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Trial efficiency

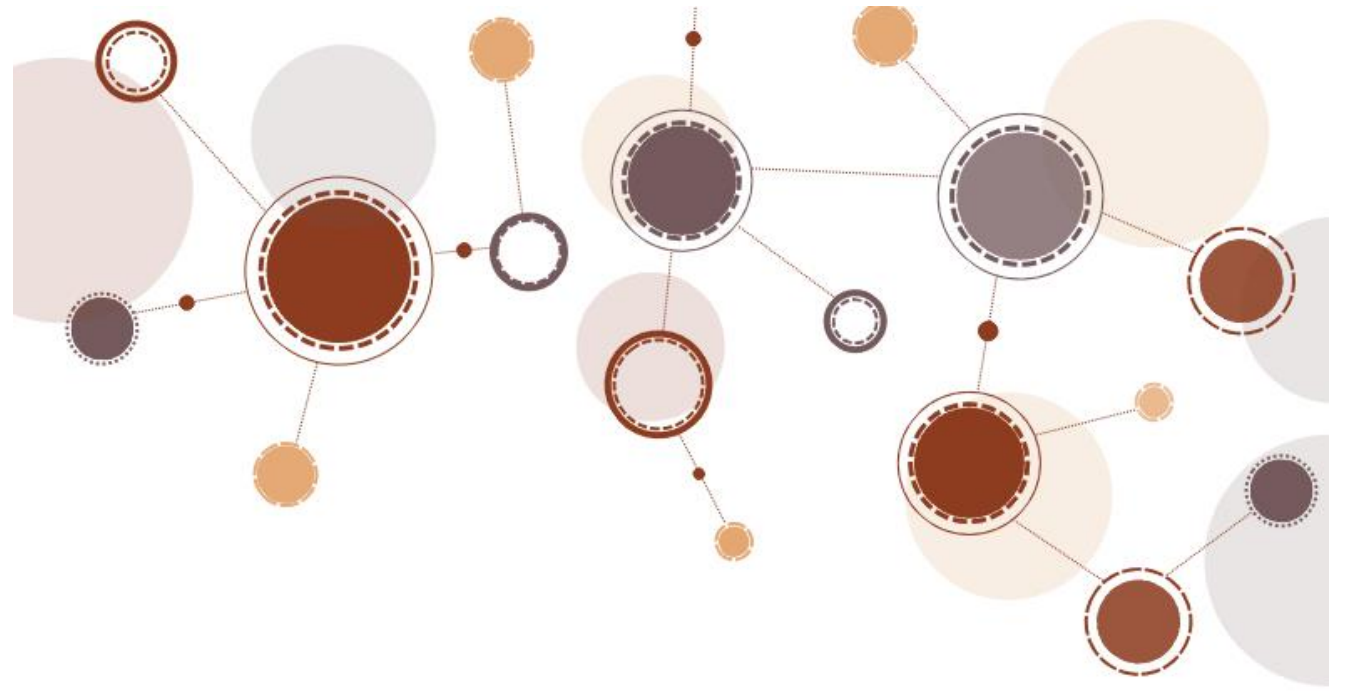
Costs, hurdles, and innovations

U-CARE Venue
13-14 October 2025

Benjamin Speich, PhD, Senior lecturer

CLEAR Methods Center, Department of Clinical Research, University Hospital Basel, University of Basel, Switzerland

Setting the Scene

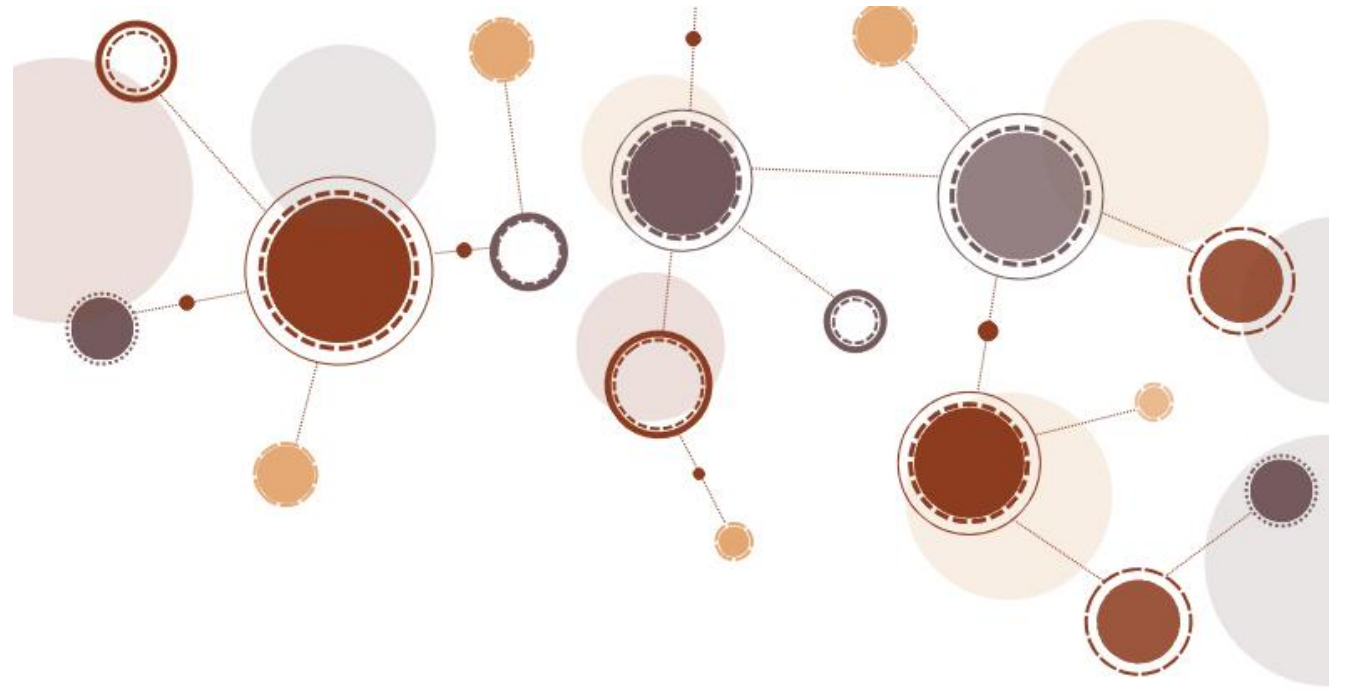


U-CARE VENUE 2025

Smarter Science

How can we conduct high-quality healthcare research more efficiently?

Setting the Scene



U-CARE VENUE 2025

Smarter Science

How can we conduct high-quality healthcare research more efficiently?

Costs

Costs of randomised trials

- R&D for 1 new drug¹: US\$ 1,400,000,000
- Average cost of phase III trial²: US\$ 11,500,000 (Dermatology)
US\$ 52,900,000 (Anaesthesia)
- NIHR-funded Trials³: £ 500,000 – £ 2,400,000

Systematic review on costs and resource use of randomised clinical trials
6650 deduplicated articles screened within title and abstract; 324 full-text articles

56 articles which contain empirical cost and/or resource data for randomised clinical trials

16 articles with overall trial costs

40 articles presenting costs for one specific aspect (i.e. 30 recruitment, 10 other)

0 articles presenting resources and costs data for all aspects of a randomised trial

¹DiMasi et al. *JHealthEcon* 2016

²Sertkaya et al. *ClinTrials* 2016

³Raftery et al. *HealthTechnolAssess* 2015

Costs of randomised trials





Journal of Clinical Epidemiology
Volume 96, April 2018, Pages 73-83



Original Article

Retrospective assessment of resource use and costs in two investigator-initiated randomized trials exemplified a comprehensive cost item list

Benjamin Speich ^{a,1}, Belinda von Niederhäusern ^{b,1}, Claudine Angela Blum ^{c,d}, Jennifer Keiser ^e, Nadine Schur ^e, Thomas Füst ^{e,f,g}, Benjamin Kasenda ^{a,h}, Mirjam Christ-Crain ^c, Lars G. Hemkens ^a, Christiane Pauli-Magnus ^b, Matthias Schwenkglenks ^{i,j,1}, Matthias Briel ^{a,k,1}  
[MAKing Randomized Trials Affordable \(MARTA\) Group](#)

cmajOPEN

► CMAJ Open. 2019 Jan 29;7(1):E23-E32. doi: [10.9778/cmajo.20180096](https://doi.org/10.9778/cmajo.20180096)

Current use and costs of electronic health records for clinical trial research: a descriptive study

[Kimberly A Mc Cord](#) ¹, [Hannah Ewald](#) ¹, [Aviv Ladanie](#) ¹, [Matthias Briel](#) ¹, [Benjamin Speich](#) ¹, [Heiner C Bucher](#) ¹, [Lars G Hemkens](#) ^{1,✉}, for the RCD for RCTs initiative and the Making Randomized Trials More Affordable Group

► [Author information](#) ► [Article notes](#) ► [Copyright and License information](#)


PMCID: PMC6375253 PMID: [30718353](https://pubmed.ncbi.nlm.nih.gov/30718353/)

PLOS One

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 OPEN ACCESS  PEER-REVIEWED
RESEARCH ARTICLE

Resource use, costs, and approval times for planning and preparing a randomized clinical trial before and after the implementation of the new Swiss human research legislation

Benjamin Speich, Nadine Schur, Dmitry Gryaznov, Belinda von Niederhäusern, Lars G. Hemkens, Stefan Schandelmaier, Alain Amstutz, Benjamin Kasenda, Christiane Pauli-Magnus, Elena Ojeda-Ruiz, Yuki Tomonaga, Kimberly McCord, Alain Nordmann, [...].
a collaboration of the MARTA (MAKING Randomized Trials Affordable) and ASPIRE (Adherence to Standard Protocol Items: REcommendations for interventional trials) Study Groups 
[view all]





