MRC-NIHR Trials Methodology Research Partnership: Webinar recording

Trials methodology: a community approach

Presented by Prof Paula Williamson

4 May 2022

On behalf of the TMRP

The slides are also available below.

For any queries, please contact uktmn@nottingham.ac.uk

https://www.youtube.com/watch?v=2tOpaxnJTFk

@MRCNIHRTMRP

http://www.methodologyhubs.mrc.ac.uk/

Trials methodology: a community approach

Professor Paula Williamson
University of Liverpool
Lead, TMRP

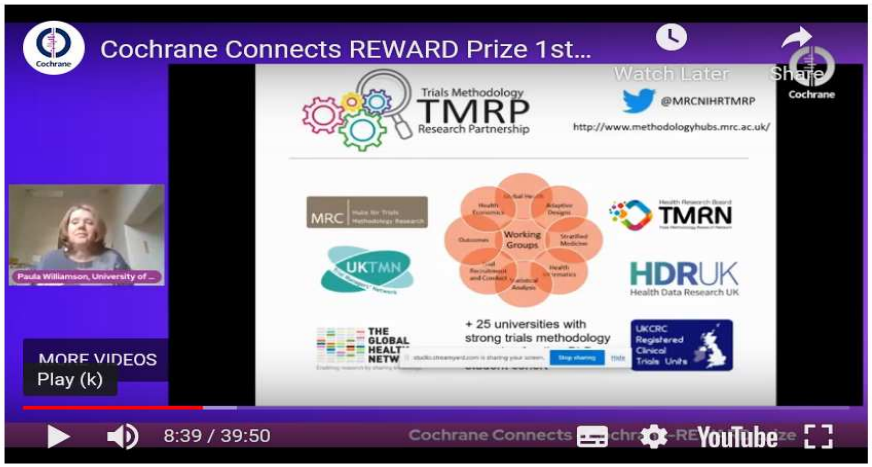
Improving health by improving trials

Cochrane

Trusted evidence.
Informed decisions.
Better health.

2021 Cochrane-REWARD prize winners

This year was particularly competitive, with many very strong contenders for the prize committee to consider. Thank you to all who submitted nominations, and congratulations to the winners below:



Trials Methodology
TMRP
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http://www.methodologyhubs.mrc.ac.uk/

MRC | Hubs for Trials Methodology Research

Health Research Board
TMRN
Trials Methodology Research Network

UKTMN
Trial Managers' Network

HDRUK
Health Data Research UK

THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

UKCRC Registered Clinical Trials Units

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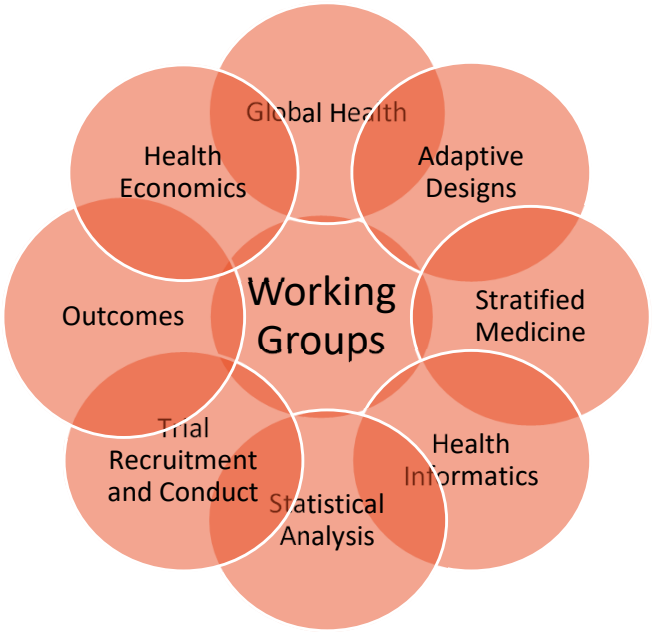

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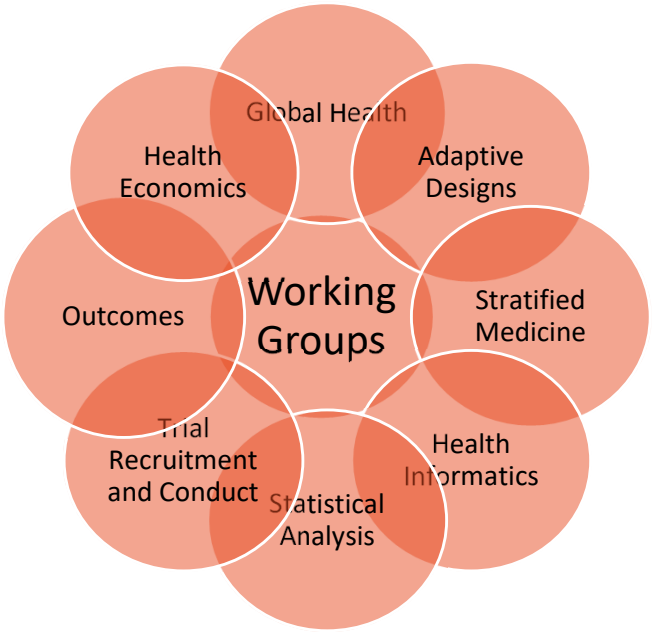

