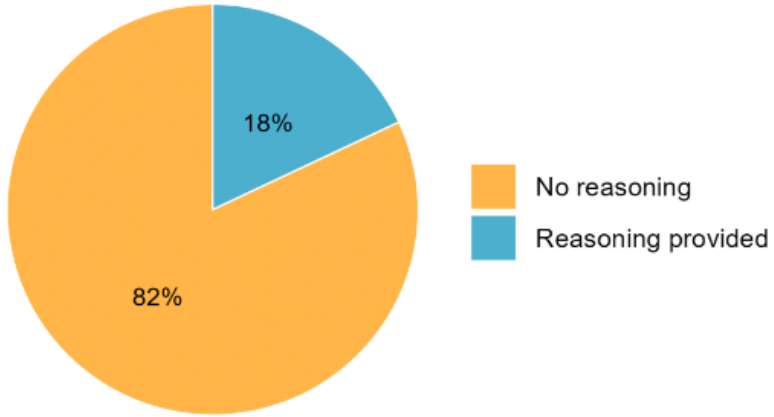
Allen et al., manuscript submitted

Questionable dosing of psychedelic substances

b Dose range of psychedelic animal studies (last decade)



c Reasoning provided by authors for chosen dose



Allen et al., manuscript submitted

Use case 2: Systematically assessing timing of animal studies in drug development

Pia Härvelid

Mia Schuster

FDA-approved drugs between 2011 and 2014

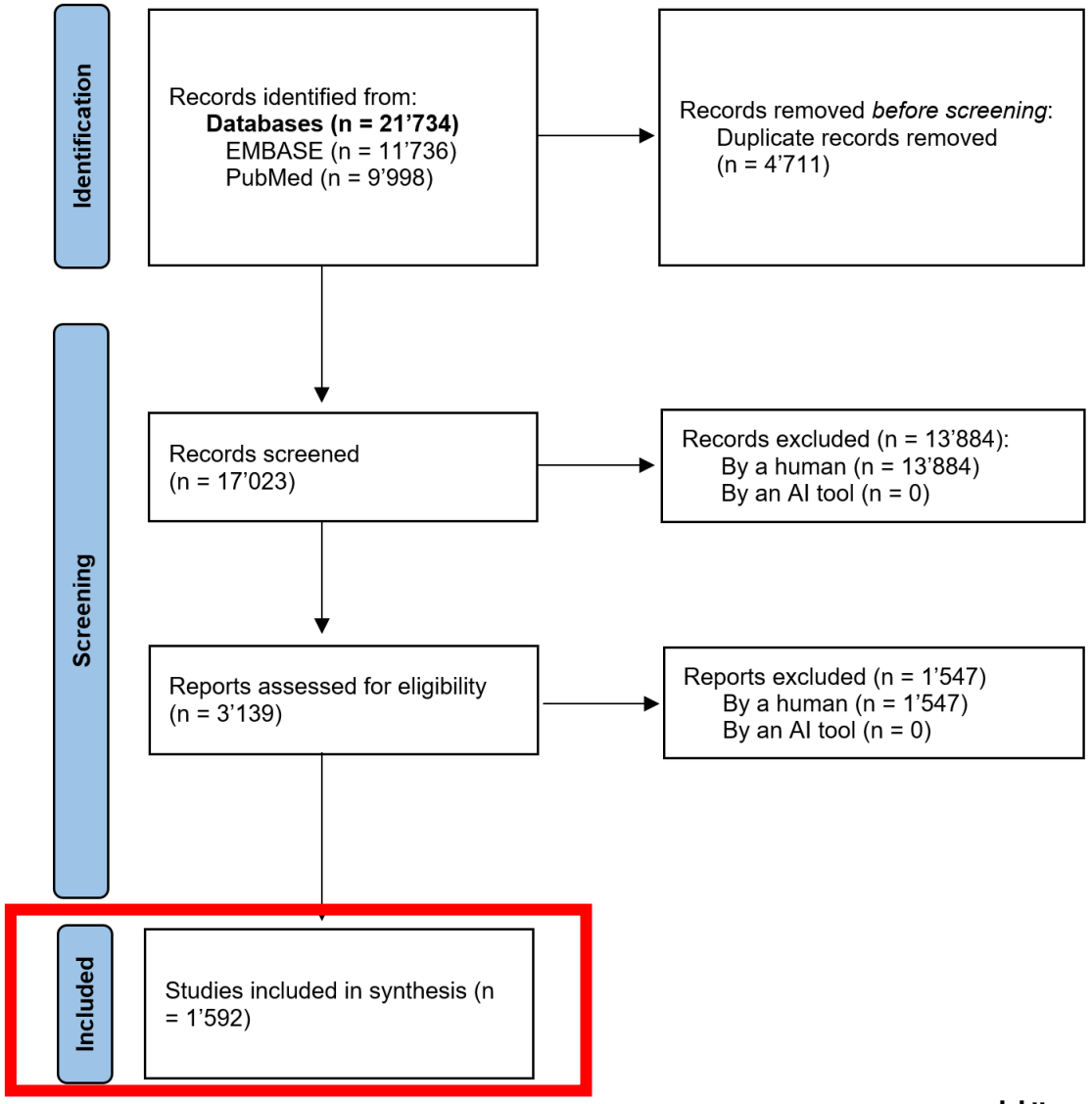
62 drugs identified
- 23 excluded (non-drugs, withdrawn, or
- Discontinued)
- 3 excluded (no eligible articles identifed)

