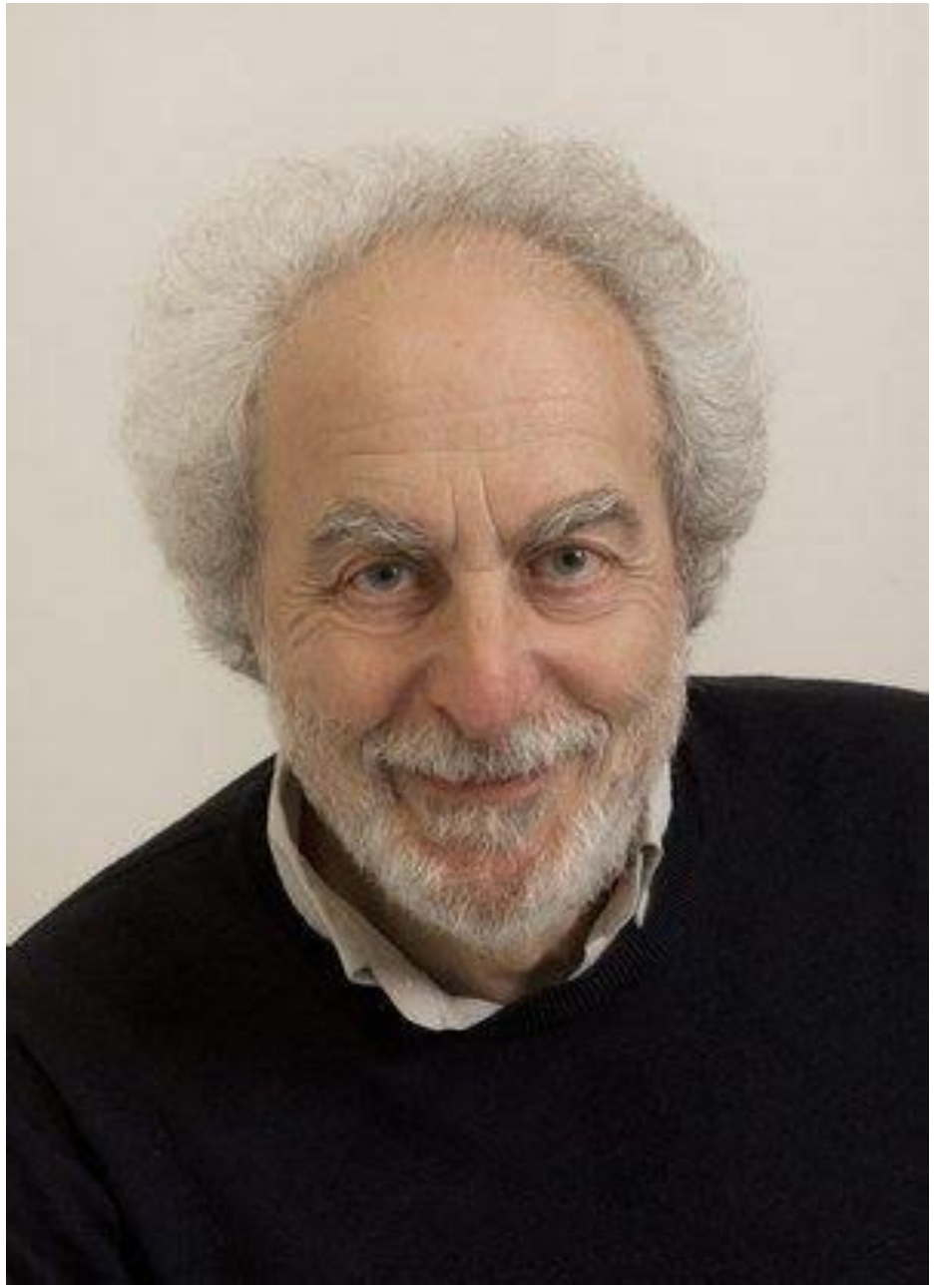
Trialblazers: Putting patients in the driving seat of trial design

Caroline Struthers
UK EQUATOR Centre

equator network

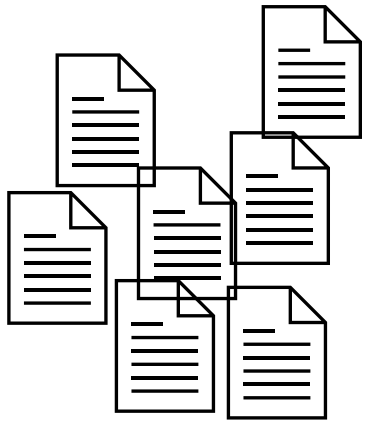
UNIVERSITY OF OXFORD



We need less research, better research, and research done for the right reasons

Doug Altman 1994

Less research?

