



MRC-NIHR Trials Methodology Research Partnership: Webinar recording

Data Integrity

Presented by Liz Allen (Cape Town University), Philip Pallman (Cardiff University), Munya Dimairo (University of Sheffield), Alex Dmitrienko (Mediana)

27 September 2022

On behalf of The Global Health Network



The slides are also available below.

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

<https://www.youtube.com/watch?v=bfw9dzwC1HU>



TMRP Webinar Series 5 The Global Health Network

Tools and resources for adaptive designs in clinical trials

Tuesday 27 September 2022

The Trials Methodology Research Partnership



- A global community of practice for improving the design, conduct, & analysis of trials everywhere
- The Global Health Working Group raises awareness of trials methodology research, signposting to technical working groups & training, facilitating collaborations & small methodology research grants for LMIC
- The Global Health Network joined the MRC-NIHR Trials Methodology Research Partnership to offer a gateway for researchers in LMICs to better contribute to & benefit from developments in this field





Contemporary Clinical Trials Communications

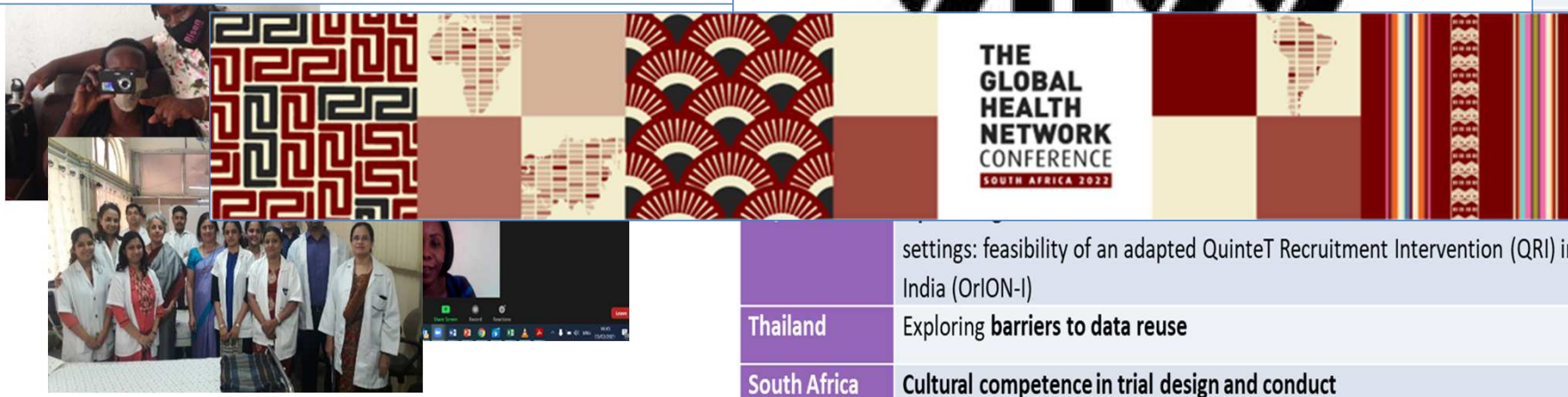
Volume 29, October 2022, 100959



The practice of pilot/feasibility studies in
informing the conduct of HIV related
clinical trials in sub-Saharan Africa
scoping review

Sylvia Nalubega ^a ✉, Lawrence Obado Osuwat ^a ✉, Poku Brenda Agyeiwaa ^b ✉
✉, John Bosco Matovu Junior ^e ✉

Join any number of WGs & interact with a
e, diverse membership
TMRP & TGHN websites for guidance,
lications, webinars, networking
www.methodologyhubs.mrc.ac.uk




	settings: feasibility of an adapted QuinteT Recruitment Intervention (QRI) in India (OrION-I)
Thailand	Exploring barriers to data reuse
South Africa	Cultural competence in trial design and conduct


The Global Health Network



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The Global Health Network enables easier, faster, and better research in the world's most challenging settings.