Health Research Board
TMRN
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HDRUK
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THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

+ 25 universities with strong trials methodology expertise funding PhD student cohort

UKCRC Registered Clinical Trials Units

A sense of community

"The TMRP has provided me with many opportunities to meet and work with researchers, including other PhD students, outside of my university. Not only has this widened my research experience beyond my PhD but it has also allowed me to meet and work with experts in this field at a time where networking can be particularly challenging in the virtual world. I have benefitted from training courses and other opportunities."

"Academics are part of a community who happen to work at a particular institution. Institutional affiliation is only a part of our identity."

What can a trials methodology network achieve?

- Better, more impactful research
- Less duplication of effort
- Value for money
- Increased knowledge exchange
- Agility - ability to pivot to COVID-19 projects

What have we done?

- Priority setting exercises – referenced in funding applications
- Small project awards (5-20K), unfunded projects, external grants
- Development and maintenance of online resources
- Open webinar series
- '*How to be a good CI*', '*How to be a good TSC Chair*', '*How to be a good TM*'

COVID-19 related activities 2020-2022

- **Adaptive Designs Working Group**

- Platform trials: RECOVERY, AGILE, HEAL-COVID

- **Statistical Analysis Working Group**

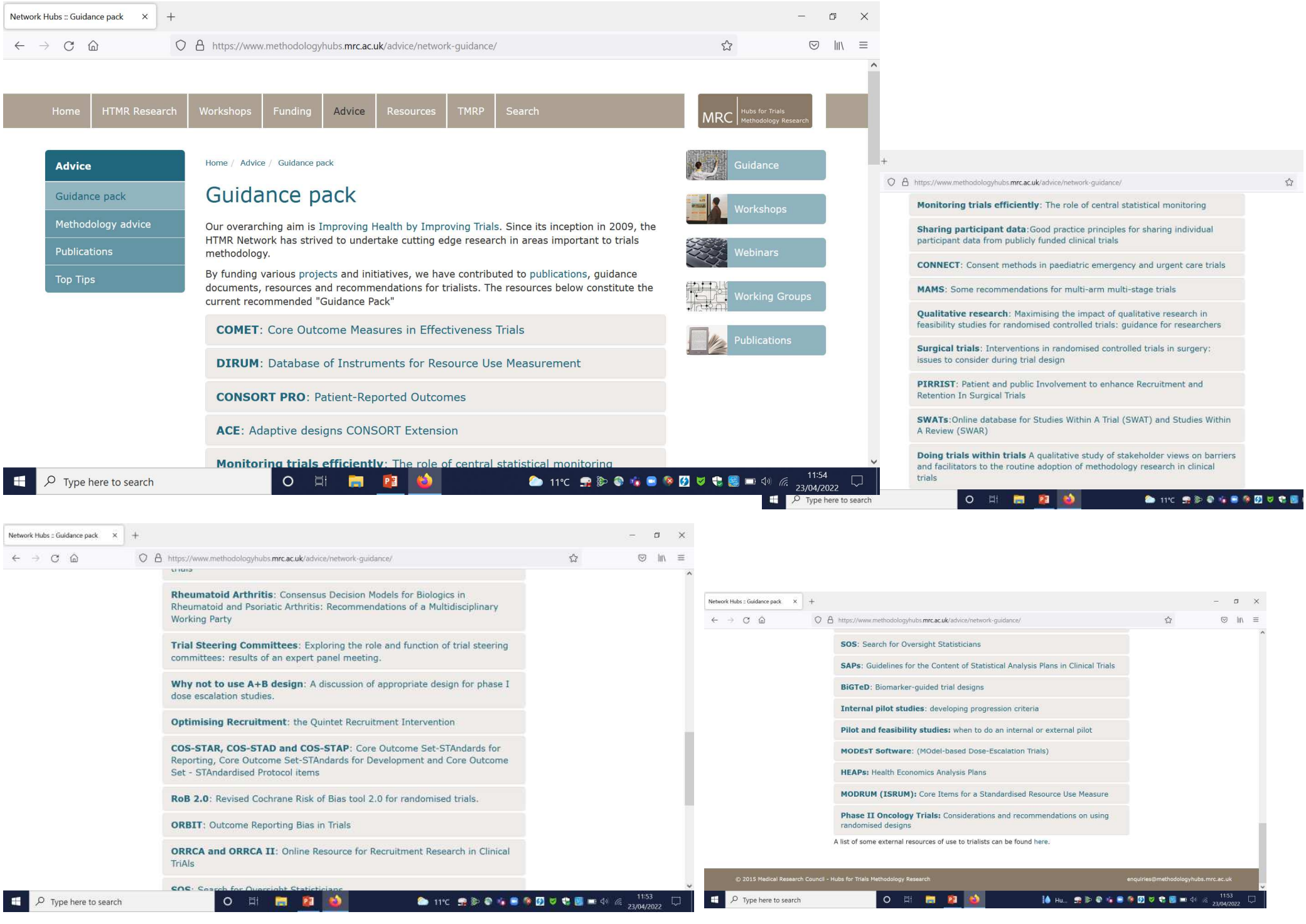
- Rapid, open reviews of protocols, preprints and publications on new COVID-19 treatments