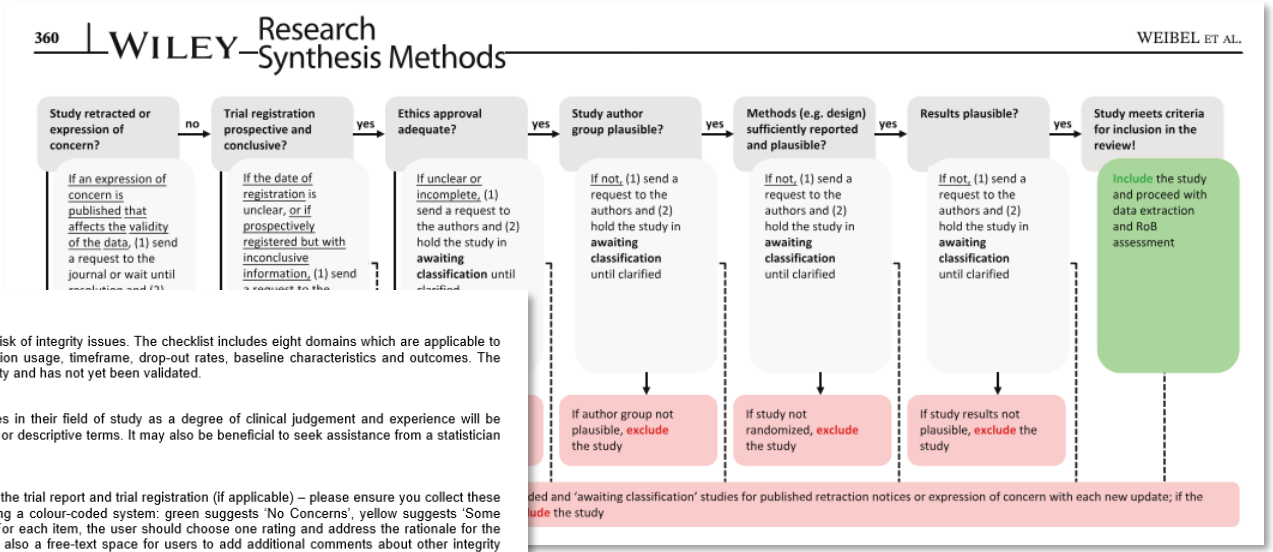


1993

Trial reports

2023

Better research?



The 'REAPPRAISED' checklist for evaluation of publication integrity

R – Research governance

☐ Are the locations where the research took place specified, and is this information plausi

☐ Is a funding source reported?

☐ Has the study been registered?

☐ Are details such as dates and study methods in the publication consistent with those in t registration documents?

E – Ethics

☐ Is there evidence that the work has been approved by a specific, recognized committee?

☐ Are there any concerns about unethical practice?

A – Authorship

☐ Do all authors meet criteria for authorship?

☐ Are contributorship statements present?

☐ Are contributorship statements complete?

Table S1: The TRACT Screening Checklist

Overview

This screening tool aims to help identify and triage studies at risk of integrity issues. The checklist includes eight domains which are applicable to every RCT; governance, author group, plausibility of intervention usage, timeframe, drop-out rates, baseline characteristics and outcomes. The tool is a proposal to optimise our awareness of research integrity and has not yet been validated.

Users

This tool is designed to be used by clinical experts on articles in their field of study as a degree of clinical judgement and experience will be required for some items, and especially those using subjective or descriptive terms. It may also be beneficial to seek assistance from a statistician for some items.

Instructions for Use

The screening tool requires information found in the full text of the trial report and trial registration (if applicable) – please ensure you collect these prior to using the tool. Each item in the checklist is rated using a colour-coded system: green suggests 'No Concerns', yellow suggests 'Some Concern/No Information', and red suggests 'Major Concern'. For each item, the user should choose one rating and address the rationale for the chosen rating in the 'Support of Judgement' section. There is also a free-text space for users to add additional comments about other integrity issues if required.