Knowledge Sharing Hubs

Transferring knowledge and exchanging methods, processes and research findings between diseases, regions and organisations.

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Capacity Development and Process Improvement

Regional and online training, resources and professional development to build skills and careers that deliver evidence to change practice.

[About](#) 

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Proud partner of the TMRP



Global Health Methodology Research

What are you looking for?

SEARCH

TMRP Global Health Pump Priming Awards

1. Photovoice to explore community members perspectives regarding health

PI: James O'Donovan and David Musoke, Makerere University School of Public Health

There have been calls for a greater number of clinical studies in low- and middle-income countries, ensuring they are contextually relevant. One useful approach towards this is Contextually Based Participatory Research (CBPR), where local stakeholders being central to the research process. CBPR is often used in research that remains contextually relevant and better understand the lived experience of the community. Photovoice is suggested as a means of diversifying participation and increasing relevance and is a method aligned to CBPR is photovoice, whereby cameras are given to individuals to capture community importance or concern. In our project, the subject of interest is community members from the Seeta Nazigo Parish, Mukono District in central Uganda. We have used 15 community members from the Seeta Nazigo Parish, Mukono District in central Uganda in the use of cameras and have undergone one round of photographic capture.



Conclusion

- The TMRP has contributed to equity in where research happens & who benefits.
- Any trial team member can explore optimal methods whatever their role
- Being part of this community can help with developing skills needed to answer questions about the way you design, operationalise, analyse & report your trials
- Including patients & participants in finding new & better trials methods is key
- Funders should consider investing in methods research within or alongside trials as a cost-effective way to sustain sites while improving the science of trials.
- It is also an excellent career development opportunity for early career researchers

The Trials Methodology Research Partnership
A global community of practice for improving design, conduct, & analysis of trials everywhere

Background

- Continual questioning of trials methods ensures they are optimal & responsive for a range of stakeholders
- Trials methodology research has led to more sophisticated trial designs & data collection platforms, better ways for recruiting / retaining participants, selecting / measuring outcomes, & collecting, analysing & sharing data
- The Global Health Network (TGHN) joined the MRC-NIHR Trials Methodology Research Partnership (TMRP) to offer a gateway for researchers in low & middle income countries (LMICs) to better contribute to & benefit from developments in this field

Objective

- To develop a new Global Health Working Group (GH WG) of the TMRP

Methods

- The TMRP & TGHN together developed a gateway for researchers in LMICs to explore & contribute to this field through a 'community of practice' model, whereby a group of people sharing a common interest come together to fulfil individual and group goals
- The aim was to raise awareness of trials methodology research, signpost to the TMRP technical working groups & training, & to facilitate collaborations & small methodology research grants for LMICs

Results

- TGHN launched the initiative by funding a competition for a member to win attendance at the International Clinical Trials Methodology Conference (ICTM) 2019
- Since then the GH WG membership has grown to approx 80 from 22 countries, including 7 students & 15 early career researchers
- Two linked websites & twitter feeds feature guidance & facilitate networking (www.methodology.mrc.ac.uk & <https://twitter.com/methodology>)
- A snapshot of traffic for the TGHN page for May 2021 was approx 425 unique page views (top 10 being US, UK, Canada, China, India, Kenya, Ghana, Ethiopia, Brazil and Nigeria), 70 being returning visitors, 280 new visitors & total membership for the page is 11428
- GH WG members have joined other TMRP technical working groups to network in their specialist area, with the top 3 technical areas of interest being: Trial Conduct, Outcomes & Adaptive Designs
- There were 270 applications for small grants from 48 LMICs, 64 eligible & 7 ultimately funded in a wide range of topics, 5 in Africa (Kenya, Uganda, Tanzania & South Africa)
- Several webinars have been held in collaboration between TGHN, TMRP & the UK Trials Managers Network (UKTMN) to feature the small grants