- **Outcomes Working Group**

- COS: acute COVID-19, transmission prevention, Long COVID

- **Trial Conduct Working Group**

- Contributed to the NIHR INCLUDE Ethnicity Framework


Network Hubs :: Guidance pack
https://www.methodologyhubs.mrc.ac.uk/advice/network-guidance/
Home
HTMR Research
Workshops
Funding
Advice
Resources
TMRP
Search
MRC Hubs for Trials Methodology Research
Advice
Guidance pack
Methodology advice
Publications
Top Tips
Home / Advice / Guidance pack
Guidance pack
Our overarching aim is Improving Health by Improving Trials. Since its inception in 2009, the HTMR Network has strived to undertake cutting edge research in areas important to trials methodology.
By funding various projects and initiatives, we have contributed to publications, guidance documents, resources and recommendations for trialists. The resources below constitute the current recommended "Guidance Pack"
COMET: Core Outcome Measures in Effectiveness Trials
DIRUM: Database of Instruments for Resource Use Measurement
CONSORT PRO: Patient-Reported Outcomes
ACE: Adaptive designs CONSORT Extension
Monitoring trials efficiently: The role of central statistical monitoring
Guidance
Workshops
Webinars
Working Groups
Publications
Monitoring trials efficiently: The role of central statistical monitoring
Sharing participant data: Good practice principles for sharing individual participant data from publicly funded clinical trials
CONNECT: Consent methods in paediatric emergency and urgent care trials
MAMS: Some recommendations for multi-arm multi-stage trials
Qualitative research: Maximising the impact of qualitative research in feasibility studies for randomised controlled trials: guidance for researchers
Surgical trials: Interventions in randomised controlled trials in surgery: issues to consider during trial design
PIRRIST: Patient and public Involvement to enhance Recruitment and Retention In Surgical Trials