Journal of Clinical Epidemiology
Volume 176, December 2024, 111536



Original Research

Resource use and costs of investigator-sponsored randomized clinical trials in Switzerland, Germany, and the United Kingdom: a metaresearch study



[Alexandra Griessbach](#) ^a  , [Benjamin Speich](#) ^a, [Alain Amstutz](#) ^{a,b,c}, [Lena Hausheer](#) ^a, [Manuela Covino](#) ^a, [Hillary Wnfried Ramirez](#) ^{a,d}, [Stefan Schandelmaier](#) ^{a,e,f}, [Ala Taji Heravi](#) ^a, [Shaun Treweek](#) ^{d,g}, [Matthias Schwenkglenks](#) ^{h,i}, [Matthias Briel](#) ^{a,j}
MAKing Randomized Trials Affordable (MARTA) Group¹

Costs of randomised trials

Eligibility:

Completed randomized non-industry trials



Data Collection:

Contacted 775 investigators over three years

→ Costs from 93 RCTs collected

Cost CRF:

Previously tested cost item list → followed by **interviews** and detailed **cost report**

Total Trial Costs		
<ul style="list-style-type: none"> • Trial Budget • Trial Funding • Total trial costs • Total trial costs adjusted for employer contributions • Total trial costs adjusted for employer contributions and 30% unaccounted time • Total trial costs adjusted for employer contributions, 30% unaccounted time and overhead 		
Planning	Conduct	Finalization
Fixed Costs <ul style="list-style-type: none"> • Ethics Committee approval fees • Health authority fees • Other approval fees • Costs for Infrastructure and Equipment • Shipping costs • Insurance fees 	Fixed Costs <ul style="list-style-type: none"> • Advertisement • Costs of Intervention • Placebo manufacturing • Additional procedures and material • Patient reimbursement • Specimen analysis • AE/SAE/SUSAR material • Travel costs • Audits and Inspections 	Fixed Costs <ul style="list-style-type: none"> • Publication fees • Conference fees and costs
Variable Costs (in days) <ul style="list-style-type: none"> • Research protocol • Budget development • Grants and funding • Application EC, • Patient-related forms • Investigational brochure • Site-specific set-up Staff training • Acquiring study drug • Statistical analysis plan • Data management plan • Monitoring plan • Initial monitoring Visit • Biobank preparation • Communication funders and authorities • Communication involved sites • Communication other stakeholders • Communication patient representatives 	Variable Costs (in days or minutes) <ul style="list-style-type: none"> • Screening • Informed consent and patient specific documents • Randomization • Baseline visit • Treatment: intervention • Treatment: control • Sample processing/analysis • Source data and data entry AEs, SAEs and SUSARs • Follow-up/Endline visit(s): • Ongoing communication • Upkeep of documentation • staff training /re-training • Amendments • Audits/ inspections • statistical services • Data management • Monitoring - Upkeep of biobank 	Variable Costs (in days) <ul style="list-style-type: none"> • Data cleaning and database lock • Biospecimen storage/destruction • Statistical analyses • Final reporting • Manuscript • Other results dissemination

Costs of randomised trials

Included RCTs (n=93)

Single center:

50/93 (54%)

Median sample size (IQR):

167 (93-438)

Median Total Costs (IQR):

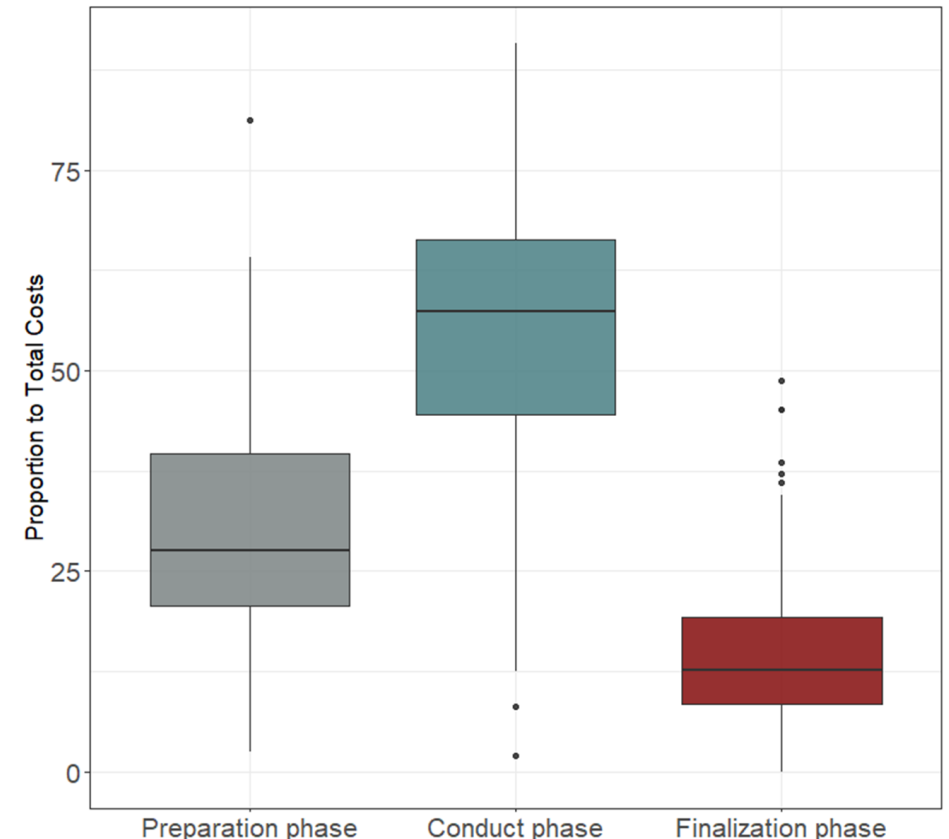
- **645'824 \$** (269'846 \$ to 1'577'924 \$)

Cost per Patient:

- **3,999 \$** (1,638 \$ to 6,658 \$)
- Comparable for Switzerland, Germany and the UK

Planned Budget vs. Actual Costs:

- **Two thirds (69.7%)** exceeded their original budget by **more than 50%**.



Median Costs USD
(median [IQR])

176'433 \$
[92'596 \$ - 424'916 \$]

313'234 \$
[103'990 \$ - 912'818 \$]

82'536 \$
[45'385 \$ - 167'744 \$]

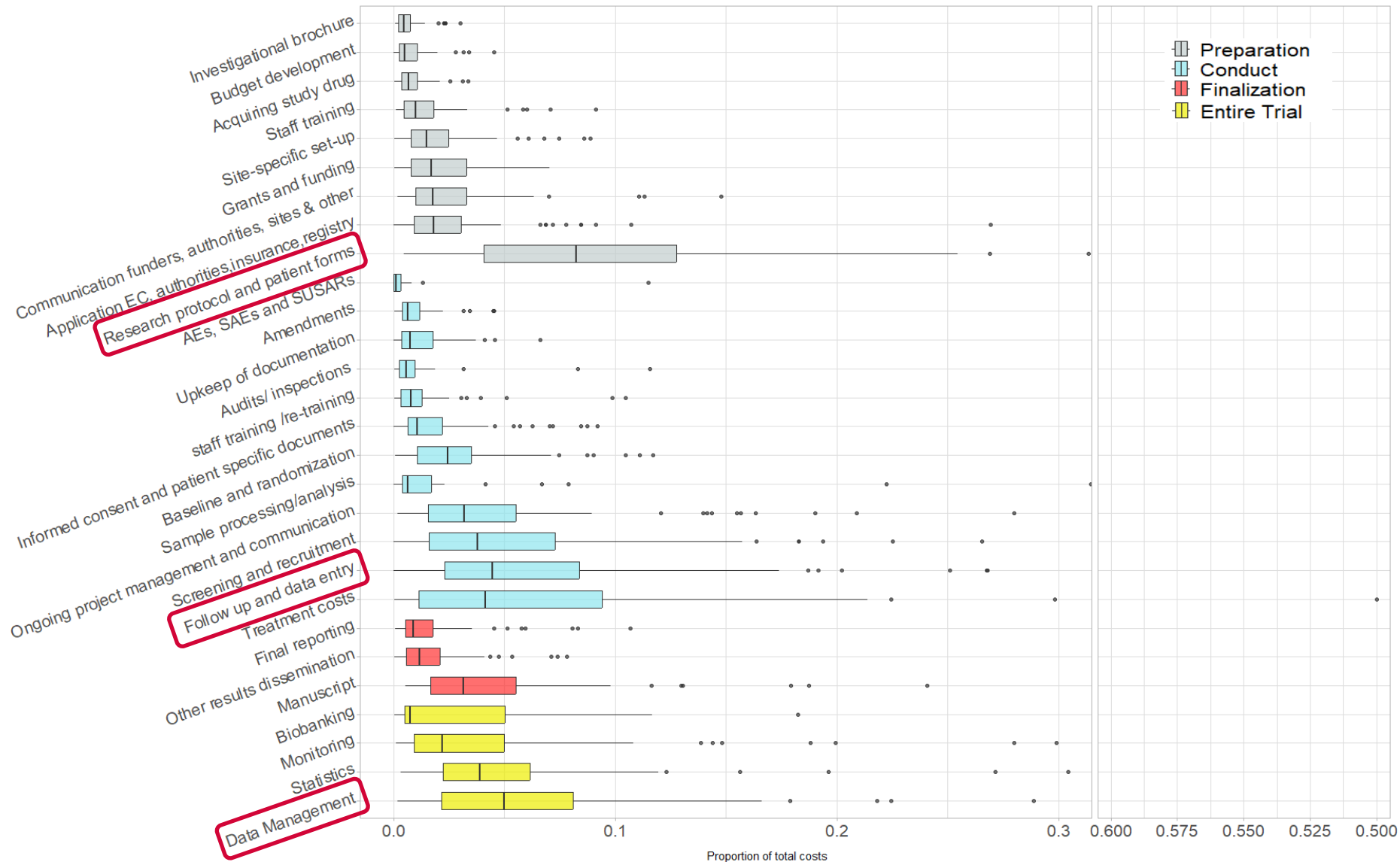
Median Proportion
of Total Costs

27.5%
(20.6% - 39.7%)

57.3%
(44.4% - 66.3%)

12.7%
(8.5% - 19.3%)

Costs of randomised trials



Most expensive items:

1.
Writing of the protocol and patient forms
(7.2%; IQR: 3.8% -10.9%)
2.
Data management
(5.0%; IQR: 3.8% -10.9%).
3.
Follow up
(4.5%; IQR: 2.3% to 8.4%)

Costs drivers & savers



Drug interventions and oncology trials were associated with **increased per patient costs**



Use of routinely collected data to assess primary outcomes was associated with **lower costs** both in **total and per patient**.

