

# How to make a randomised trial informative, relevant, and useful

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# Let's start with a conclusion

'Most randomised trials are bad and most trial participants will be in one. The research community has tolerated this for decades.'

Pirosca et al. *Trials* (2022) 23:458  
<https://doi.org/10.1186/s13063-022-06415-5>

Trials

COMMENTARY

Open Access

## Tolerating bad health research: the continuing scandal

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<https://doi.org/10.1186/s13063-022-06415-5>

### Abstract

**Background:** At the 2015 REWARD/EQUATOR conference on research waste, the late Doug Altman revealed that his only regret about his 1994 *BMJ* paper 'The scandal of poor medical research' was that he used the word 'poor' rather than 'bad'. But how much research is bad? And what would improve things?

**Main text:** We focus on randomised trials and look at scale, participants and cost. We randomly selected up to two

# A cohort of trials

- Used Cochrane systematic reviews published between May 2020 and April 2021.
- Randomly selected two reviews from across all Cochrane groups.
- Look at every trial included in those reviews.
- We called high risk of bias trials Bad, low risk Good and uncertain, er, Uncertain. Or Ugly.



# The Good



**133 (8%)**

# The Bad



**1013 (62%)**

# The Ugly



**494 (30%)**



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# Money

Using the low and high estimates, these high risk of bias trials spent..

..between £726 million and £8 billion  
(roughly 9 billion SEK to 101 billion SEK)

This would fund the UK's NIHR Health Technology Assessment programme for between just under a decade or just over a century.



# Gates Foundation

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# INFORM

Based around the Zarin *et al* informativeness framework (<https://jamanetwork.com/journals/jama/article-abstract/2740057>):

- 1.Importance – the trial question
- 2.Design – the trial methods
- 3.Feasibility – the trial is likely to be feasible
- 4.Integrity – the trial is conducted and analysed in a scientifically valid manner
- 5.Reporting – the trial must full report methods and results



# Improving trial informativeness: the plan

1. A rapid review of global literature: what have others done or said?
2. A content review: what do e.g., funders ask researchers to do?
3. A global interview study: what do people think?
4. Map what should be done, what is being done, what works and where are the gaps?
5. Package everything



# The rapid review: published

*Journal of Evaluation in Clinical Practice*

WILEY



REVIEW ARTICLE **OPEN ACCESS**

## Improving Trial Informativeness: A Rapid Review of Global Research on How to Ensure Trials Are Useful

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### ABSTRACT

**Rationale:** Randomised controlled trials are considered the ‘gold standard’ in clinical research and decision-making. However, many trials have significant flaws that current review processes fail to identify early enough for corrections to be made. Flaws in trial design, conduct and reporting ultimately lead to research waste. This rapid review provides insights from global research aimed at improving trial ‘informativeness’ as described by Zarin and colleagues.

**Methods:** A rapid review was conducted with a focus on research addressing trial design processes that might improve informativeness aligned with one or more of the five key conditions outlined by Zarin and colleagues: 1) Importance, 2) Design, 3) Feasibility, 4) Integrity and 5) Reporting. A further thematic analysis was conducted using NVivo 12.

**Results:** The final review includes 42 texts. Of the 27 recommended processes or actions to improve trial informativeness, most were relevant to the second condition of trial design (2) Design: 44%. A key recommendation was the use of ‘tools’ to enhance



<https://onlinelibrary.wiley.com/doi/10.1111/jep.70147>



# The content analysis: under review



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## Do Funders, Regulators, and Ethics Bodies Support Informative Trials? A Content Analysis of Global Guidance Documents

23 Pages • Posted: 8 Aug 2025

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[https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=5383112](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=5383112)



# The interview study: close to submission

<b>Participants</b>		
<b>Trial role</b>	<b>N (=55)</b>	<b>%</b>
Investigator	21	38.2%
Funder	12	21.8%
Ethics	6	10.9%
Regulator/standards	4	7.3%
Industry	4	7.3%
Contract research organisation	3	5.5%
Operations	1	1.8%
Sponsor	1	1.8%



# The interview study: countries

Country	N	%		Country	N	%
USA	12	21.8%		France	2	3.6%
UK	11	20.0%		India	2	3.6%
South Africa	5	9.1%		Norway	2	3.6%
Australia	3	5.5%		The Netherlands	2	3.6%
Canada	3	5.5%		Nigeria	1	1.8%
Ireland	3	5.5%		Germany	1	1.8%
Kenya	3	5.5%		Ethiopia	1	1.8%
Switzerland	3	5.5%		Italy	1	1.8%



# 55 people said many things: here one quote

“If I had to pick one [something to improve], it would be really honing down on **asking applicants to provide a compelling case for how they will recruit, target, and retain the participants**, because without that it doesn't matter how valid the methods are, how great the question is, nothing informative will come of that.”

Investigator, Canada, Late 40s, Male, Chinese



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# So, what did we find?

- Many of the same things came up across all three studies.
- The **rapid review had 27 recommended actions**, 13 (48%) on *Design*. **Content analysis had 34**, 11 (32%) on *Design*. **Interviews had 24**, 10 (42%) on *Design*. *Importance* also mentioned a lot in interviews.
- *Feasibility* was only 3/27 actions in the literature review, and wasn't mentioned much in the content analysis. It was mentioned in interviews.
- There were differences between industry and academia in the interviews for *Importance*.



# It's complicated but..

..we think\* this boils down to 12 things grouped into three areas  
*Design, Conduct and Knowledge mobilisation.*

Everyone connected with trials needs to do something. For now we're thinking of these as actions for good practice.

\*For now. We might combine a couple.



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# Design

1. **Set research priorities** [funder/investigator/regulator].
2. **Engage patients and communities early** [funder/investigator/patient].
3. **Use design tools** [funder/investigator].
4. **Ensure accountability for robust designs**, including multidisciplinary teams with statistical expertise [funder/investigator].
5. **Have pre-funding scientific assessment** and regulatory consultation [funder/investigator/regulator].
6. **Apply quality-by-design to critical determinants of quality** [funder/investigator]



# Conduct

- 7. Use future-proofing measures** [funder/investigator].
- 8. Assess feasibility** and integrate qualitative evidence of lived experience into process design [funder/investigator/healthcare staff].
- 9. Provide continual training** beyond Good Clinical Practice [funder/investigator/professional bodies].
- 10. Have oversight throughout trial lifetime**, [funder/investigator/ethical approval/oversight committee].



# Knowledge mobilisation

- 11. Ensure trial registration, and that complete results are published** in timely way [funder/investigator/regulator].
- 12. Disseminate findings in accessible, inclusive formats,** mobilise knowledge to support equity and uptake into policy and practice [funder/investigator/policymaker/patient].



# Conclusions

- How to make trials more informative is not a mystery. We know how to make them better, and who has a role to play.
- The challenge is implementation and how to stop doing things that are likely to lead to bad trials.
- We think INFORM will help to stop bad trials, and help to ensure that more are good.





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