-> 36 drugs included

Active substance(s)	Medical indications
Vilazodone	Depression
azilsartan medoxomil	Hypertension
roflumilast	COPD, bronchitis
vandetanib	medullary thyroid cancer
linagliptin	Diabetes, glycemic control
belatacept	Organ transplantation
icatibant	angioedema
Vismodegib	Basal cell carcinoma
Tafluprost	glaucoma, intraocular pressure
Avanafil	erectile dysfunction
Aclidinium bromide	Bronchitis, COPD, bronchospasm
Aflibercept	colon cancer
Linaclotide	Irritable bowel syndrome, constipation
Ocriplasmin	vitreomacular adhesion
Omacetaxine mepesuccinate	chronic myeloid leukemia, leukemia
Cabozantinib	medullary thyroid cancer
Raxibacumab	Bacillus anthracis, Anthrax
Pasireotide	Cushing
Lomitapide	hypercholesterolemia, dyslipidemia
Alogliptin benzoate	Diabetes, glycemic control
Radium Ra-233	cancer
Vortioxetine	Depression
Bazedoxifene/estrogens	menopause
Riociguat	Pulmonary Hypertension, pulmonary arterial hypertension
Macitentan	Pulmonary Hypertension, pulmonary arterial hypertension
Elosulfase alfa	Mucopolysaccharidosis
Droxidopa	hypotension, dizziness, lightheadedness
Metreleptin	lipodystrophy, leptin deficiency
Siltuximab	lymphoproliferative disorders, Castleman
Vorapaxar	myocardial infarction, peripheral arterial disease, stroke, coronary artery disease
Belinostat	lymphoma, cancer
Tavaborole	onychomycosis, fungus
Idelalisib	leukemia, cancer
Olodaterol	COPD, bronchitis
Oritavancin	antibiotic
Suvorexant	sleep problems, insomnia
Eliglustat	Gaucher, accumulation disease
Netupitant/palonosetron	nausea, vomiting
Pirfenidone	pulmonary fibrosis

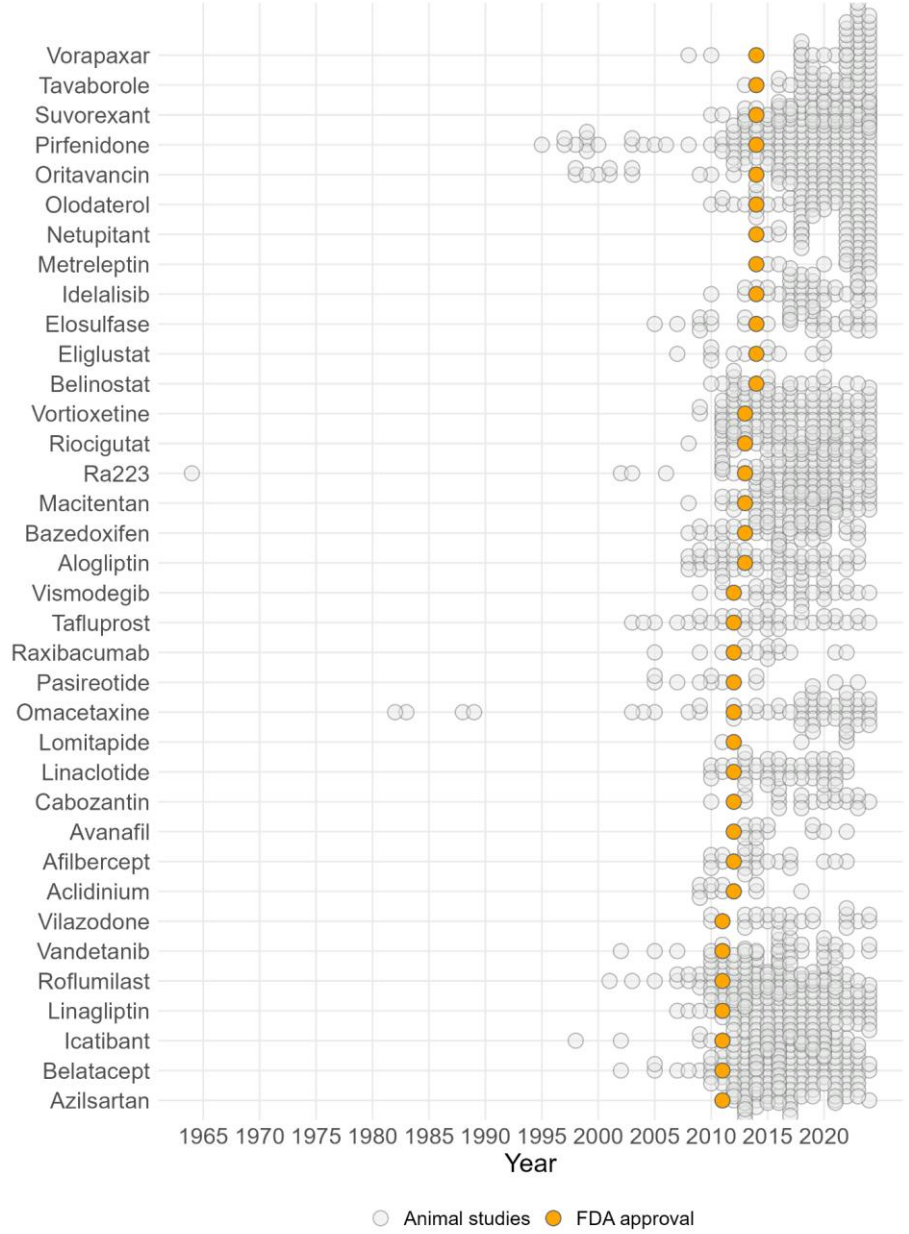
Härvelid et al., manuscript in preparation