Country	Title
Uganda	The practice of pilot studies in informing the conduct of HIV clinical trials in sub-Saharan Africa: a review of study protocols
Kenya	Five implementation of Short Message Service for medication adherence in multiple programs: technical description in Kenya (PROMS Sub)
Uganda	Photovoice to explore community members' perspectives regarding health and health care challenges in Mukono District, Uganda
Tanzania	Assessment of the challenges encountered in implementing waste disposal WfM methodologies in low income countries

Home About Us Resources Global Methodology Projects MRC/NIHR Trials Methodology Research Partnership

Get started

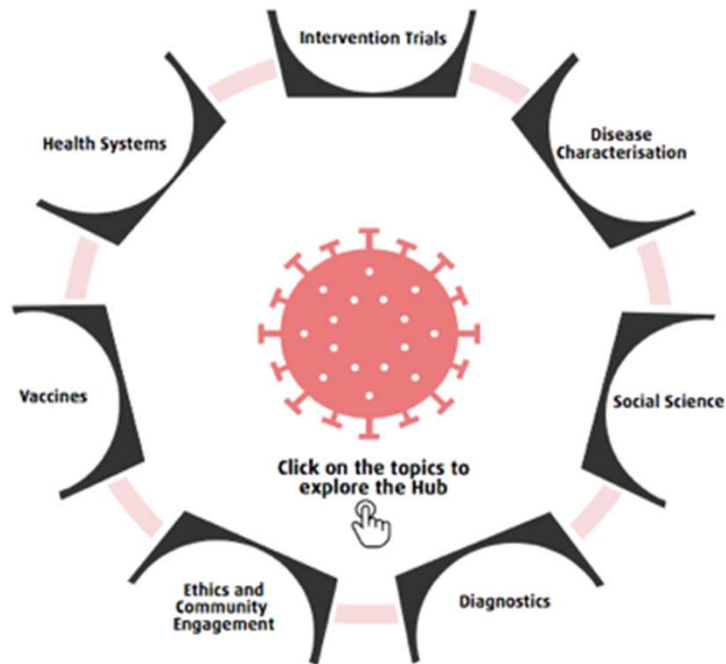
Home

This is a community of researchers who are interested in supporting the generation of more improvements in health across the globe. Clinical research needs evidence-led improved methods.

What is methodology Research? Methodology Research is research about the way we design, conduct, analyse, report. Conducting methodology research research studies will generate evidence-led improvements in the way we design research on research! For examples of methodology research, visit the [MRC-NIHR Trials Methodology Research Partnership](#)



- All diseases need an ecosystem of different types of research
- Each study requires a cycle of steps for accurate, safe & ethical data
- Findings should then be taken up into practice and policy



Steps & processes do not differ between diseases/type of research
 Need to address gaps in evidence & tackle research inequity by sharing knowledge & know-how
 between diseases, organisations & settings
 And embed research in every healthcare setting

A network of digital & physical spaces

A powerful mechanism for exchanging know-how & mobilising information

Research capacity development & knowledge exchange delivered through overlapping & interconnected focus areas

Not duplicating, but connecting excellence



Vast space for research organisations & networks to come together with research teams, health workers & policy makers



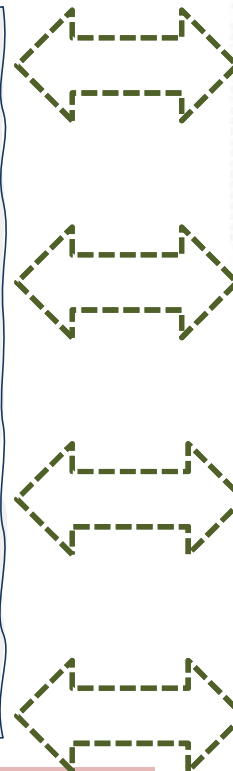
Research skills training, career development & knowledge mobilisation

- Online learning
- Webinars & workshops
- Regional capacity building programmes
- Resources & toolkits
- Process mapping
- Education & tacit learning
- Professional Development for researchers
- Essential Curriculum for health research