Results from multivariable regression


Limitations

- Potential **recall bias** (when inquiring about resource use)
- Only 12% of 775 contacted PIs shared costs (bias towards **more successful, smaller, low-cost trials**)
- **Sample too small** to provide precise estimates for small subgroups (medical fields, pilot trials, trials with routinely collected data)



Methodology | [Open access](#) | Published: 12 March 2024

Trial Forge Guidance 4: a guideline for reporting the results of randomised Studies Within A Trial (SWATs)

[C. E. Arundel](#) , [L. K. Clark](#), [A. Parker](#), [D. Beard](#), [E. Coleman](#), [C. Cooper](#), [D. Devane](#), [S. Eldridge](#), [S. Galvin](#), [K. Gillies](#), [C. E. Hewitt](#), [C. Sutton](#), [D. J. Torgerson](#), [S. Treweek](#) on behalf of the PROMETHEUS GROUP

[Trials](#) **25**, Article number: 183 (2024) | [Cite this article](#)

Reporting Item 17c

Costs associated with the SWAT.

Example: *The total cost of the SWAT was [insert cost], which equates to [insert cost] per participant.*

Why do we not have this level of transparency at trial level?

→ CONSORT statement ?

Hurdles

Hurdles

RESEARCH

Open Access



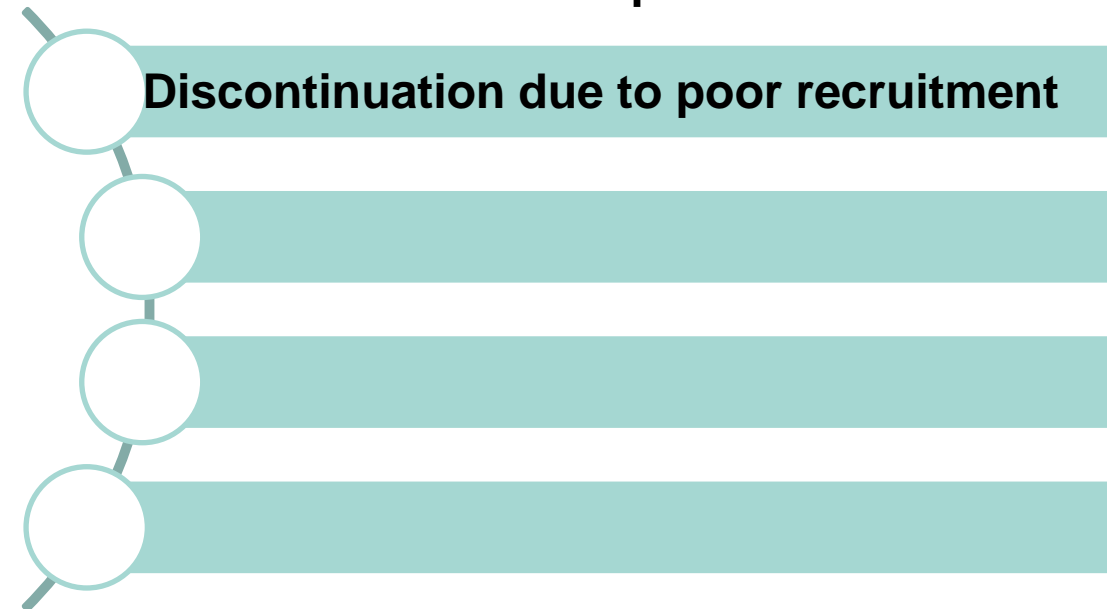
What are the main inefficiencies in trial conduct: a survey of UKCRC registered clinical trials units in the UK

Lelia Duley^{1*}, Alexa Gillman², Marian Duggan³, Stephanie Belson⁴, Jill Knox⁵, Alison McDonald⁶, Charlotte Rawcliffe⁷, Joanne Simon⁸, Tim Sprosen⁹, Jude Watson¹⁰ and Wendy Wood¹¹

Planning phase



Conduct phase





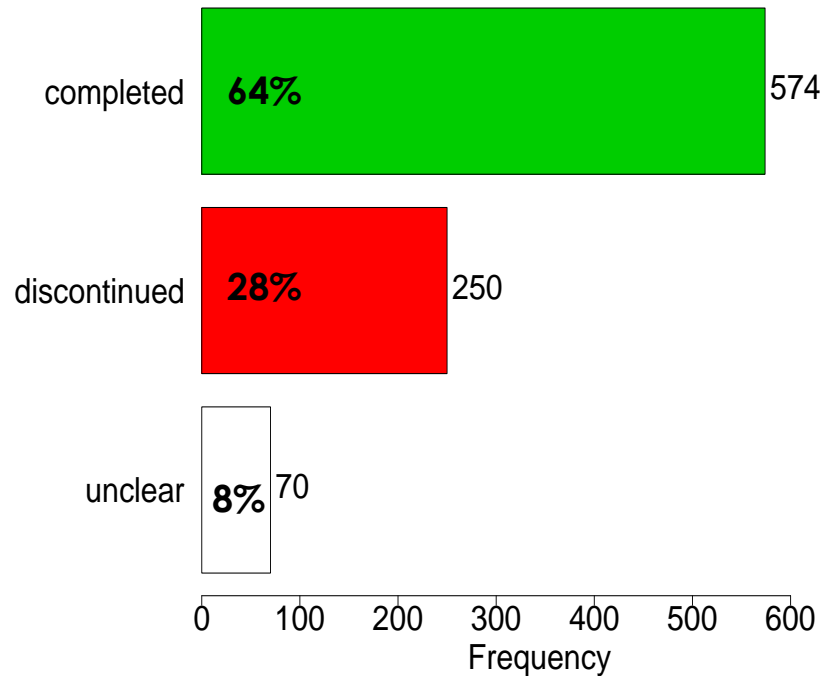
DISCO

DISCO I - RCTs with ethical approval 2000-2003



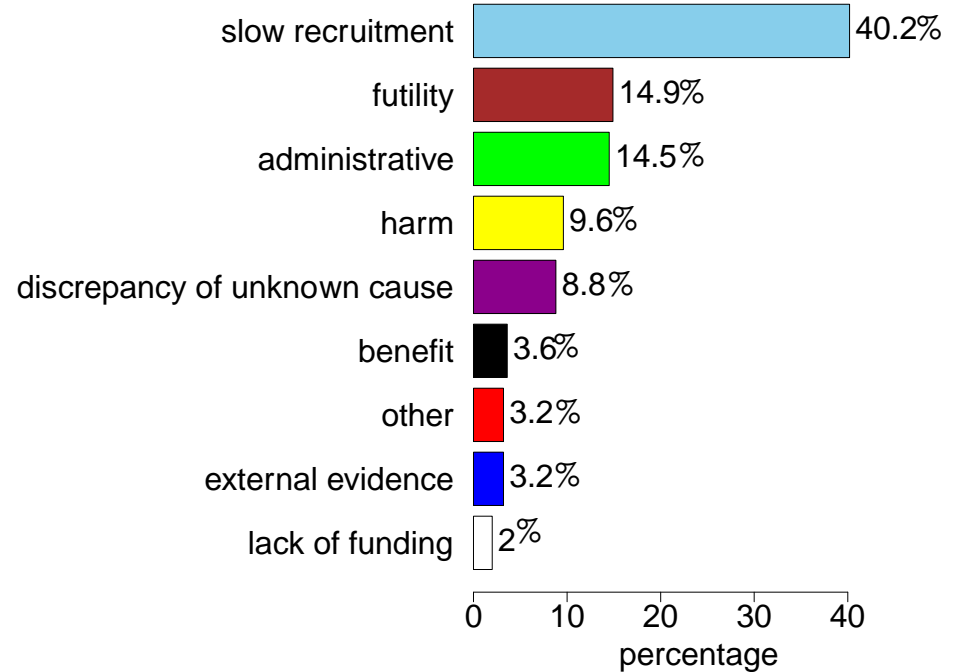
N=894

Completion Status



N=250

Reasons for discontinuation



- **Non-industry RCTs stronger affected by poor recruitment than industry-initiated**
- **Overall only 59% of RCT results published**