Included studies



Härvelid et al., manuscript in preparation

Proportion of post-approval studies

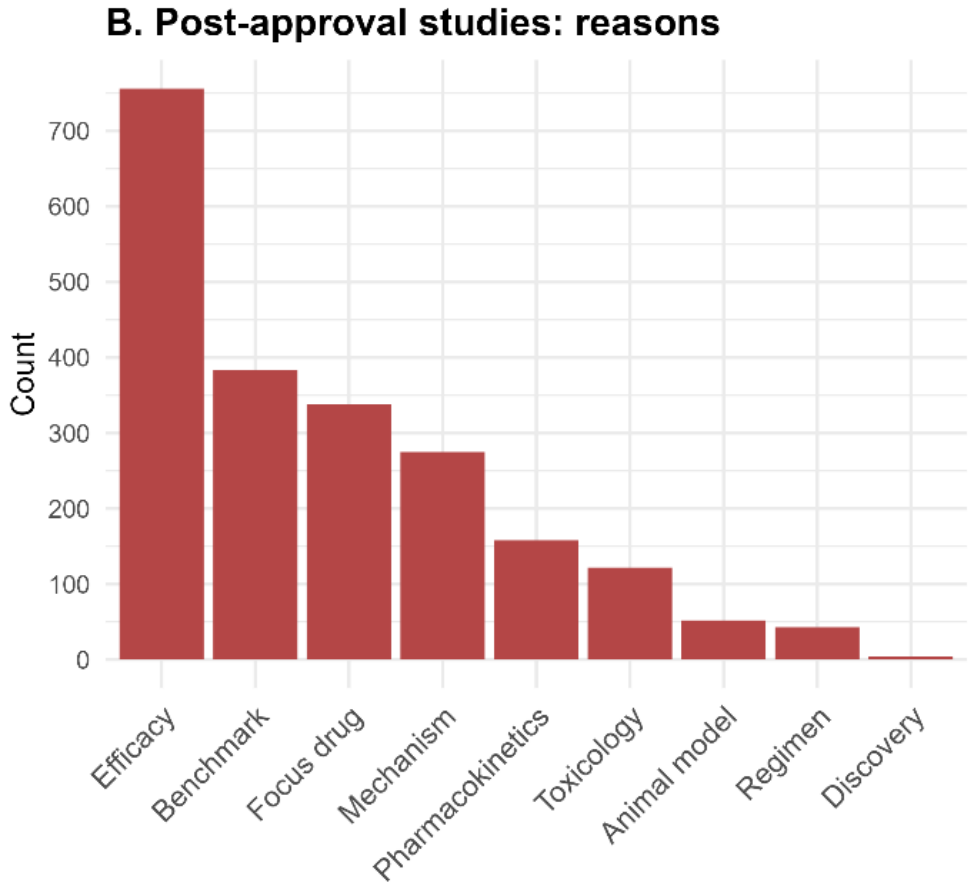


84% of animal studies published after regulatory approval (1345/1592 studies)

If considering a time gap of 3 years post-approval: **67%** published after regulatory approval (1063/1592 studies)

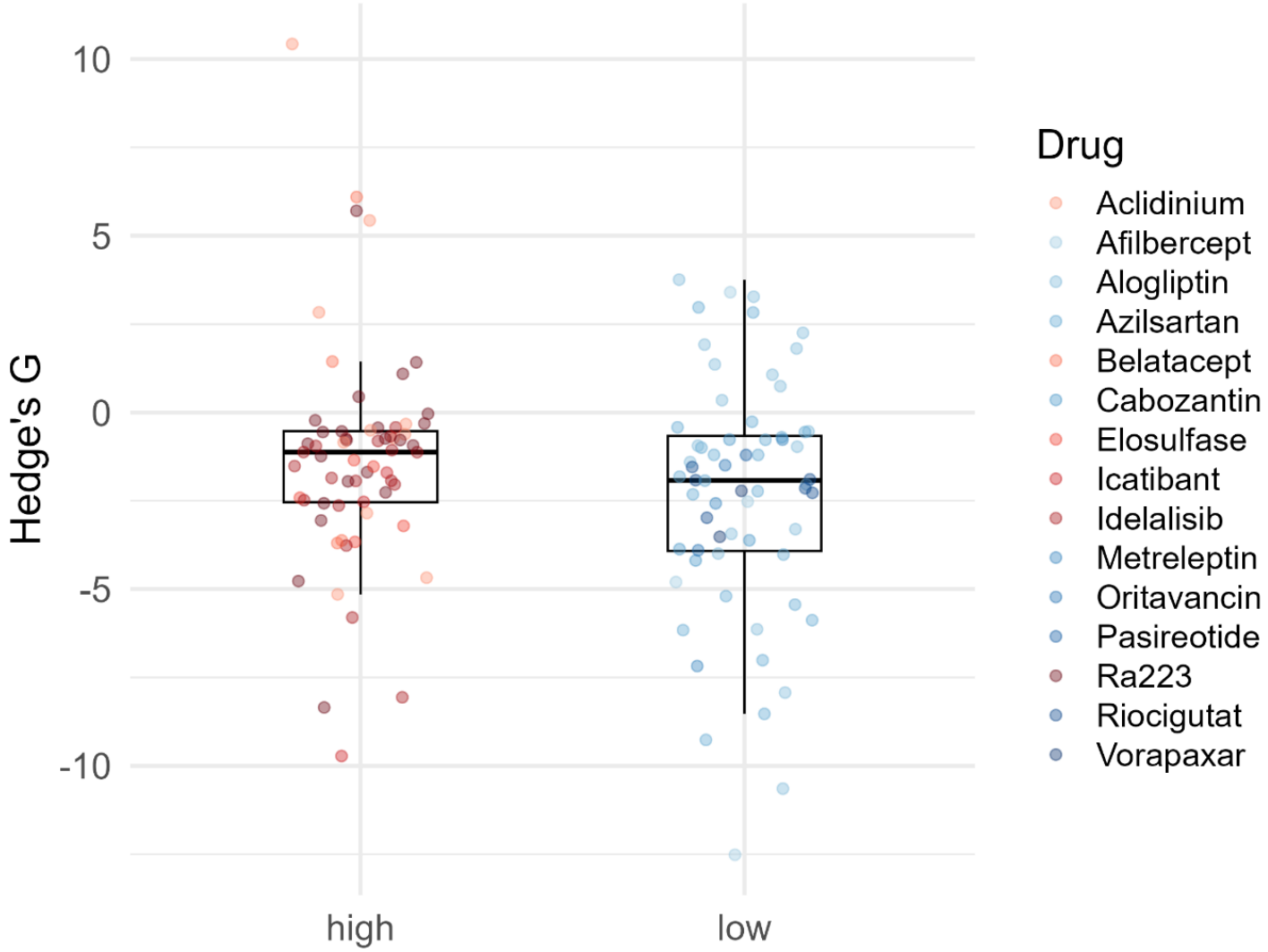
Härvelid et al., manuscript in preparation