SWATs: Online database for Studies Within A Trial (SWAT) and Studies Within A Review (SWAR)
Doing trials within trials A qualitative study of stakeholder views on barriers and facilitators to the routine adoption of methodology research in clinical trials
Rheumatoid Arthritis: Consensus Decision Models for Biologics in Rheumatoid and Psoriatic Arthritis: Recommendations of a Multidisciplinary Working Party
Trial Steering Committees: Exploring the role and function of trial steering committees: results of an expert panel meeting.
Why not to use A+B design: A discussion of appropriate design for phase I dose escalation studies.
Optimising Recruitment: the Quintet Recruitment Intervention
COS-STAR, COS-STAD and COS-STAP: Core Outcome Set-STAndards for Reporting, Core Outcome Set-STAndards for Development and Core Outcome Set - STAndardised Protocol items
RoB 2.0: Revised Cochrane Risk of Bias tool 2.0 for randomised trials.
ORBIT: Outcome Reporting Bias in Trials
ORRCA and ORRCA II: Online Resource for Recruitment Research in Clinical TriAls
SOS: Search for Oversight Statisticians
SAPs: Guidelines for the Content of Statistical Analysis Plans in Clinical Trials
BiGTeD: Biomarker-guided trial designs
Internal pilot studies: developing progression criteria
Pilot and feasibility studies: when to do an internal or external pilot
MODEsT Software: (MOdel-based Dose-Escalation Trials)
HEAPs: Health Economics Analysis Plans
MODRUM (ISRUM): Core Items for a Standardised Resource Use Measure
Phase II Oncology Trials: Considerations and recommendations on using randomised designs
A list of some external resources of use to trialists can be found here.
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enquiries@methodologyhubs.mrc.ac.uk
Type here to search
11:54
23/04/2022
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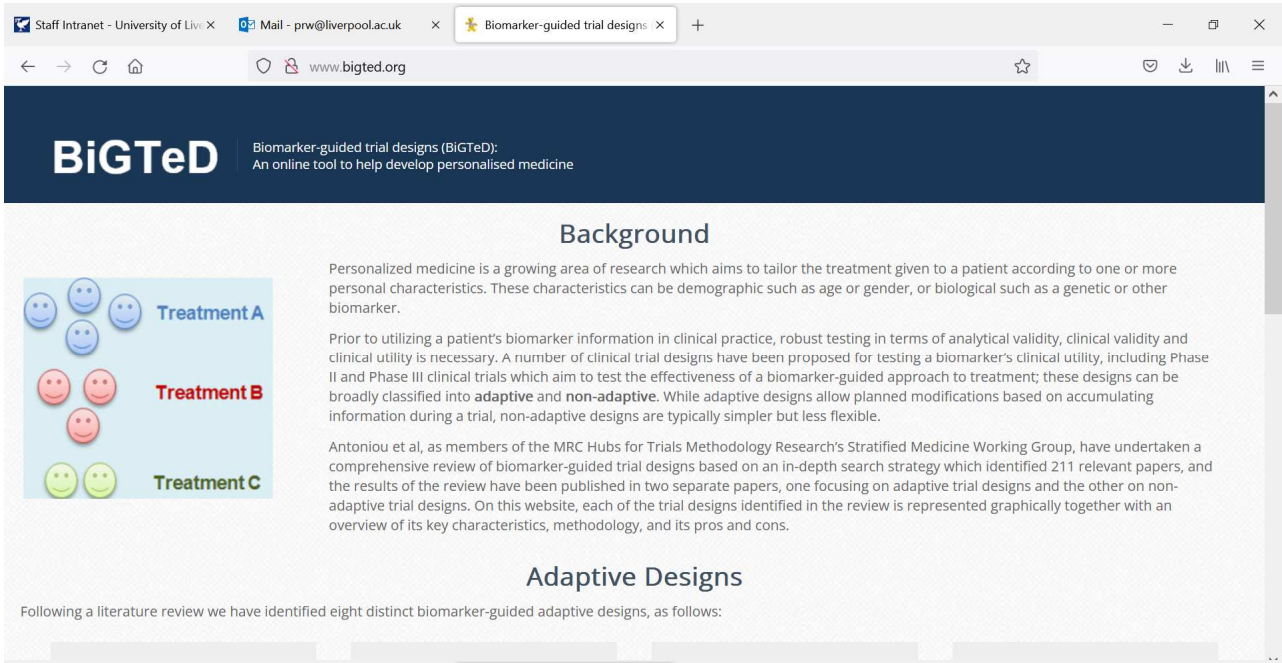
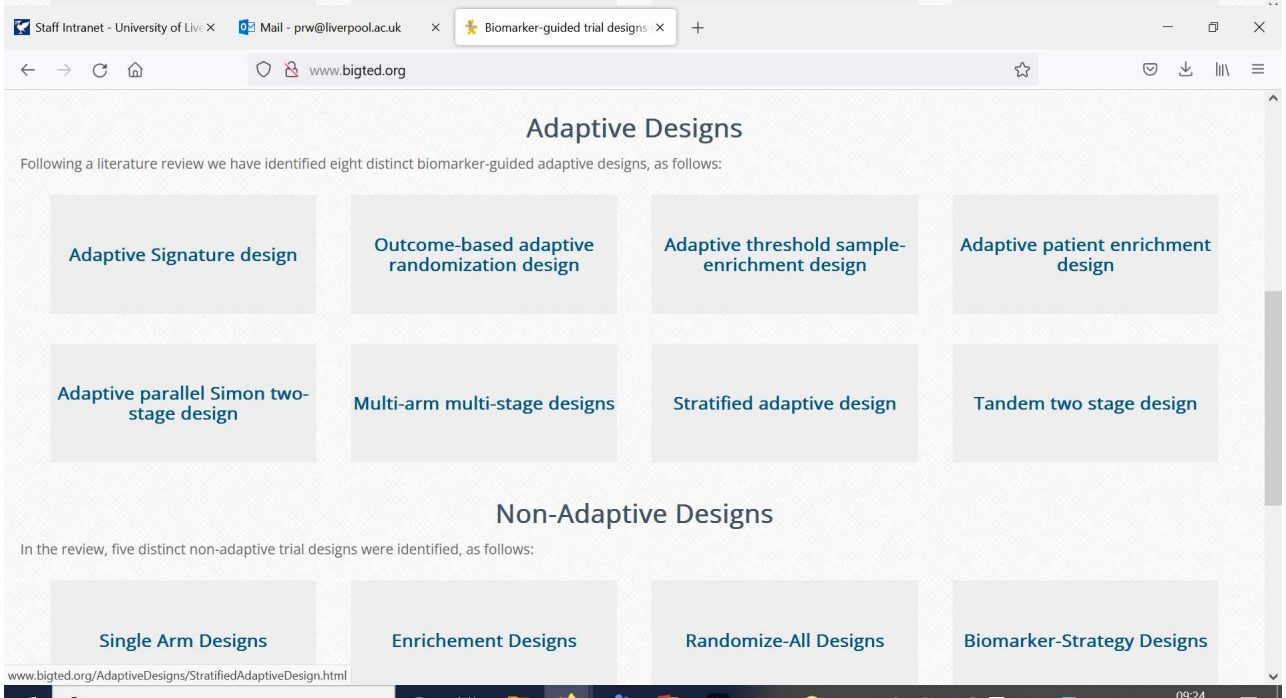
23/04/2022