Details

Article Title, Year	
Author(s)	

Checklist

DOMAIN	*ITEM*	N Conc
Governance	Absent or retrospective registration of RCTs. This is relevant for RCTs commencing after 2010	
	Discrepancy of >15% between the intended sample size in the trial registration compared to the actual sample size achieved in the RCT	
	Absent or vague description of research ethics or apparent concerns regarding ethics	
	Number of authors ≤3 or low author to study size ratio	
	Other studies of authors have been retracted not on request of	

TACIT

Tool for Addressing Conflicts of Interest in Trials

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Welcome to the TACIT website

TACIT stands for Tool for Addressing Conflicts of Interest in Trials and is a tool that provides review authors with a framework for addressing conflicts of interest in trials included in Cochrane Reviews and other systematic reviews.

We aim to develop a tool that facilitates a systematic and transparent judgement of "notable concern" about conflicts of interest in relation to funders and researchers involved in randomised clinical trials included in Cochrane reviews and other systematic reviews.

In addition, TACIT also address the sufficiency of information that the conflicts of interest assessment was based on. These assessments can then be used in exploratory meta-analyses to examine whether results in trials with notable concern differ from those of trials with no notable concern.

Open access Protocol

BMJ Open

Protocol for the development of a tool (INSPECT-SR) to identify problematic randomised controlled trials in systematic reviews of health interventions

PREREGISTERED

equator network

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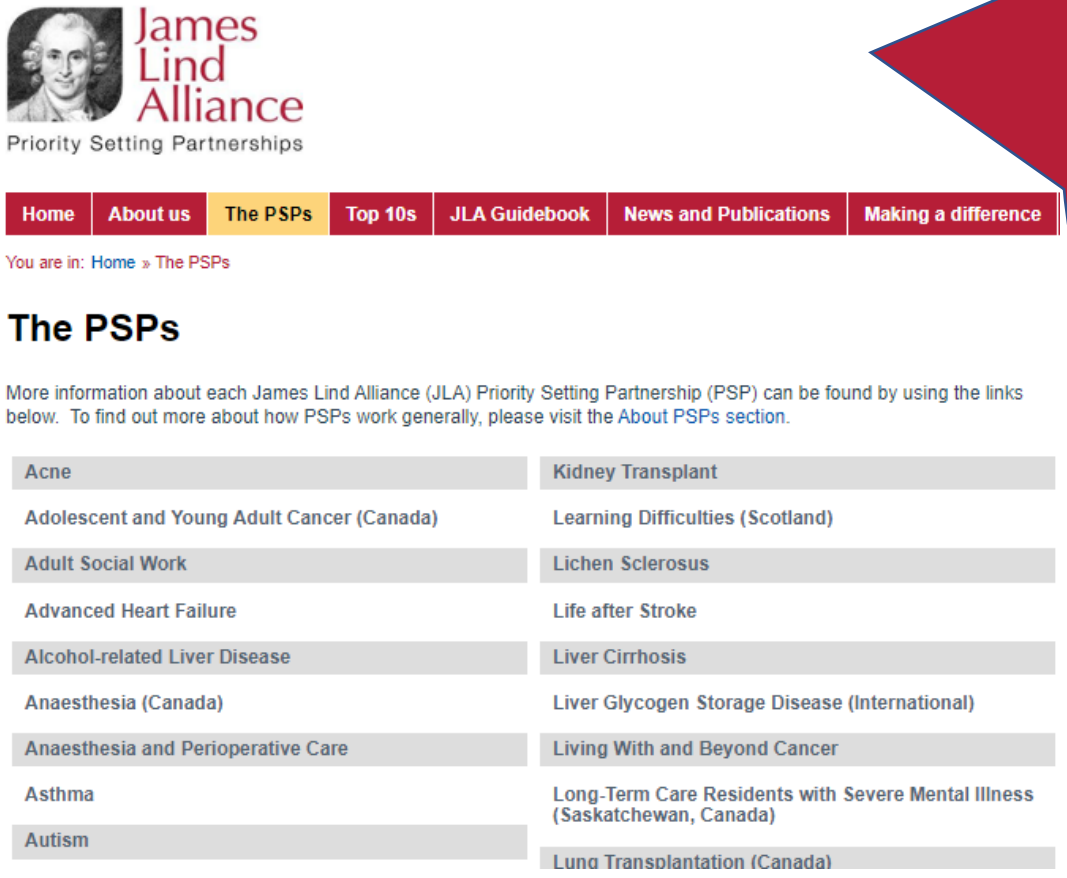
Our analysis of public involvement in clinical trials

Last updated on 21 Mar 2023

NHS
Health Research Authority

…clinical trials have much less public involvement than other types of research.