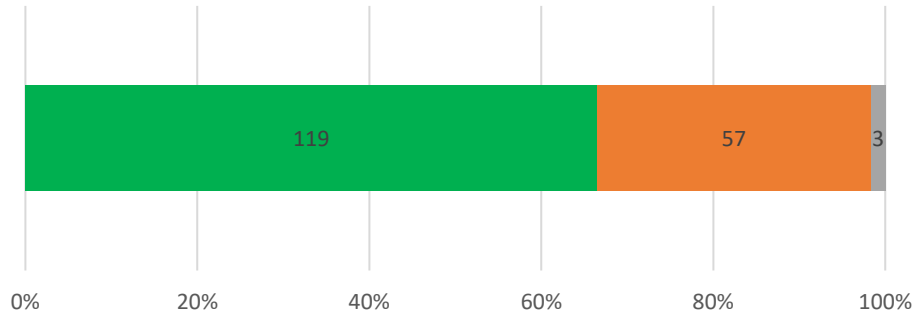
DISCO II and III - RCTs with ethical approval in 2012 and 2016



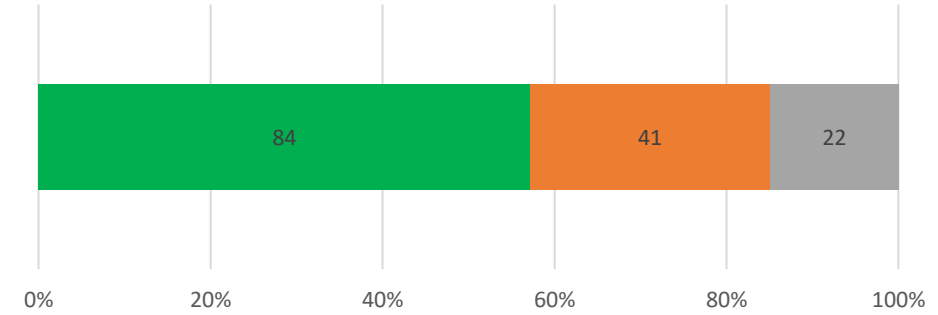
Industry-sponsored

Non-industry-sponsored

2012

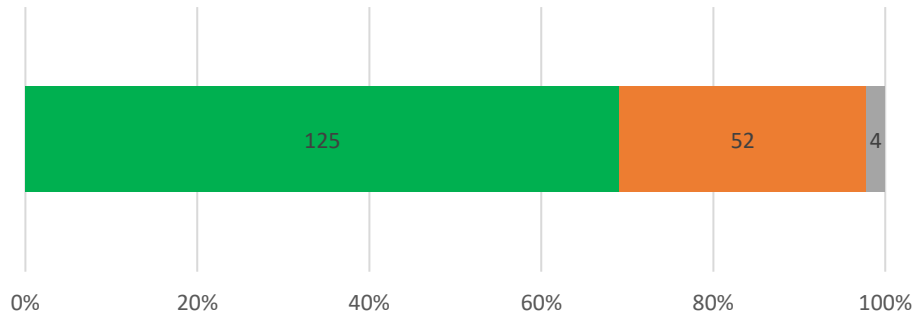


32% (57/179) Discontinued

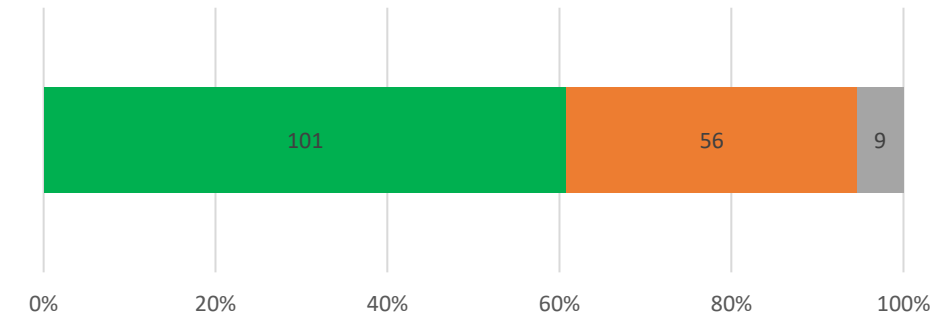


28% (41/147) Discontinued

2016



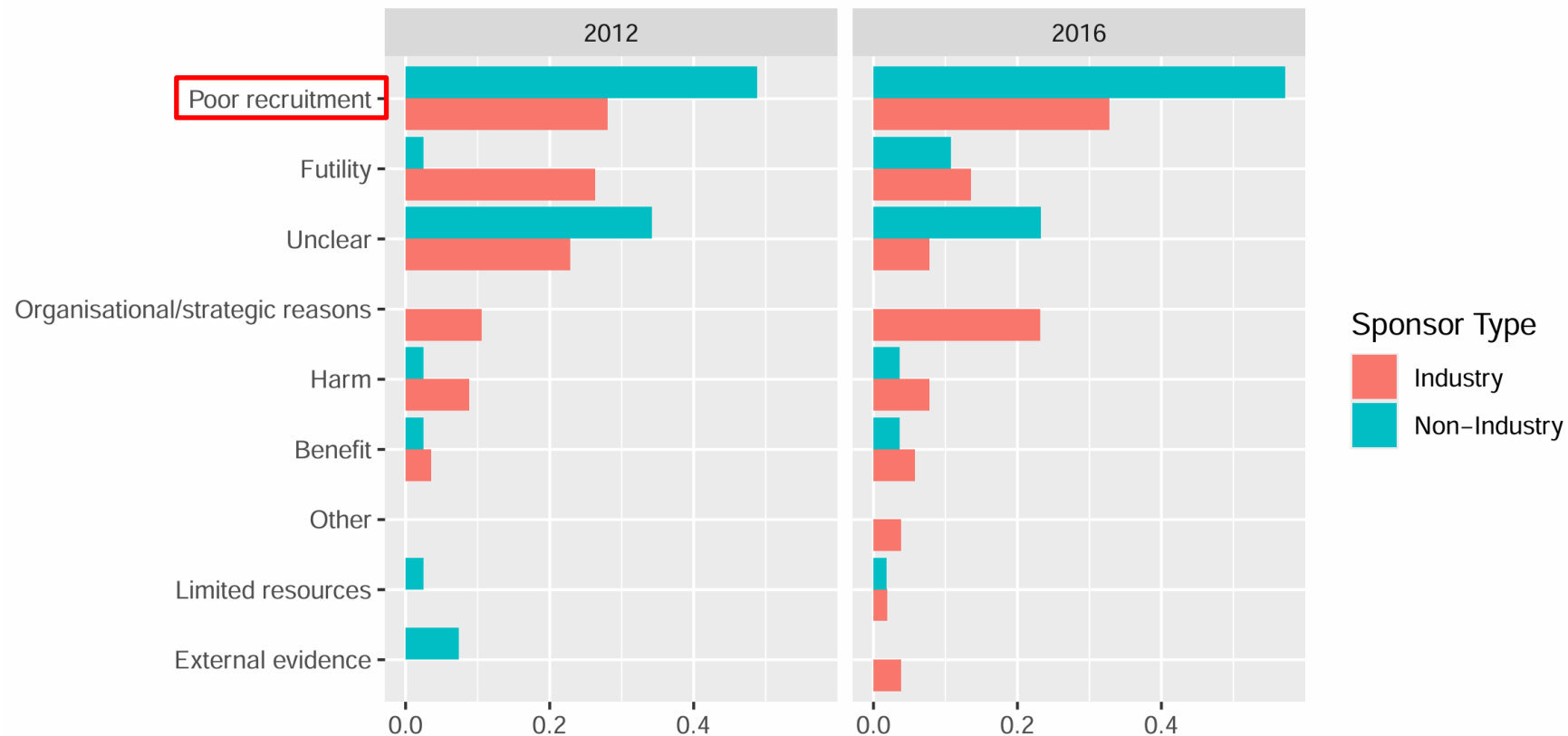
29% (52/181) Discontinued



34% (56/166) Discontinued

■ Completed
 ■ Discontinued
 ■ Unclear

Reasons for Discontinuation



- **Discontinuation: DISCO I: 28% vs DISCO II: 30% vs DISCO III: 31%**

→ **No improvement**

- **Non-availability of results: DISCO I: 41% vs DISCO II: 18% vs DISCO III: 20%**

→ **Improvement compared to DISCO I**

Hurdles

RESEARCH

Open Access



What are the main inefficiencies in trial conduct: a survey of UKCRC registered clinical trials units in the UK

Lelia Duley^{1*}, Alexa Gillman², Marian Duggan³, Stephanie Belson⁴, Jill Knox⁵, Alison McDonald⁶, Charlotte Rawcliffe⁷, Joanne Simon⁸, Tim Sprosen⁹, Jude Watson¹⁰ and Wendy Wood¹¹

REGULATIONS

Planning phase

Conduct phase

Permissions and approvals

Contracts

Study design and document development

Discontinuation due to poor recruitment

Implementation of amendments

Regulations

RESEARCH ARTICLE

Open Access

Bureaucracy stifles medical research in Britain: a tale of three trials

Helen Snooks^{1*}, Hayley Hutchings¹, Anne Seagrove¹, Sarah Stewart-Brown², John Williams¹ and Ian Russell¹

the **bmj** opinion

Latest

Authors ▾

Topics ▾

Bureaucracy is hampering the success of clinical research

January 13, 2020

Reducing Bureaucracy in Clinical Research: A Call for Action

By John Gribben¹, Elizabeth Macintyre², Pieter Sonneveld³, Jeanette Doorduijn³, Christian Gisselbrecht⁴, Ulrich Jäger⁵, Steven Le Gouil⁶, Simon Rule⁷, Martin Dreyling⁸

Correspondence: Martin Dreyling (e-mail: Martin.Dreyling@med.uni-muenchen.de).

Clinical Trials 2006; 3: 496–502

ARTICLE **CLINICAL TRIALS**

Clinical trials bureaucracy: unintended consequences of well-intentioned policy


Robert M Califf

**RMD
Open**

Rheumatic &
Musculoskeletal
Diseases

LETTER

Reducing bureaucracy in clinical trials, now is the time!