Planning – stratified medicine





Planning – adaptive designs

Wilson *et al. BMC Medicine* (2021) 19:251
https://doi.org/10.1186/s12916-021-02124-z

BMC Medicine

RESEARCH ARTICLE Open Access

Costs and staffing resource requirements for adaptive clinical trials: quantitative and qualitative results from the Costing Adaptive Trials project

Nina Wilson[1], Katie Biggs[2], Sarah Bowden[3], Julia Brown[4], Munyaradzi Dimairo[2], Laura Flight[2], Jamie Hall[2], Anna Hockaday[4], Thomas Jaki[5,6], Rachel Lowe[7], Caroline Murphy[8], Philip Pallmann[7], Mark A. Pilling[9], Claire Snowdon[10], Matthew R. Sydes[11], Sofía S. Villar[5], Christopher J. Weir[12], Jessica Welburn[2], Christina Yap[10], Rebecca Maier[1,13], Helen Hancock[1,13] and James M. S. Wason[1*]

Abstract

Background: Adaptive designs offer great promise in improving the efficiency and patient-benefit of clinical trials. An important barrier to further increased use is a lack of understanding about which additional resources are required to conduct a high-quality adaptive clinical trial, compared to a traditional fixed design.
The Costing Adaptive Trials (CAT) project investigated which additional resources may be required to support adaptive trials.

Planning – choosing the outcomes to measure

Network Hubs :: Guidance pack | COMET Initiative | Resources

https://www.comet-initiative.org/Resources

Home | Search the COMET Database | Resources | COS Endorsement | COS Uptake | Patients and the Public | Events | About us

COMET VIII

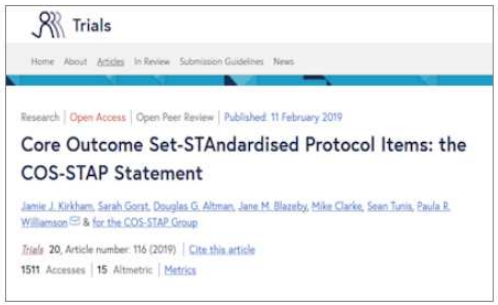
- Database
- Systematic reviews of COS
- Newsletter
- Plain language summaries
- Patients and the Public
- Downloadable slide set

Resources

This section of the website includes useful resources and tools. A trio of guidance for COS development now exists, in addition to the COMET Handbook. Click the links below for more information.