Research done for the right reasons



…a truly collaborative effort…… clinical research will be relevant, focused and cohesive

Participant, Neuro-oncology PSP

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Home > Researchers > Funding opportunities

24/40 NIHR James Lind Alliance Priority Setting Partnerships rolling call

Opens

24 April 2024

Closes

13:00 on 20 August 2024

Contact

- For help with your application contact eme@nihr.ac.uk
- For more information about the funding Programme, visit the EME Page
- Got a research idea and not sure how to turn it into a funding

We would particularly welcome proposals within MRC remit that address 1 or more of the research areas identified by the ME/CFS Priority Setting Partnership for ME/CFS research:

- post-exertional malaise
- use of existing drugs for other conditions
- diagnosis
- autoimmunity
- ME/CFS sub-types
- post-infective cause
- neurological symptomology
- genetics
- severe ME/CFS
- mitochondrial dysfunction
- oxygenation dysfunction

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Funding opportunity

Researching ME/CFS: highlight notice

n Council (MRC)

date

Timeline

1 May 2003
Opening date

Closing dates throug
usually September,
depending on the gr
you apply for
Depending on the grant
apply for

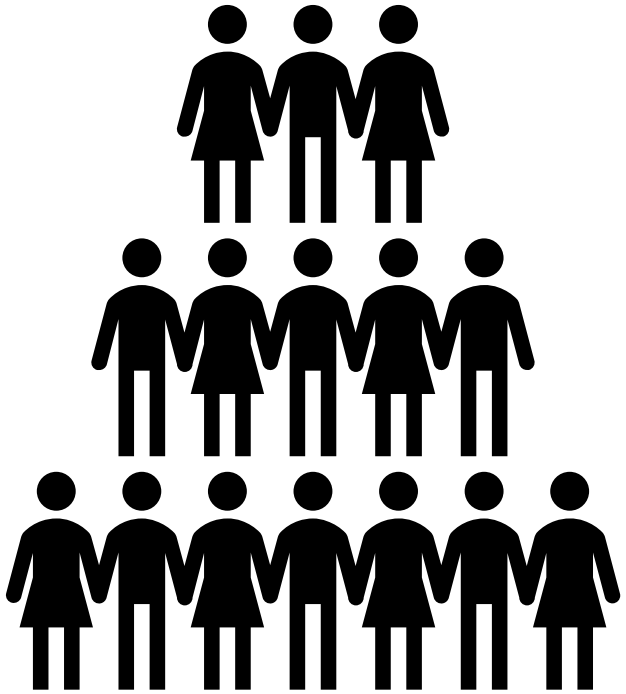
Priority setting

Seeking funding

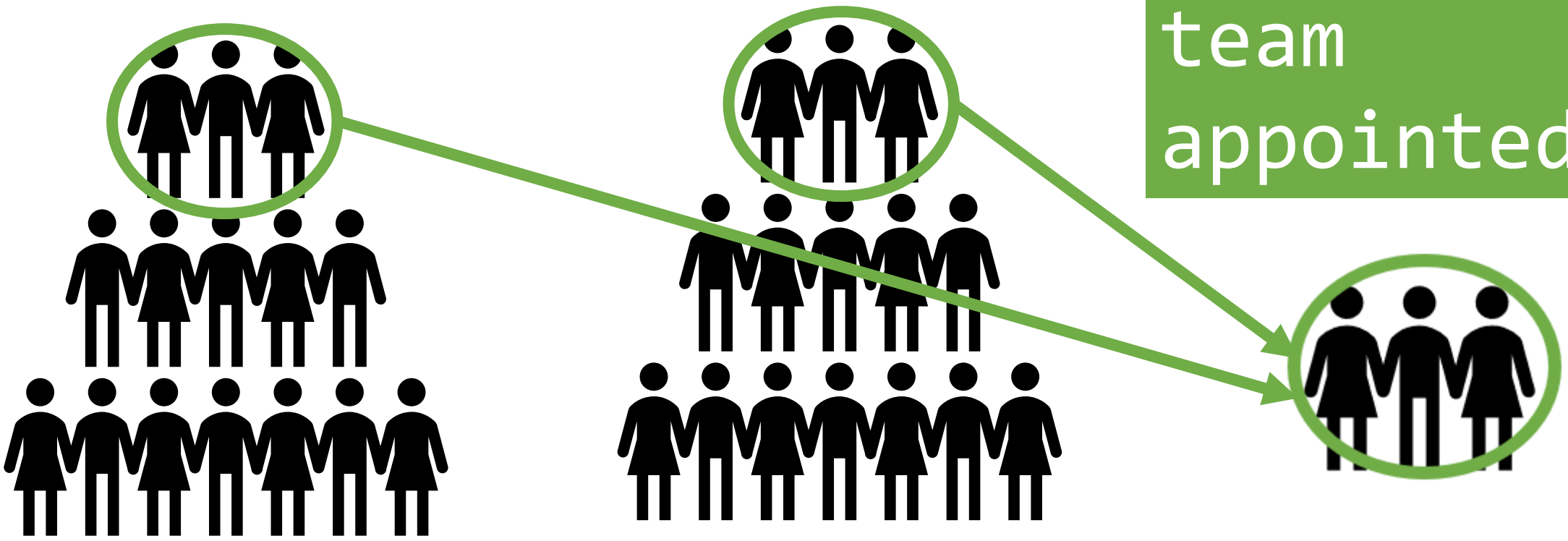
Designed and funded

James Lind

Research team in place



Priority setting	Design trial	Commission trial
James Lind	Trialblazers	Research team appointed



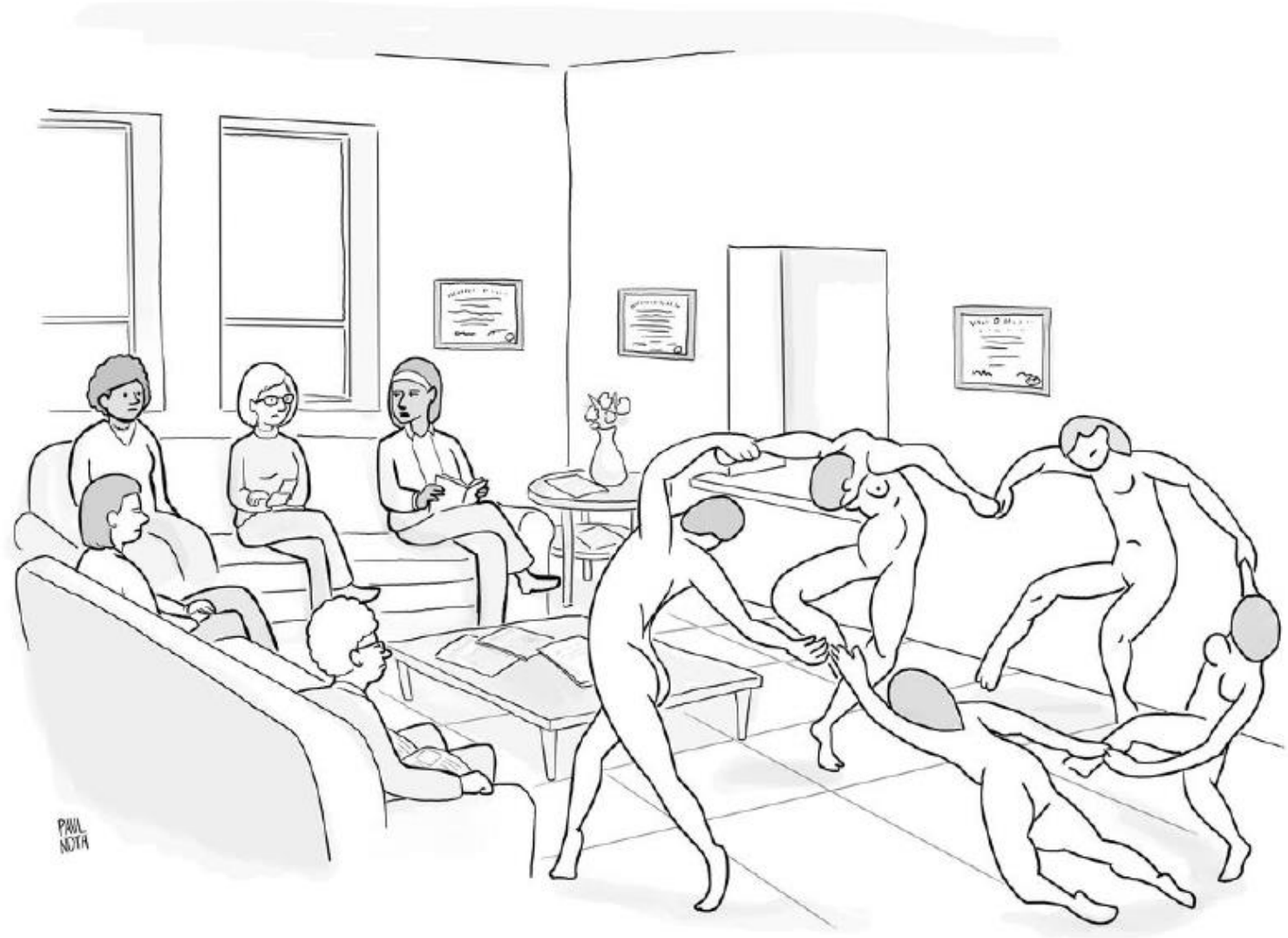
Treweek et al. Trials (2022) 23:537
https://doi.org/10.1186/s13063-022-06348-z