Loreto Carmona 

Regulations

[Home](#) | [JAMA](#) | [Vol. 311, No. 15](#)

Viewpoint

Ethics, Regulation, and Comparative Effectiveness Research Time for a Change

Richard Platt, MD, MS¹; Nancy E. Kass, ScD²; Deven McGraw, JD, LLM, MPH³

[» Author Affiliations](#) | [Article Information](#)

 RELATED ARTICLES

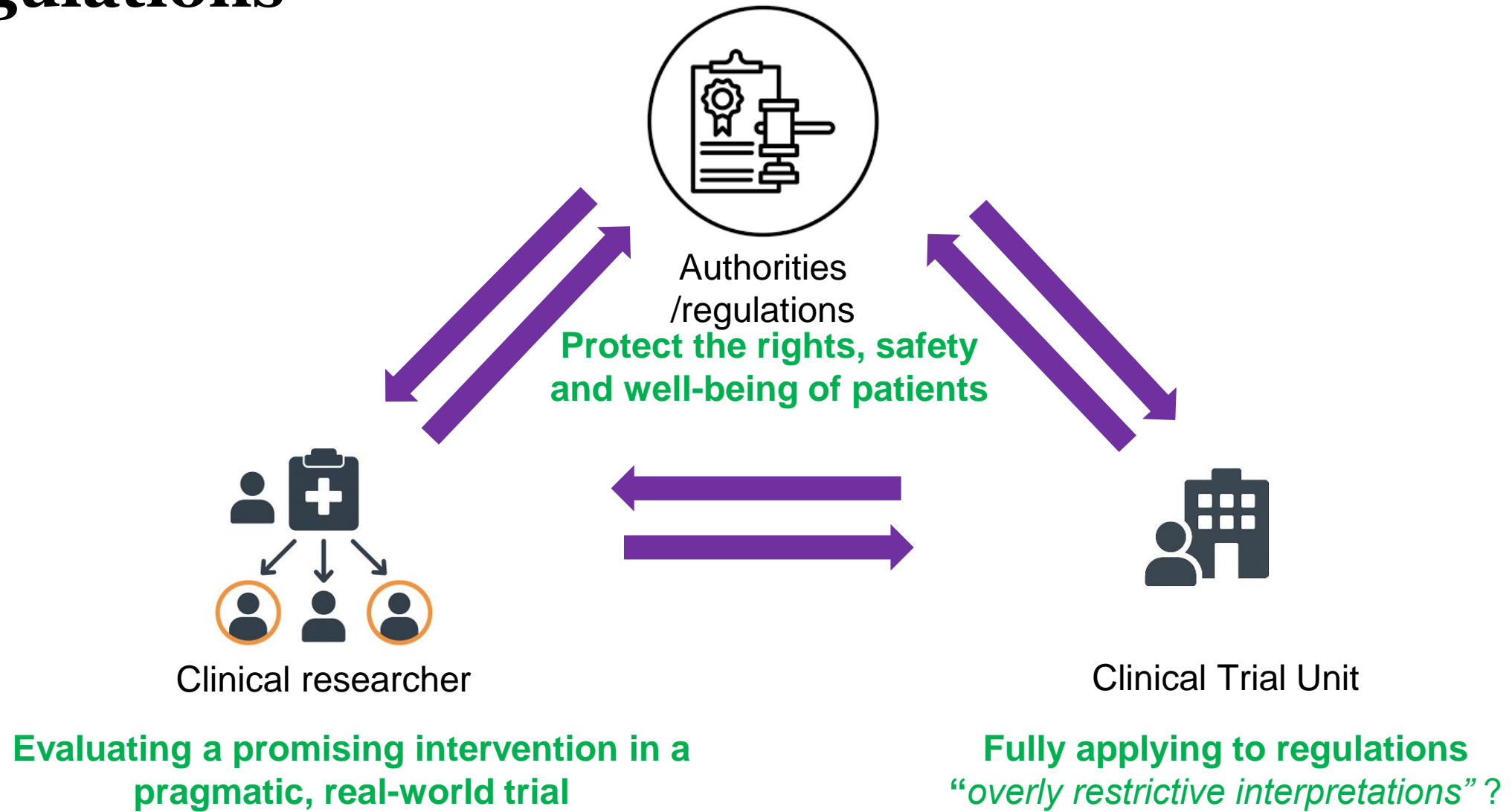
Recommendations Within Current Regulatory Regimens

Policies regulating clinical research **should consider whether studies pose greater risks and burdens to patients than they would encounter in usual clinical care**, both with respect to the intervention being studied and to patients' other interests, including the privacy, security, and confidentiality of health information. Addressing this issue will require revisions to current federal regulations, but in the shorter term, the following recommendations would be welcome.

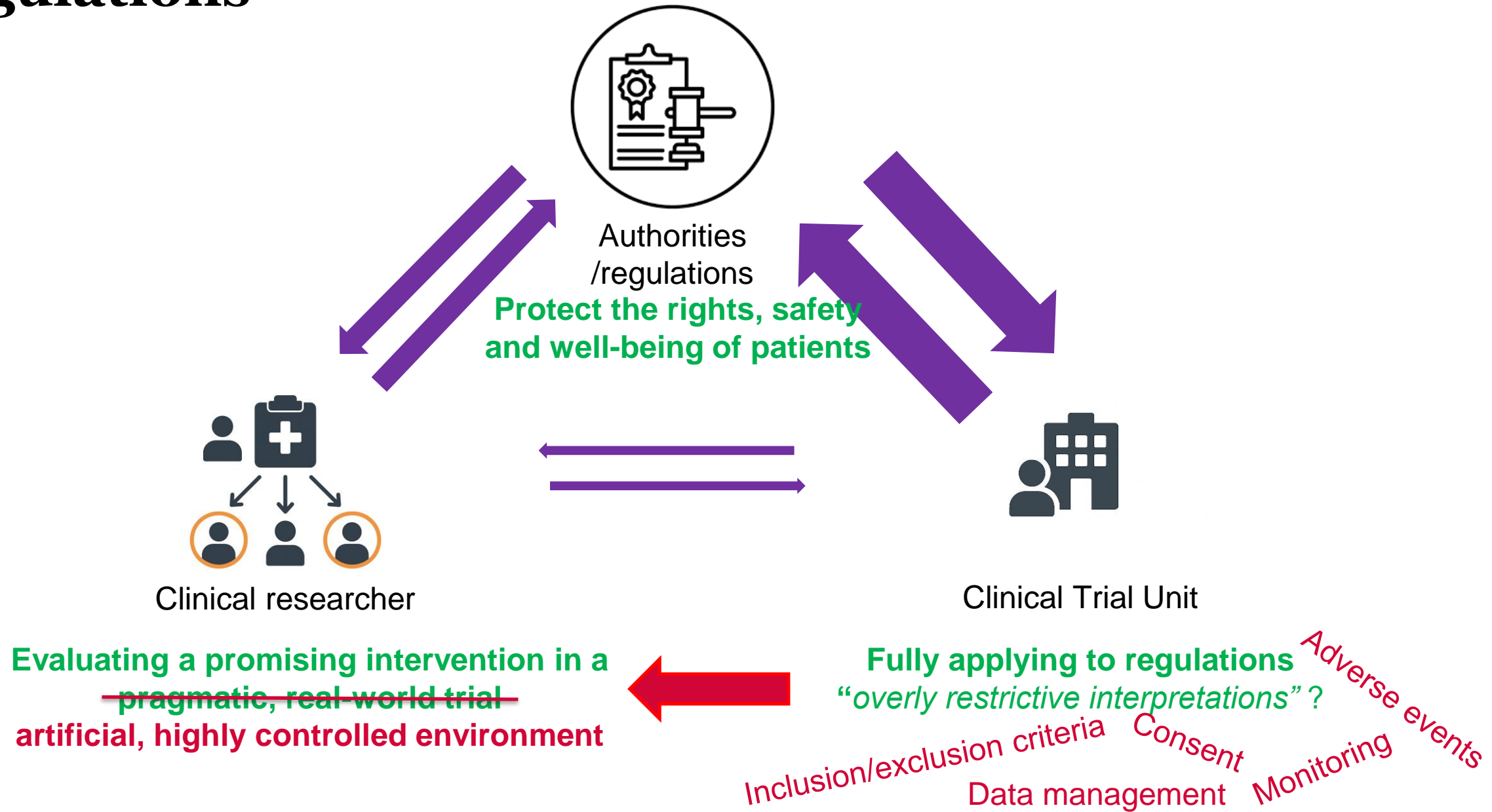
“Guidance

Some barriers to research in the name of ethical protection result from misinterpretations or overly restrictive interpretations of regulations.”