COS-STAD

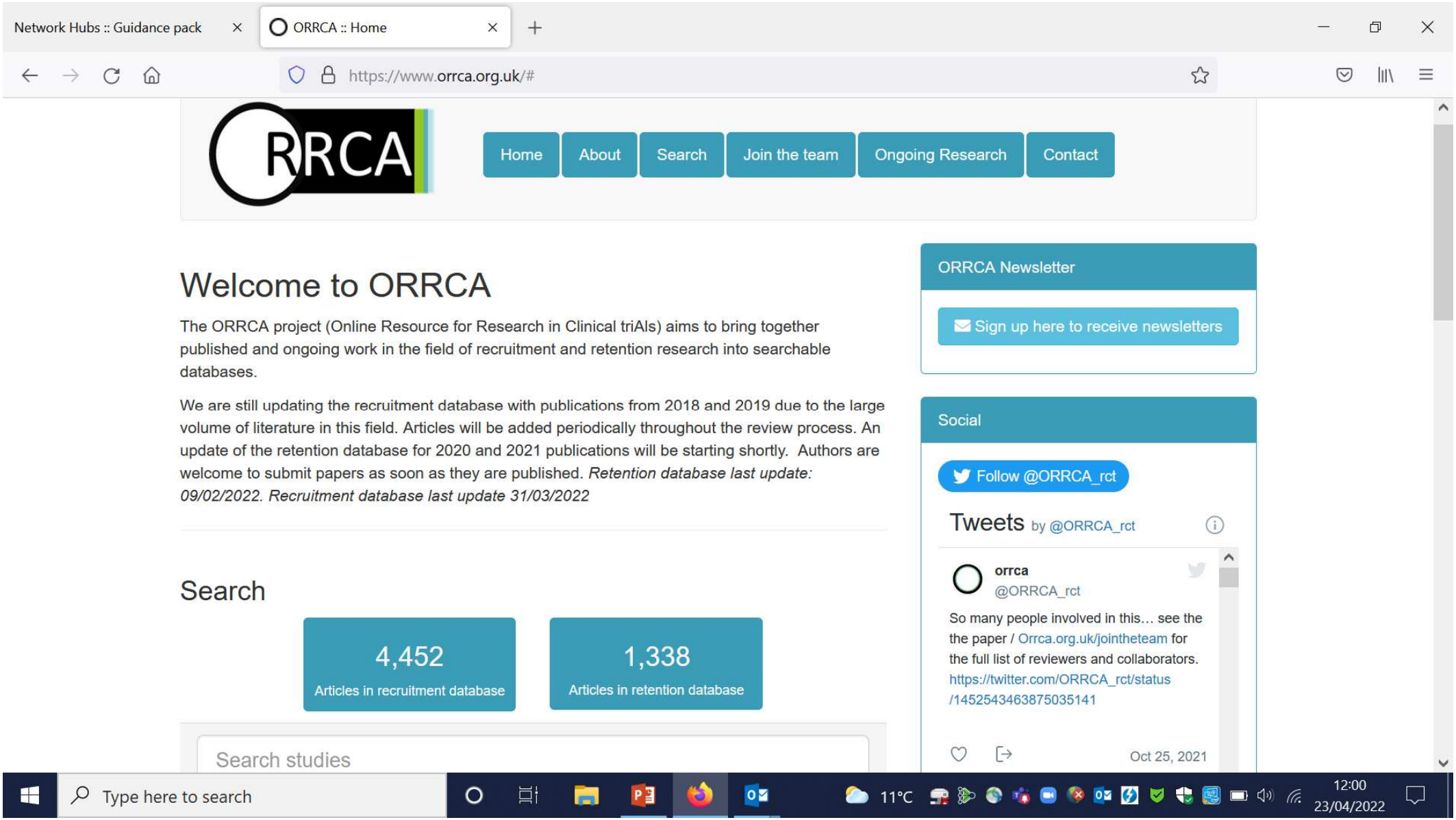
COS-STAP



COS-STAR

Type here to search 11°C 11:58 23/04/2022

Conduct – recruitment and retention research



Trial Conduct Working Group - Funding Awards

INITIAL: Involving patients and the public In sTatistIcal Analysis pLans

Determining the most important methodological areas requiring methodological research for routine data in trials: a consensus

Minority ExpeRiences In Trials (MERIT): Understanding why ethnic minority groups are under-represented in trials through a rapid qualitative evidence synthesis, and mapping evidence to find solutions

Beyond "must speak English": In search of a fairer way to operationalise patient screening for language proficiency in trial recruitment

Analysis

BMJ

RESEARCH

Frequency and reasons for outcome reporting bias in clinical trials: interviews with trialists

"When I take a look at the data I see what best advances the story, and if you include too much data the reader doesn't get the actual important message, so sometimes you get data that is either not significant or doesn't show anything, and so you, we, just didn't include that"

Citation Analysis for JAMA article

November 2020: viewed 80K times with >22K downloads, 124 citations

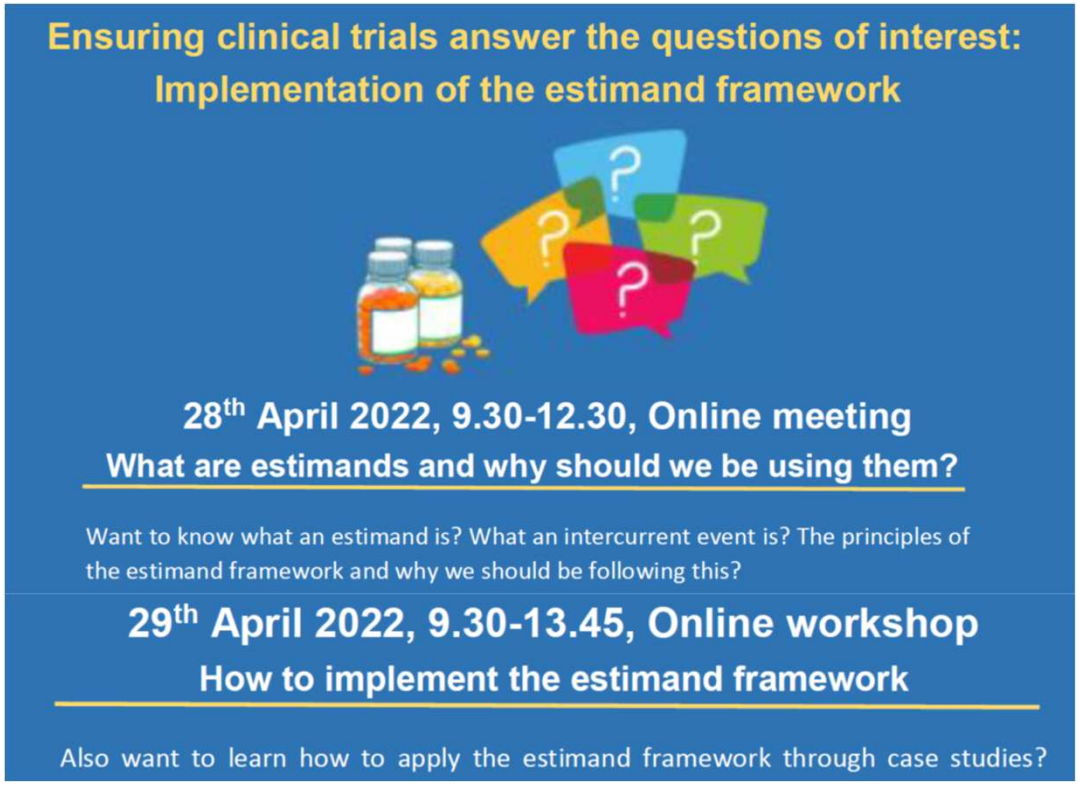
Primary reason for citation	2018	2019	2020	Grand Total
Guidance used as a template	6	8	28	42
Reporting and transparency	7	8	11	26
Recommending use of guidance	1		9	10
Future SAP will follow guidelines	1	4	3	8
Discussion of statistical methods	2	2	2	6
Justification for a SAP element	1	3	2	6
Other guideline development	1	1	2	4
Other		1	2	3
Application outside RCT		2		2
Data sharing methods		1		1
Cross referencing guidelines			1	1
Grand Total	19	30	60	109*