Testing efficacy as common reason for post-approval animal studies



22% of post-approval animal studies conducted exclusively for efficacy reasons

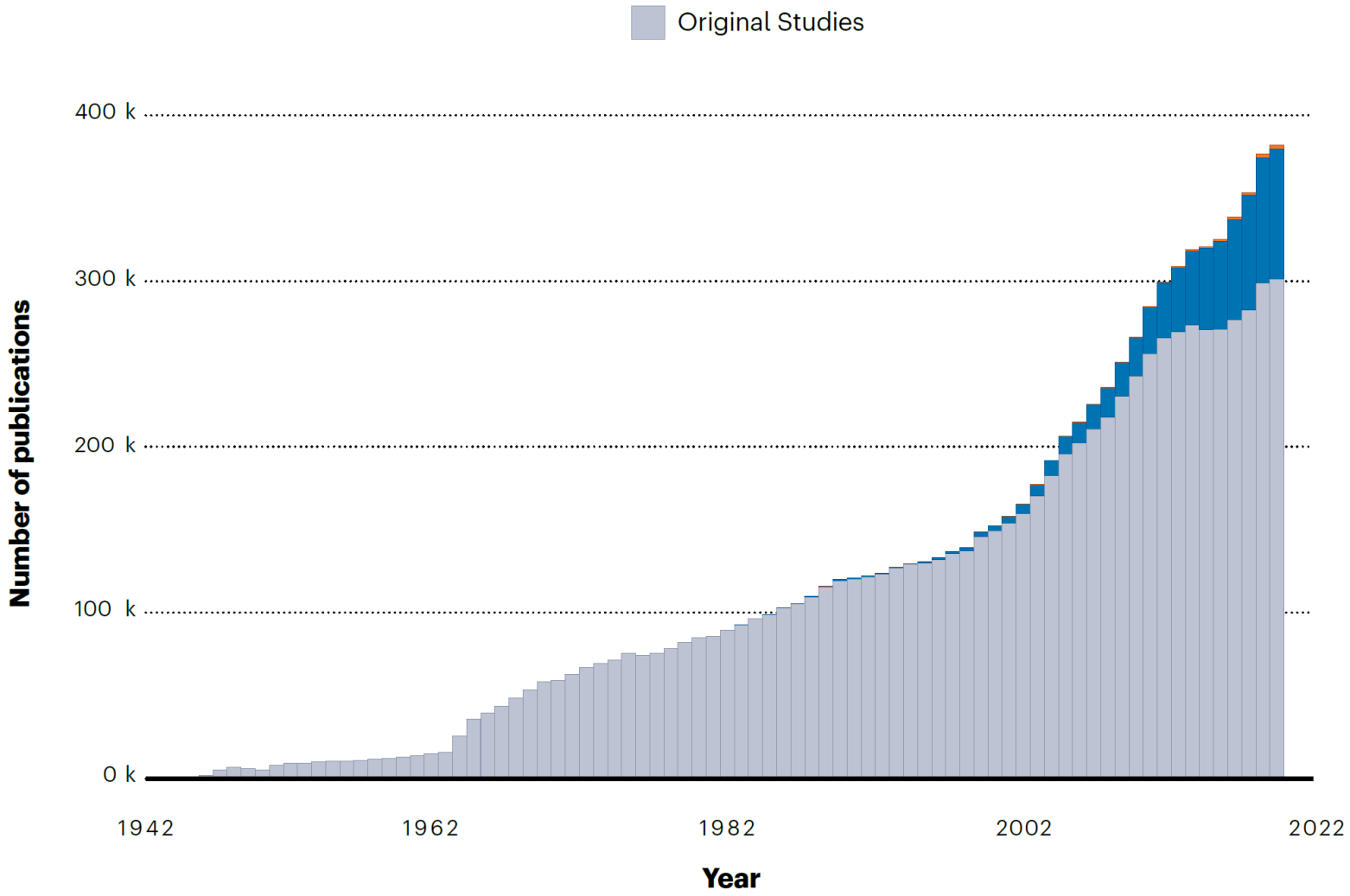
Animal effect sizes are not associated with clinical drug value



Härvelid et al., manuscript in preparation

Where is this Going?