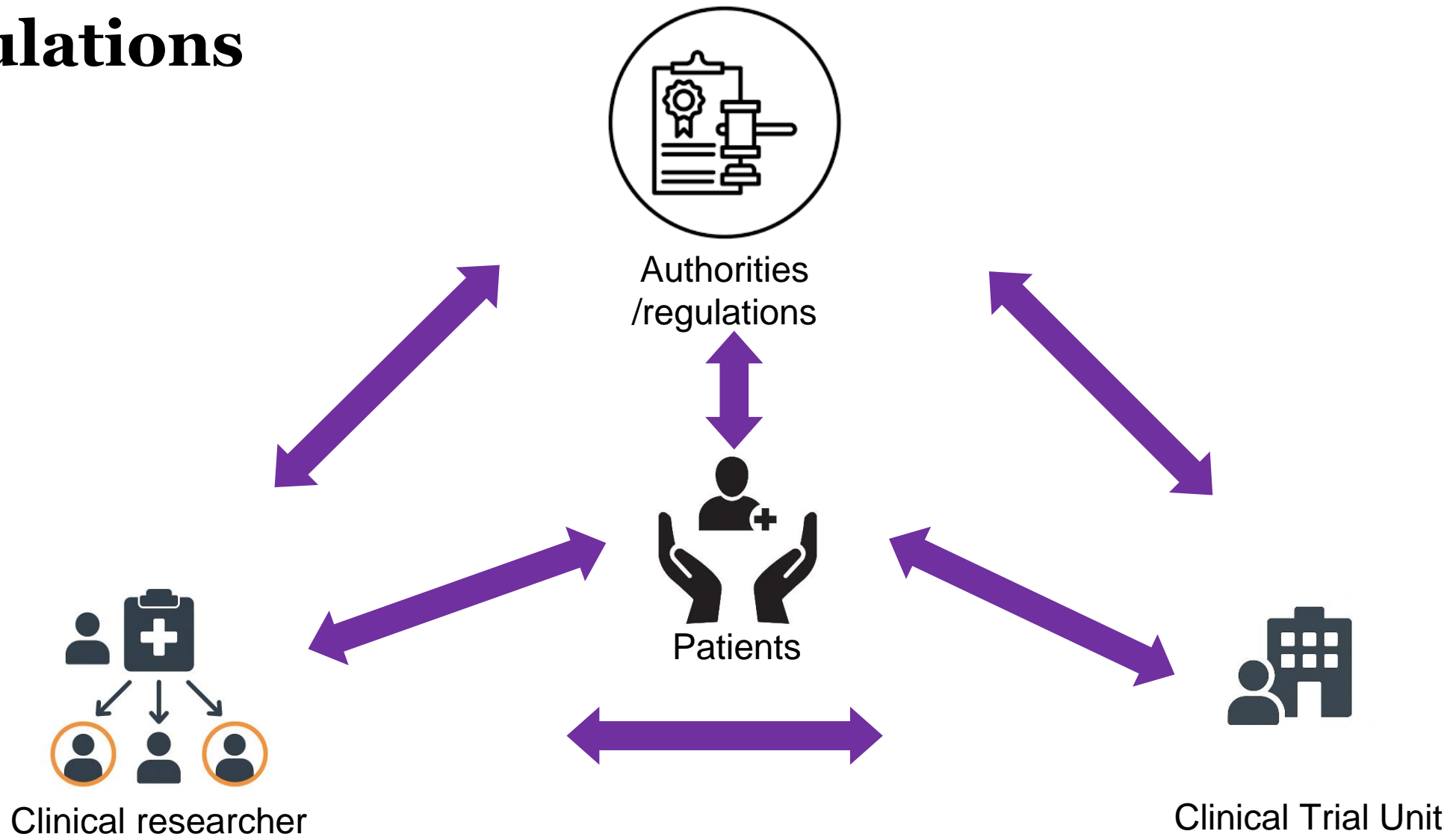
Regulations



Regulations



Regulations



Exchange and Guidance needed

“Some barriers to research in the name of ethical protection result from misinterpretations or overly restrictive interpretations of regulations.”

Hurdles

RESEARCH

Open Access



What are the main inefficiencies in trial conduct: a survey of UKCRC registered clinical trials units in the UK

Lelia Duley^{1*}, Alexa Gillman², Marian Duggan³, Stephanie Belson⁴, Jill Knox⁵, Alison McDonald⁶, Charlotte Rawcliffe⁷, Joanne Simon⁸, Tim Sprosen⁹, Jude Watson¹⁰ and Wendy Wood¹¹

Planning phase

Permissions and approvals

Contracts

Study design and document development

Recruitment of staff

...issues with study drug

Conduct phase

Discontinuation due to poor recruitment

Implementation of amendments

Data management (incl. CRF design)

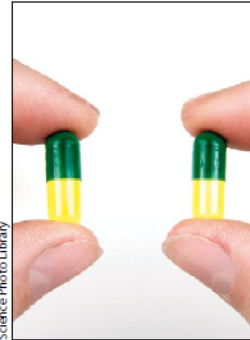
Preparation and submission of publication

Unobtainable Placebo

EDITORIALS

Products at Risk

Gregory D. Curfman, M.D., Stephen Morrissey, Ph.D., and Jeffrey M. Drazen, M.D.



Science Photo Library

The unobtainable placebo: control of independent clinical research by industry?

Independent researchers might end up compromising—or even abandoning—their research design because of the unwillingness of some pharmaceutical companies to deliver placebo drugs or devices. We believe that this could be a major way for the pharmaceutical industry to control scientific information about their drugs.



In this issue of the *Journal*, we publish the results of a clinical trial investigating step-up control in adult patients with asthma whose disease was not well controlled by low-dose inhaled glucocorti-

SmithKline has supported past ACRN studies, and we hope that they will in the future.

Many drug companies realize that it is in their best interest to provide these materials, not only

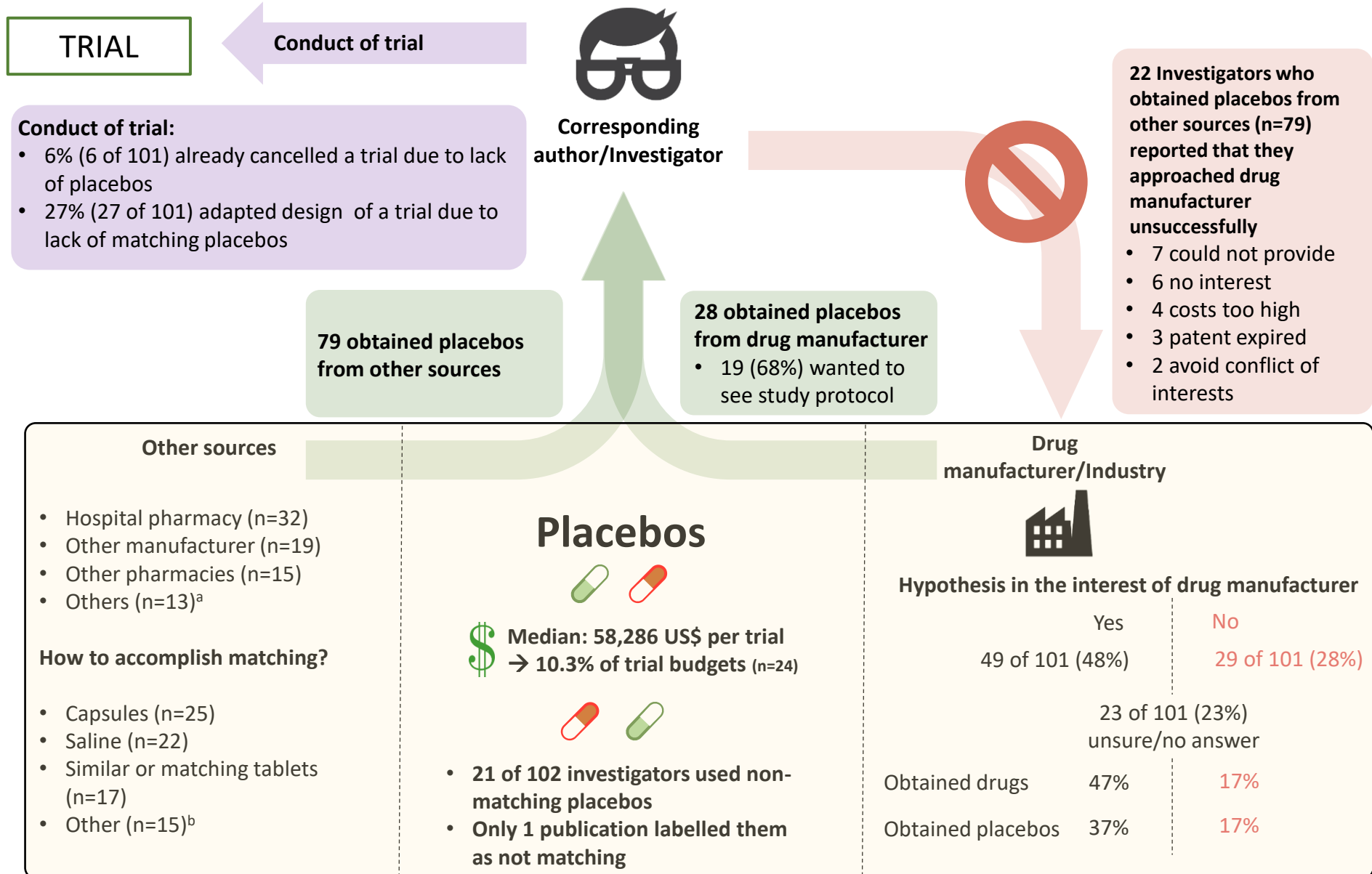
LETTER: An update on changes to the design of the ODIN trial

Sigrid Sandner^{1,2}, MD, MSCE; Björn Redfors³⁻⁵, MD, PhD; Marc Ruel⁶, MD, MPH; Mario Gaudino^{2*}, MD, PhD, MSCE

*Corresponding author: Department of Cardiothoracic Surgery, Weill Cornell Medicine, 525 E 68th St, New York, NY 10065, USA. Email: mfg9004@med.cornell.edu

- Pharmaceutical company...
 - ...only agreed to provide the placebo if the trial protocol was changed following their review
 - ...“charged an extraordinary amount of money for providing a simple placebo tablet”
 - ...refused to provide placebos

Unobtainable Placebo



Innovations

1. Hierarchical Composite Endpoints

Resources limited (e.g. money; # patients) to design the ideal trial

Traditional Composite Endpoint: Combine endpoints of interest to observe more events → smaller sample size needed



Pitfall:

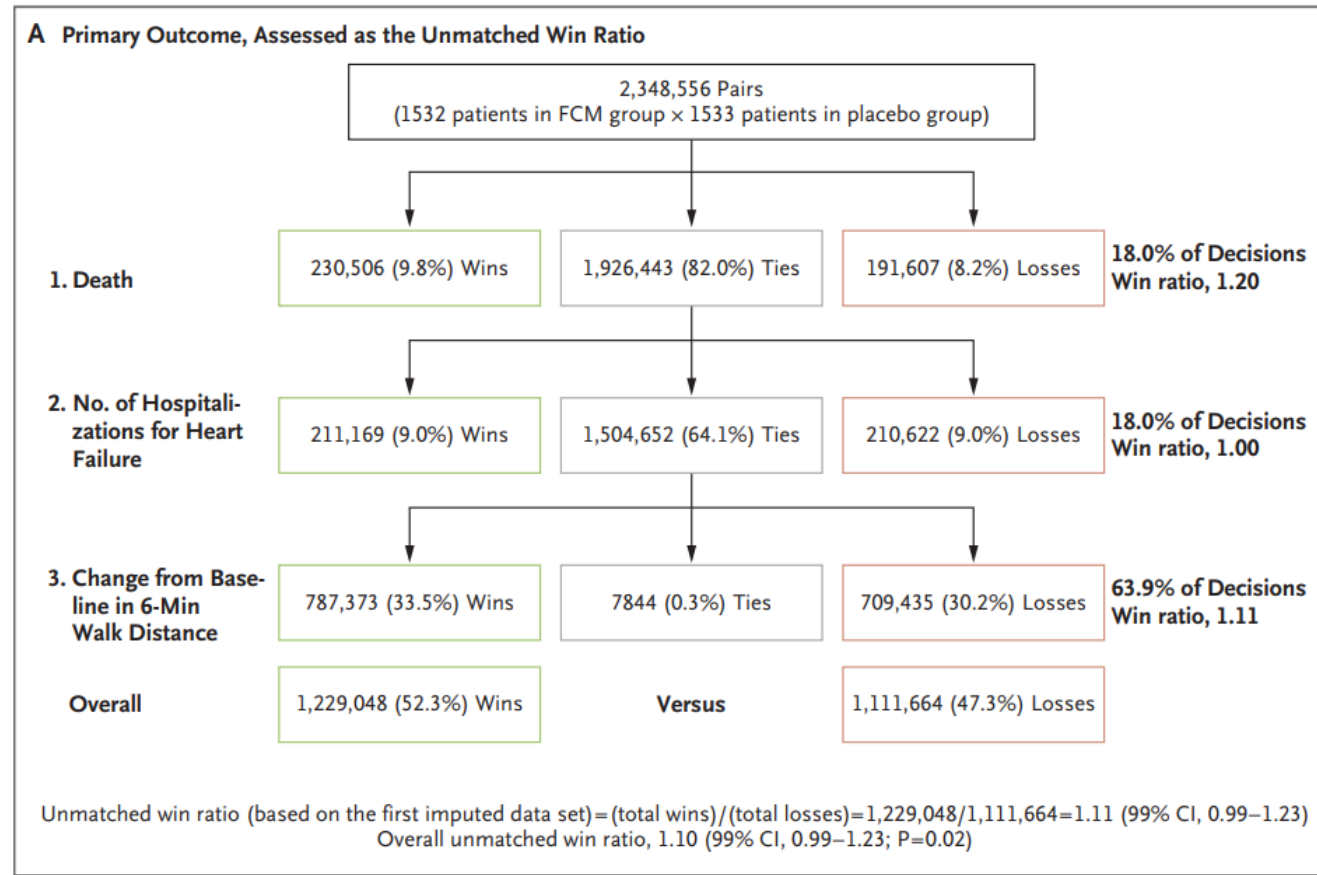
- Treating events of different importance equally
- Effects might go in different directions (e.g. fewer participants in the control group are hospitalized because more participants died and could therefore not reach the endpoint)



Hierarchical Composite Endpoints

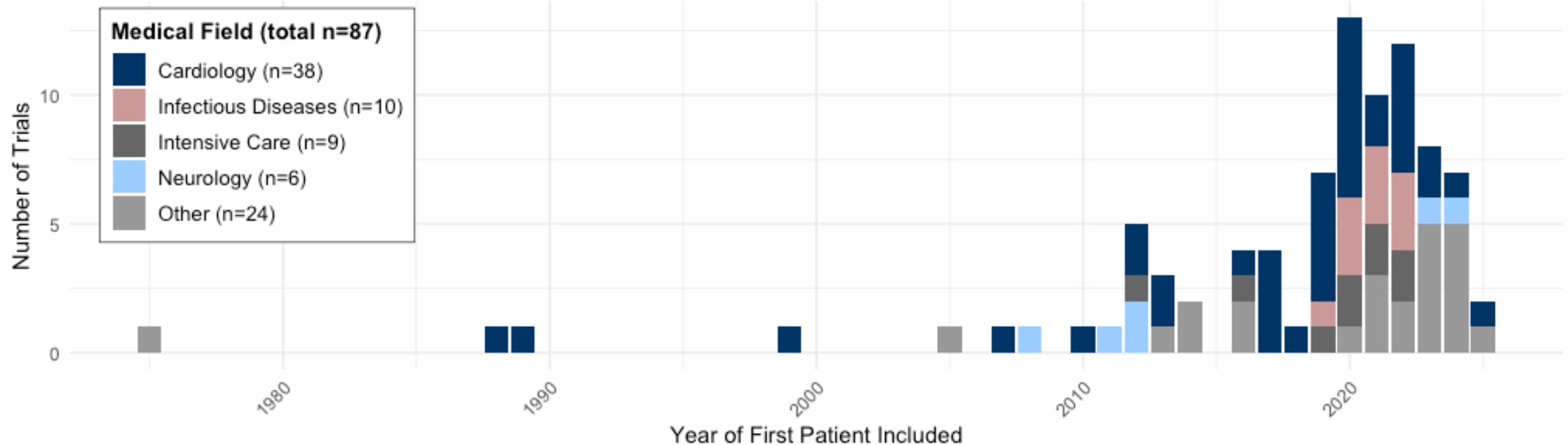
Hierarchical Composite endpoint:

Components are arranged hierarchically, giving the most important event the highest priority!



Hierarchical Composite Endpoints

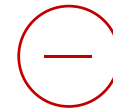
Systematic scoping review on RCTs using a hierarchical composite endpoint as the primary outcome



- 2-7 components (majority 2-4)
- Highest component of HCE: Mortality (80%)
- Last component of HCE: Continuous (65%)
- Majority did not mention how hierarchy was established (78%)

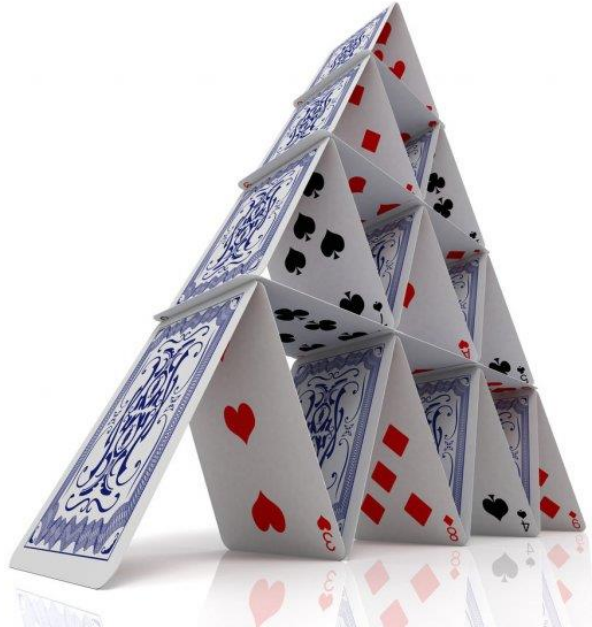


- Better than traditional composite
- Better reflects overall health
- Increased power