Country of first author	
UK	15
Denmark	6
Australia	4
USA	4
Canada	3
Netherlands	2
unknown	2
Saudi Arabia	1
China	1
Chile	1
Italy	1
Finland	1
Germany	1

15 citations excluded (7 duplicates, 4 awaiting access, 1 citation could not be confirmed, 3 editorial /letters associated with the original publication)

Analysis

"Subgroup analyses in randomised controlled trials frequently categorise continuous subgroup information"
(Faye Williamson et al, submitted)



Reporting and sharing findings

- CONSORT-PRO
- CONSORT-Adaptive Design
- CONSORT- and SPIRIT-Surrogate
- SPIRIT-Routine

- Tool to assess outcome reporting bias, http://www.outcome-reporting-bias.org/

- Data sharing guidance

- Recommendations for sharing qualitative data in trials

Global Health project awards

- **Sylivia Nalubega**, Soroti University, Uganda: *The practice of pilot studies in informing the conduct of HIV clinical trials in sub Saharan Africa: a review of study protocols*

- **Naomi Waithira**, MORU Tropical Health Network, University of Oxford, UK: *Exploring barriers to data reuse*

- **Nandi Siegfried**, MRC Alcohol, Tobacco and Other Drug Research Unit, South Africa: *Cultural competence in trial design and conduct*

- **Mercy Chepkirui Terer**, KEMRI-Wellcome Trust Research Programme, Kenya: *Pilot implementation of Short Message Service for randomisation in a multisite pragmatic factorial clinical trial in Kenya (PRISMS Study)*

Global Health project awards

- **Sangeetha Paramasivan**, University of Bristol, UK: *Optimising Informed CONsent in clinical trials in low- and middle-income settings: feasibility of an adapted QuinteT Recruitment Intervention (QRI) in India (OrION-I)*

- **Wigilya Mikomangwa**, Muhimbili University of Health and Allied Sciences,Tanzania: *Assessment of the challenges encountered in implementing vaccine clinical trial methodologies in low income countries*

- **David Musoke and James O'Donovan**, Makerere University, Uganda: *Photovoice to explore community members perspectives regarding health and healthcare challenges in Mukono District, Uganda*

MRC Doctoral Training Programme in Trials Methodology, 2021-2028

Statistics

Computer science

Data science

Health informatics

Health economics

Psychology

Social science

Behavioural science

Bioethics

International Clinical Trials Methodology Conference

THE TRIALS METHODS RESEARCH AGENDA: A PRIORITY SETTING EXERCISE, 2022

Inviting input from:

- members of the public
- patients
- researchers involved in clinical trials and/or trials methodology research
- clinicians and health professionals
- funders
- research ethics organisations
- those involved in the conduct of clinical trials (including investigators, research nurses, trials operations staff, statisticians, health economists, clinical trial pharmacists, regulators)
- editorial board members of journals that publish clinical trial protocols, clinical trials results and trials-relevant methodology

Collaborating countries:

UK
IRELAND
SWITZERLAND
FRANCE
AUSTRALIA

Contact:
sinead.holden@ucd.ie

UCD School of Medicine
Scoil an Leighis UCD

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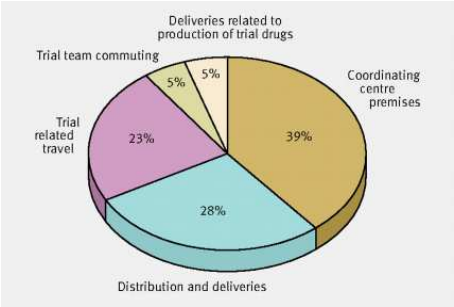
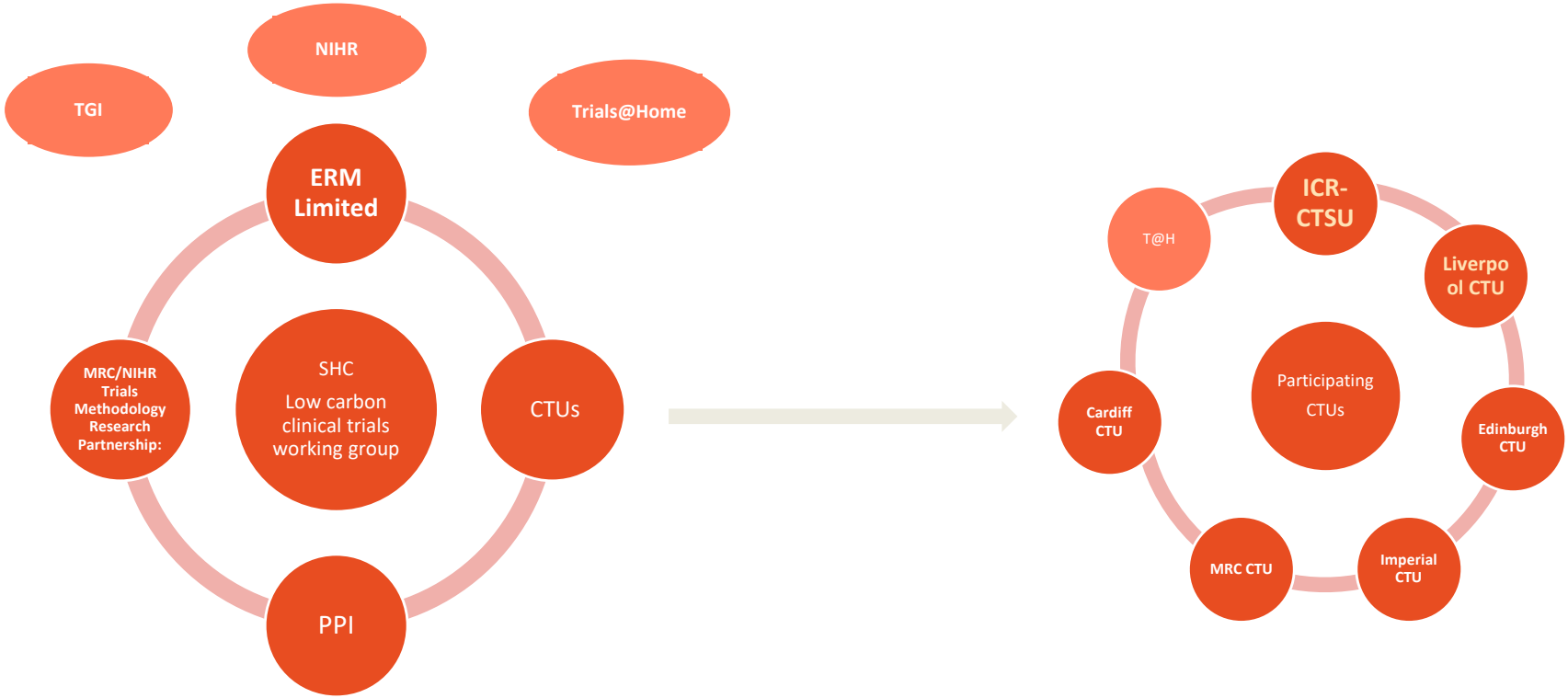
UNIVERSITY OF LIVERPOOL

Enabling lower carbon clinical trials: *Development and prototype testing of a method to quantify the carbon footprint of current clinical trials to inform future lower carbon clinical trial design*



Proportions of greenhouse gas emissions in CRASH Trial Case study
BMJ 2007;334:671



TMRP – the future

- Partner organisations and Working Group Co-Leads

- Funding:

- TMRP Coordinator
- DTP 2021-2028
- Re-investment from ICTMC 2022

- Strengthening collaborations with: international organisations, Patient Research Partners, industry

- Future funding applications – for TMRP and for specific projects

- ICTMC 2024 ☺

- Delivering impact of work to date

Impact of/KT for methods research

- *What's been the most impactful methods research or guidance you are aware of, and why?*
- What do we mean by 'impact'?
- Who or what do we want to be 'impacted'?
- Is there a translational gap?
- How can we achieve impact?
- How can we demonstrate impact?