Trials

METHODOLOGY Open Access

Getting it wrong most of the time? Comparing trialists' choice of primary outcome with what patients and health professionals want

Trial area	trials	primary outcomes	patient/HP primary outcome agreement	% agreement
Breast cancer management	20	21	8	38%
Nephrology	24	25	5	20%



PAUL NOTH

"So I'm guessing we're in the placebo group."

Engagement practices that join scientific methods with community wisdom: designing a patient-centred, randomized control trial with a Pacific Islander community

You listened to us. We are doing it together. It is hard to make the meetings…but we are not just being studied by some outsiders, we are doing the research…on something that we want, not just what the researchers want.

Clinical effectiveness of symptomatic therapy compared to standard step-up care for the treatment of low impact psoriatic oligoarthritis: a 2-arm parallel group feasibility study (The POISE Trial)

	Population	Intervention	Control	Outcome measures	Follow-up
POISE 1 (feasibility)	Existing cohort (MONITOR-PsA)	symptomatic therapy (NSAIDs) and local steroid injection	'step-up' DMARD therapy	n/a feasibility	n/a feasibility

Not Feasible

Over the 15-month study period, only one eligible patient was randomised…

…many patients refused treatment in the observational cohort prior to an invitation into the trial as they did not wish to be treated with DMARDs

Clinical effectiveness of symptomatic therapy compared to standard step-up care for the treatment of low impact psoriatic oligoarthritis: a 2-arm parallel group feasibility study (The POISE Trial)

	Population	Intervention	Control	Outcome measures	Follow-up
POISE 1 (feasibility)	Existing cohort (MONITOR-PsA)	symptomatic therapy (NSAIDs) and local steroid injections	'step-up' DMARD therapy	n/a feasibility	n/a feasibility
POISE 2 (full trial if feasible)	Screen for undiagnosed PsA as well as recruit already diagnosed	symptomatic therapy (NSAIDs) and local steroid injections	Menu of non-drug and/or self-help treatments (rescue meds if necessary)	Minimal questionnaires Non-invasive/objective (e.g. activity monitors) + clinical observations	At least one year including active personal monitoring and support to participants

Not Feasible

It means a lot to me, to belong to your group

I would be very happy to be part of a PsA community

…your idea is fascinating and could well become a benchmark for future research

Report for July 2023 Build-a-Trial workshop participants in Oxford and on Zoom

Caroline Struthers, Research Fellow, University of Oxford

INTRODUCTION

In April 2023 I was awarded funding via a university scheme to conduct a public engagement project. I wanted to find and work with a patient community to test out a project idea called Trialblazers, aiming to develop a way to put patients in the driving seat of clinical trial design.