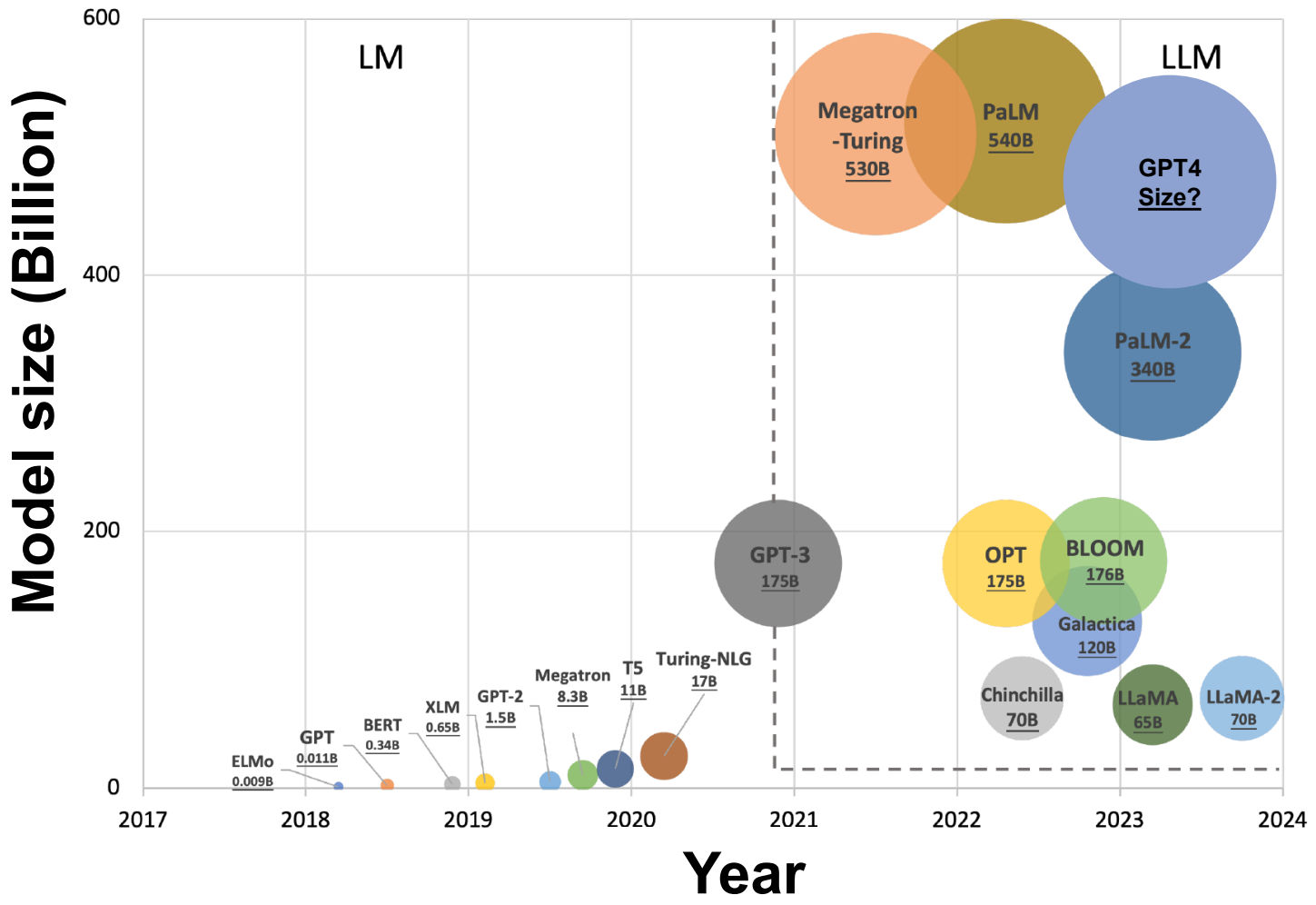
The problem: skyrocketing evidence…



Ineichen et al., Lab Animal, 2023

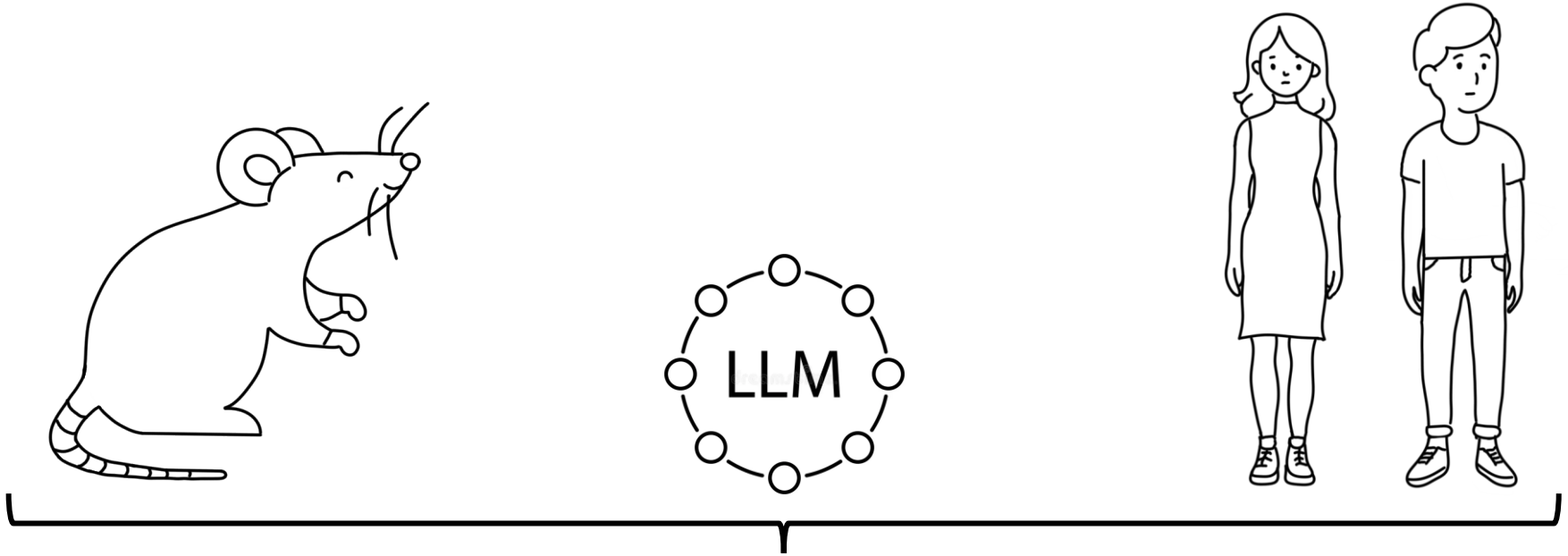
What are (Large) language models (LLMs)?