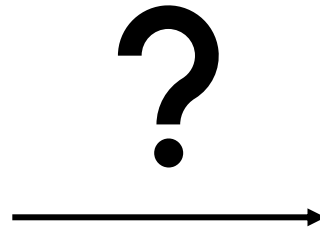


- Interpretation of effect size difficult
- Adjustment in analysis not possible

2. Platform trials



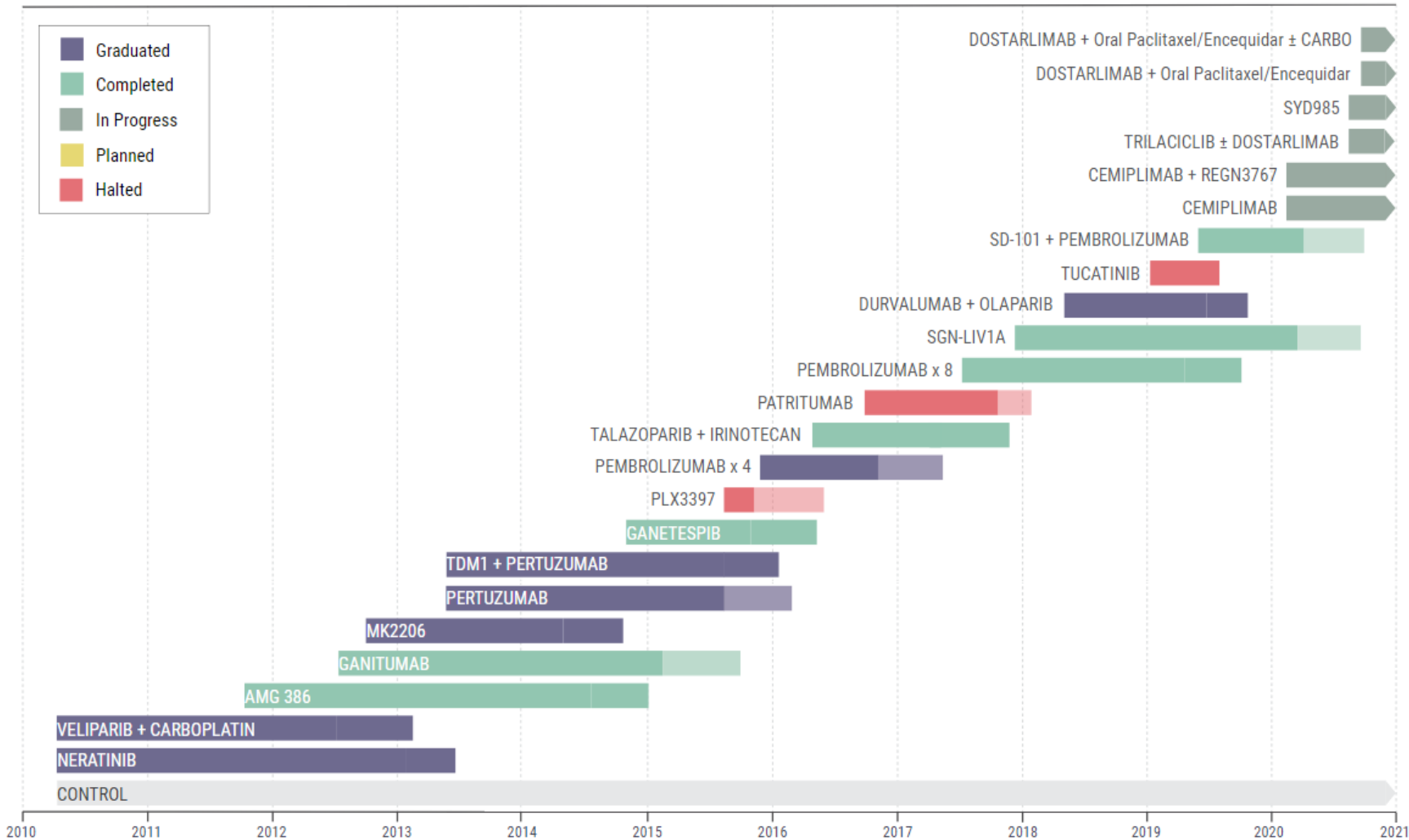
Classic RCT



Platform trial

Definition: *“Platform trials study multiple interventions in a single disease (or condition) [...], with interventions allowed to enter or leave the platform [...].”*¹

Platform trials



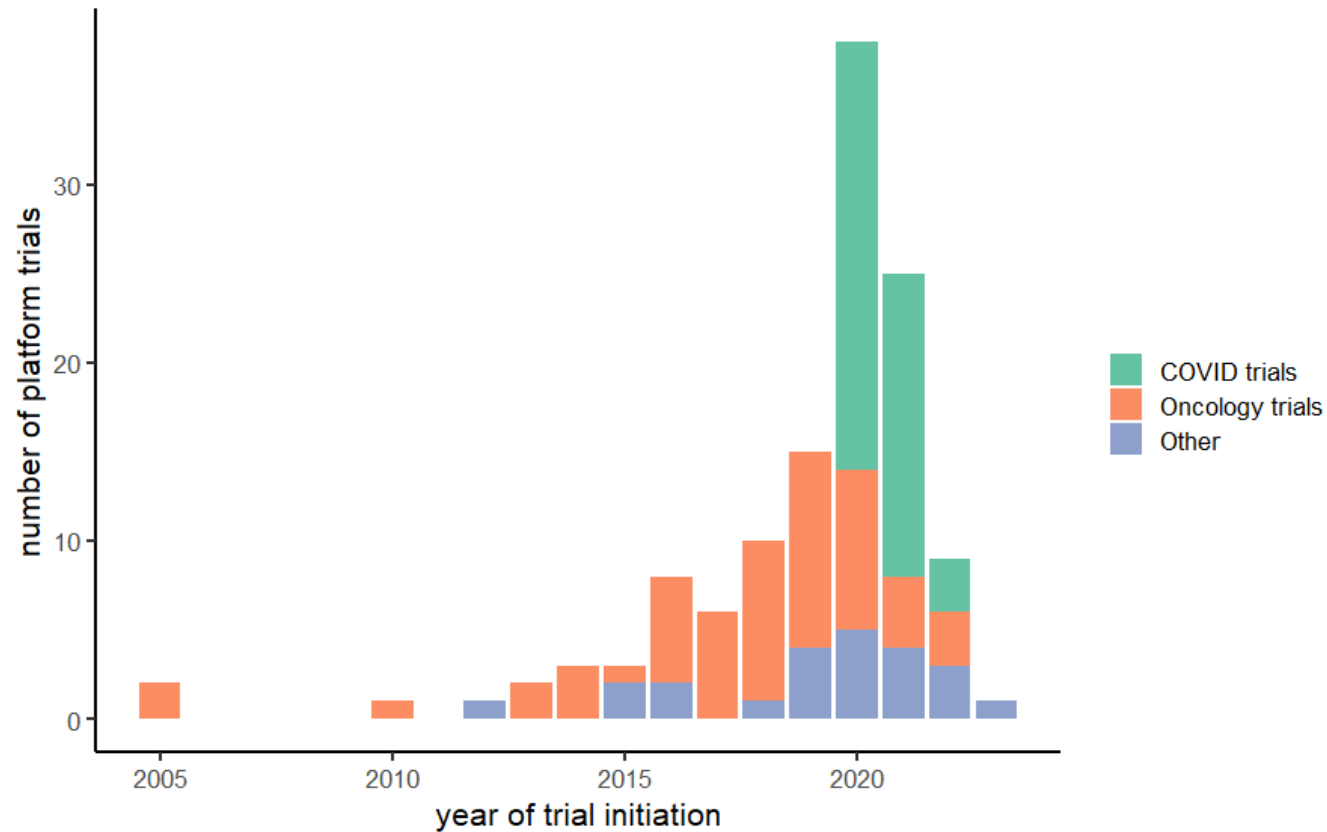
Example:

I-SPY 2 Trial

Neoadjuvant treatment for locally advanced breast cancer

Platform trials

Systematic overview of all platform trials (n=127)

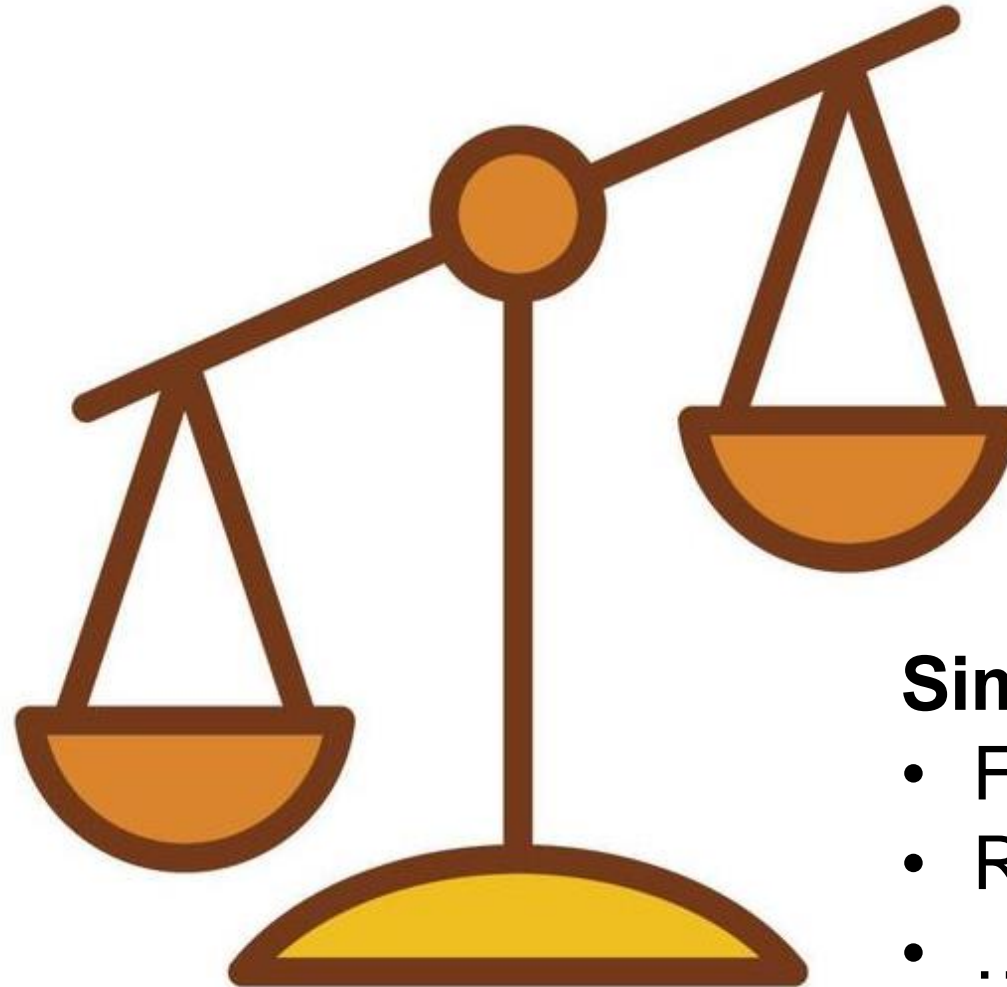


- ~40% never added a new treatment arm
- High operational complexity
- Careful consideration if platform trial is the best design
- Might be the preferred design for rapid, multi-intervention evidence generation (e.g., pandemics, evolving therapies)

Smarter Science

Innovations

- Platform trials
- HCE
- TwiCs
- ...



Simpler trials

- Fewer regulatory hurdles
- Risk based regulations
- ...

Thank you for your attention!