Open Arms Public Involvement Group

Louise Hailey and rheumatologist Dr Laura Coates, leaders of the "Open Arms" Public involvement group in my department kindly agreed to support me.

Louise and Laura led on the 2021 publication of the top 10 research priorities in psoriatic arthritis: a James Lind Alliance Priority Setting Partnership https://www.jla.nihr.ac.uk/priority-setting-partnerships/psoriatic-arthritis/

The POISE trial

In 2019 Laura and colleagues had tested if it were possible to recruit people with mild psoriatic arthritis to a randomised trial testing an alternative

Sir Sajid Javid, UK Secretary of State for Health and Social Care 2021-2022

People with ME have been ignored for far too long

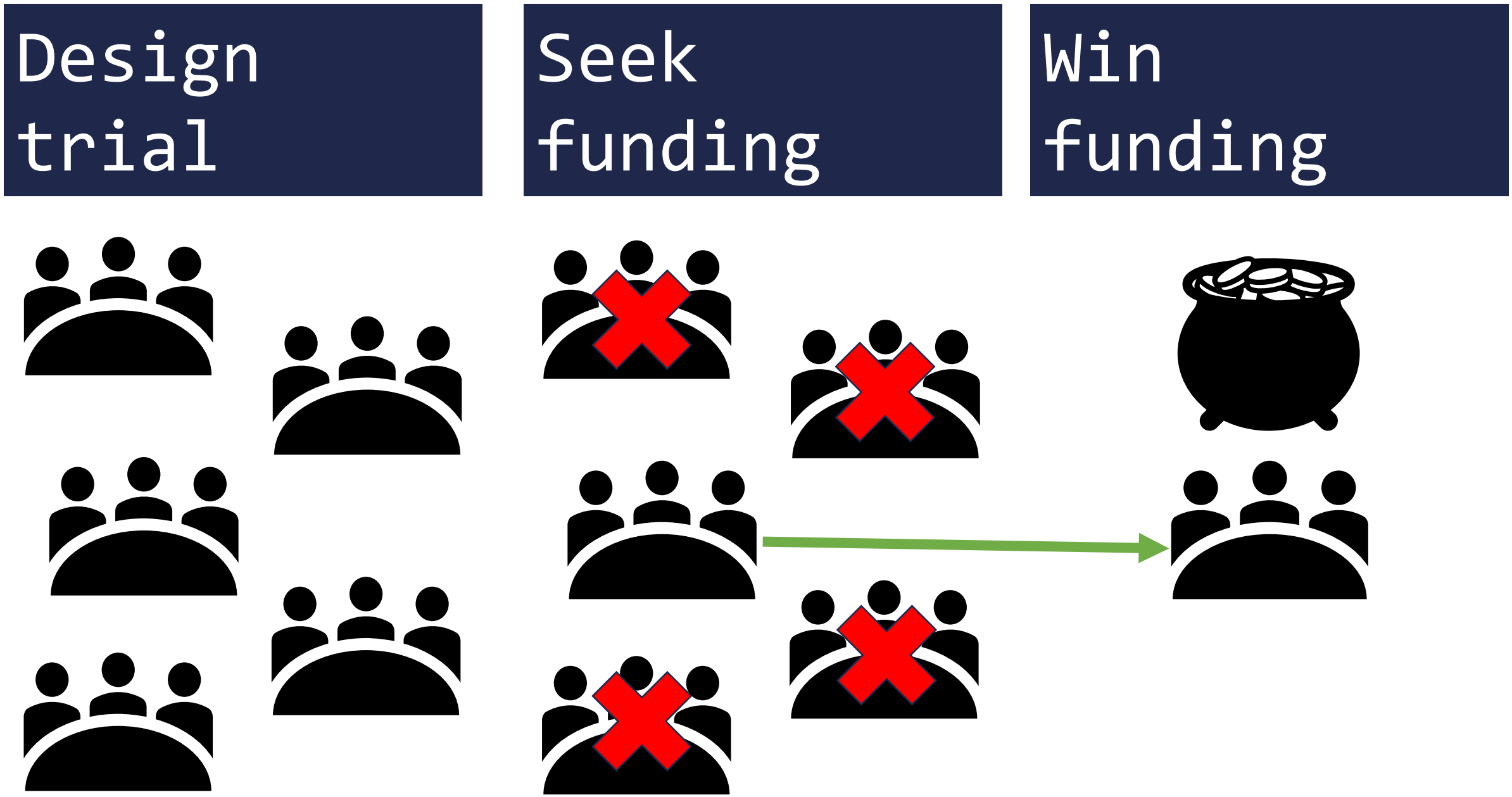
The Times, May 2024

Priority 1 What is the biological mechanism that causes post-exertional malaise (symptoms caused or made worse by physical, mental or emotional effort, which can be delayed) in people with ME/CFS? How is this best treated and managed?	**Priority 2** Which existing drugs used to treat other conditions might be useful for treating ME/CFS, such as low dose naltrexone, or drugs used to treat Postural Orthostatic Tachycardia Syndrome (POTS)?	**Priority 3** How can an accurate and reliable diagnostic test be developed for ME/CFS?	**Priority 4** Is ME/CFS caused by a faulty immune system? Is ME/CFS an autoimmune condition?