A computational model capable of "understanding" and generating human language, performing tasks like text generation, translation, summarization, and classification.



He et al., Arxiv, 2024
(L)LM = (Large) language model

Trialomics: Curating large scale data on drug development



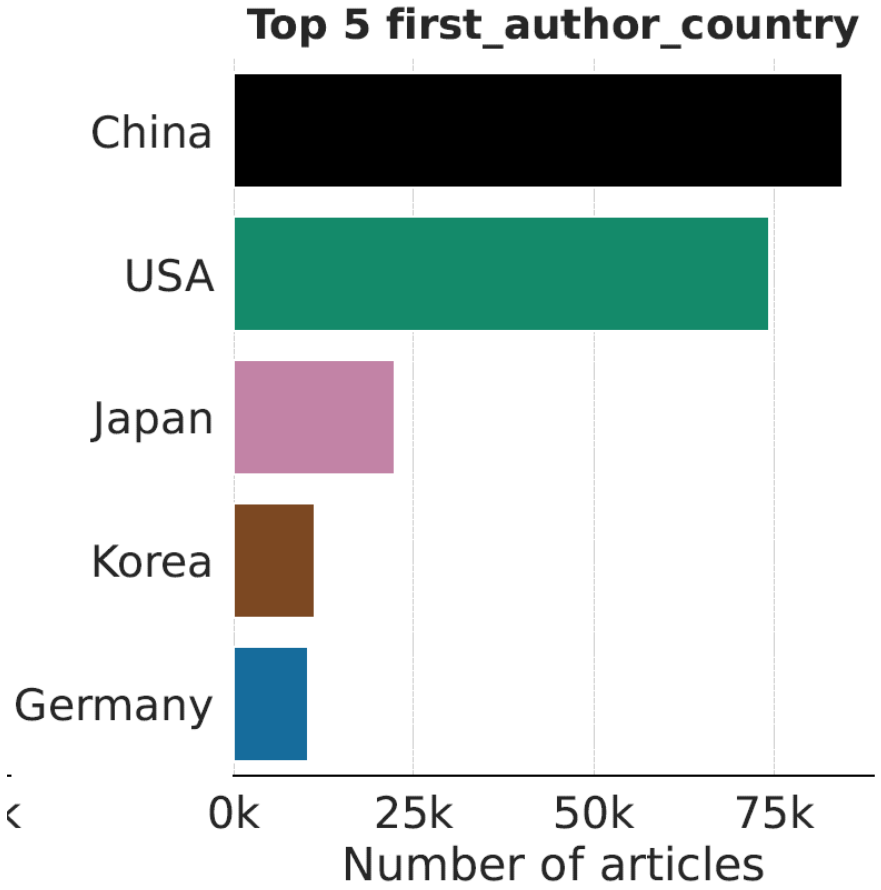
Simona Doneva

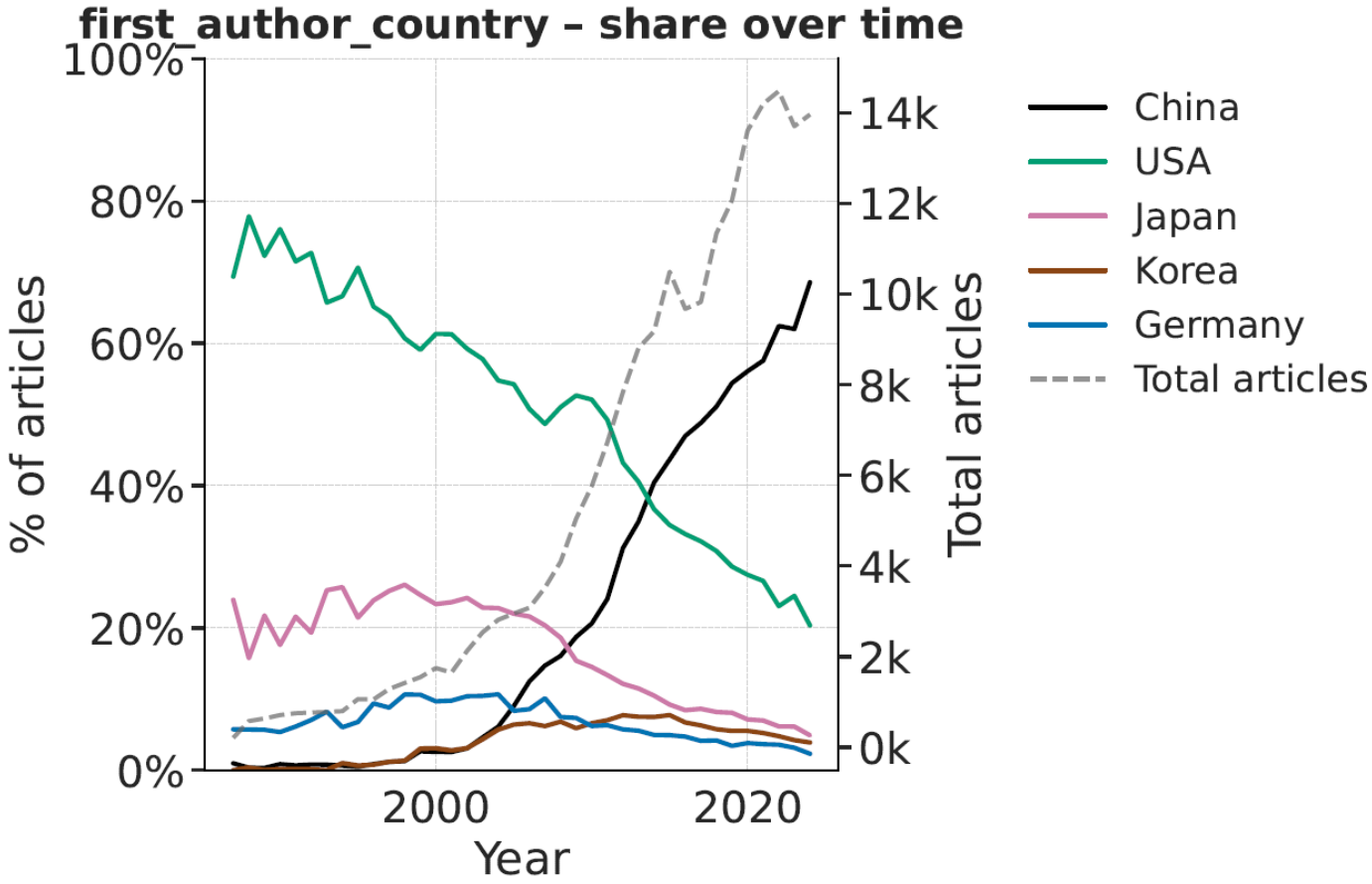
Which factors govern successful development of drugs?

TrialSim

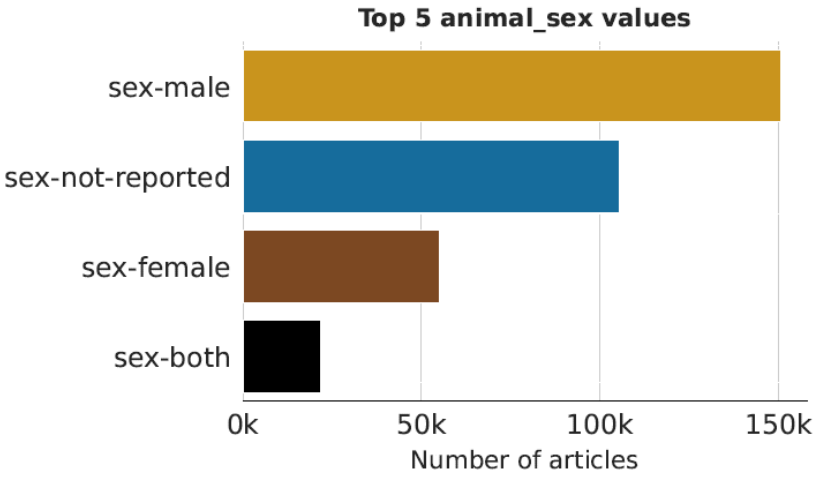
Drug trial – omics: **Trialomics**

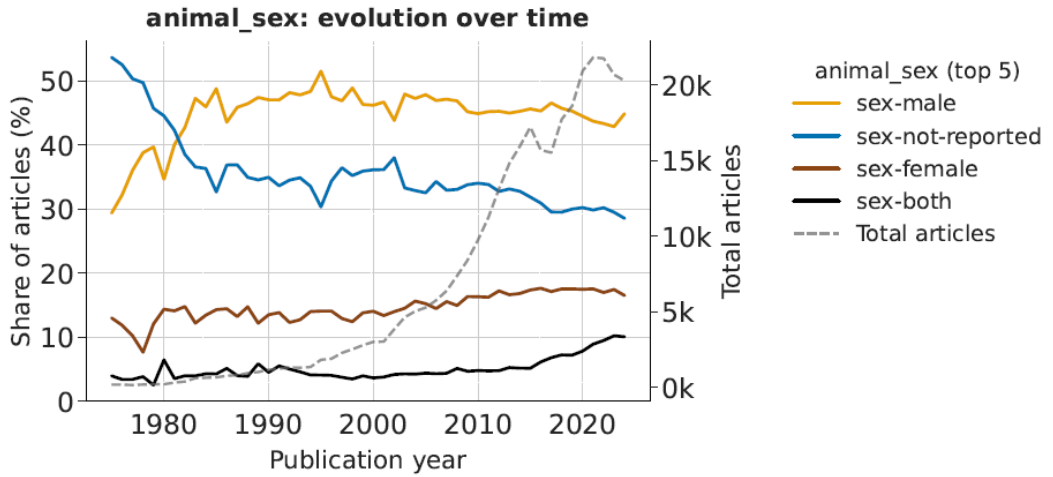
AI for large scale assessment of animal-to-human translation