Priority 5 Are there different types of ME/CFS linked to different causes and how severe it becomes? Do different types of ME/CFS need different treatments or have different chances of recovery?	**Priority 6** Why do some people develop ME/CFS following an infection? Is there a link with long-COVID?	**Priority 7** What causes the central and peripheral nervous systems (brain, spinal cord and nerves in the body) to malfunction in people with ME/CFS? Could this understanding lead to new treatments?	**Priority 8** Is there a genetic link to ME/CFS? If yes, how does this affect the risk of ME/CFS in families? Could this lead to new treatments?
Priority 9 What causes ME/CFS to become severe?	**Priority 10** How are mitochondria, responsible for the body's energy production, affected in ME/CFS? Could this understanding lead to new treatments?	**Priority 10+** Does poor delivery or use of oxygen within the body cause ME/CFS symptoms? If so, how is this best treated?	

Priority 2

Which existing drugs used to treat other conditions might be useful for treating ME/CFS, such as low dose naltrexone, or drugs used to treat Postural Orthostatic Tachycardia Syndrome (POTS)?

- New clinical studies to answer PSP Top 10 priorities
- Map priorities to evidence gaps
- Raise awareness of funding opportunities
- Raise awareness of effective public involvement methods
- Case studies and exemplars of good research practice


Design trial
Seek funding
Win funding

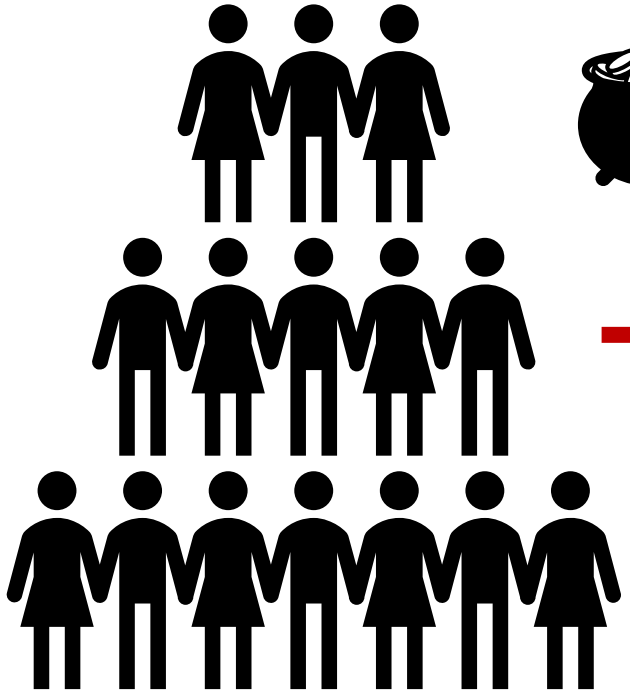
Design trial

Allocate funding

Appoint researchers

Trialblazers

Funders



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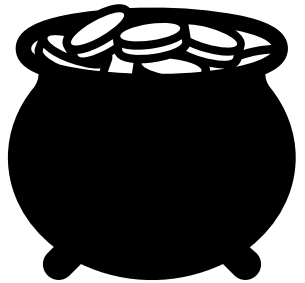

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