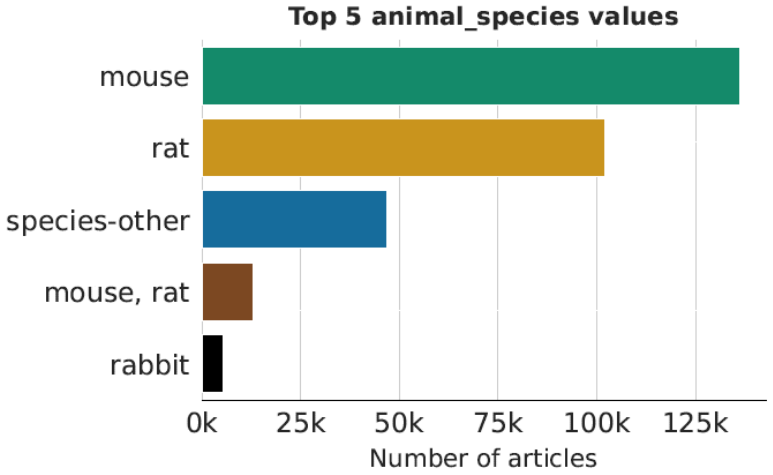


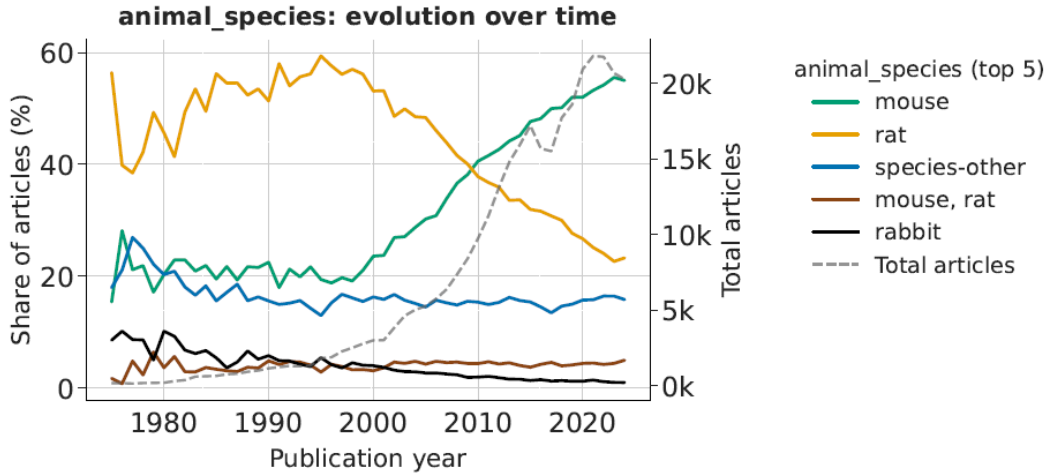


AI for large scale assessment of animal-to-human translation

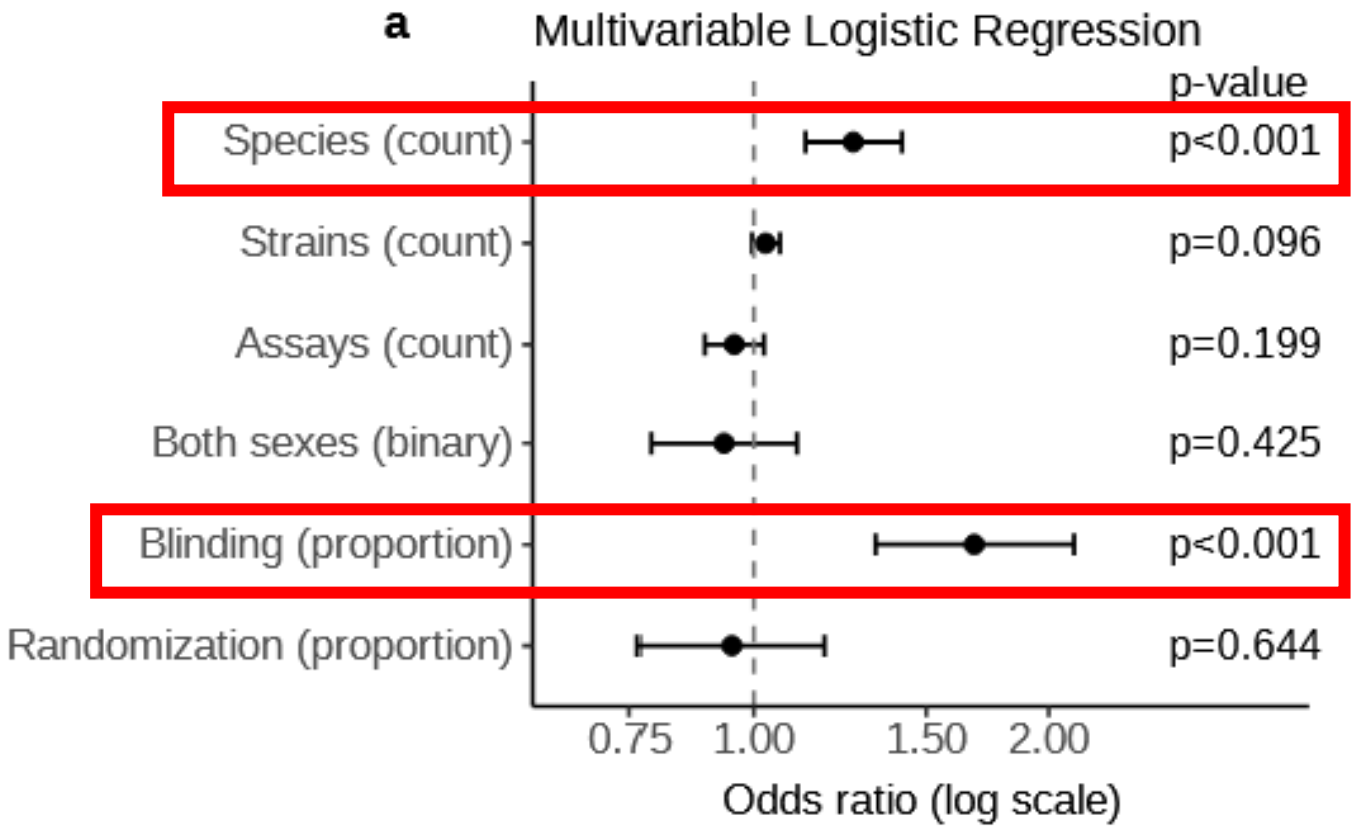








How to improve drug testing in animals?



Conclusions

- Animal research is (still) important.
- There are **systemic** problems in animal research.
- Animal research should overall be more rigorous to optimize **value** for human health and **credibility**.
- AI as critical tool to understand drug development and to make it more evidence-based.

Recommendation:

1. Training and awareness
2. Connecting animal and human researchers (reverse translation?)

Quiz

- Go to joinmyquiz.com
- Enter quiz number: 473345

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MS Schweizerische Multiple Sklerose Gesellschaft