*Over 3 million courses taken
100,000's documents shared*

*Standards raised by providing access to tools,
methods and how-to
Delivering equity to access to knowledge*

Embedded with research capacity building mechanisms to develop lasting capable teams



Member areas (63)

Search SORT BY TITLE

Coronavirus COVID-19 Research implementation and knowledge hub to support equitable access to conducting research the globe. Implementing research within this pandemic is critical, both for understanding... VISIT SITE >	Sub-Saharan Congenital Anomalies Network sSCAN The sub-Saharan African Congenital Anomalies Network (sSCAN) is a regional Congenital Anomalies (CA) surveillance network established to provide support for congenital anomaly... VISIT SITE >	Global Health Data Science [Image] VISIT SITE >	Africa CDC African Union AFRICA CDC VISIT SITE >
ARCH Welcome to the ARCH Hub: Applying Research to Policy and Practice for Health If research is to deliver its maximum impact and positively change health outcomes, findings from health... VISIT SITE >	DAC Trials DESIGN, ANALYZE, COMMUNICATE Excellence in Clinical Studies through Better Design, Analysis and Communication VISIT SITE >	INTERNATIONAL HEALTH REGULATIONS The International Health Regulations Strengthening Programme is a UK Aid funded technical assistance programme contributing to international efforts to improve global health... VISIT SITE >	Virtual Biorepository knowledge hub - a forum for sharing and gathering information about a proposed virtual biorepository (VBR) resource for equitable and efficient access to pathogens... VISIT SITE >
Epidemic Preparedness Innovations Epidemic Preparedness Innovations (EPI) aims to bring together knowledge, tools and methods to support vaccine researchers, developers, funders and anybody working on or... VISIT SITE >	Global Consortium for Injury Research GCR Global Consortium for Injury Research (GCR) is an online consortium for people working in injury-related research. VISIT SITE >	CONNECT is a collaborative open-access web forum aimed at strengthening the capacity of health workers connecting with research and society. Health workers based in various work... VISIT SITE >	Welcome to the UK Public Health Rapid Support Team open access forum, for everyone interested in responding to outbreaks of infectious diseases. VISIT SITE >

Over 60 knowledge Hub exchanging how-to between diseases, regions & teams

This works as the barriers don't differ

Communities of practice building lasting capable research teams



Home

Welcome to the Epidemic Preparedness Innovations (EPI) web space. This platform has been set up by the Coalition for Epidemic Preparedness Innovations (CEPI). It aims to bring together knowledge, tools and methods to support vaccine researchers, developers, funders and anybody working on or interested in the field of epidemic preparedness innovations.

CEPI opens search for experts to join its Scientific Advisory Committee
 CEPI call for individuals to join its Scientific Advisory Committee, or SAC – an expert group providing broad guidance and recommendations to CEPI on R&D programmes – is now open through 12 February 2021.

CEPI funding call launches to rapidly generate additional clinical research on COVID-19 vaccines
 Launched on 28 January 2021

News

CEPI Sponsored OSMB Training Course
 The deadline for applications is Friday April 9, 2021.

Articles

Operation Warp Speed: implications for global vaccine s...
 Lancet Glob Health. 2021; Mar 26;20(2):14-16. doi: 10.1016/S2468-2667(21)00140-6. Online ahead of print. ABSTRACT Several global efforts are underway to develop COVID-19 vaccines, and experts analyse their path.

Correction to: Risks of ventilator-associated pneumonia.
 Crit Care. 2021; Mar 23;26(1):115. doi: 10.1186/s13054-021-03617-5. NO ABSTRACT PMID: 33727161. PMC: PMC7939701. DOI: 10.1186/s13054-021-03617-5#read-more.

Resources

1. Resource filter

2. Use the search box

These resources are sorted by date of publication, with the most recent displayed first.

You can filter the resources depending on their type, the region they are focused on, or the subject area using the filters below. You can further refine your search using the drop-down menus.

Are you looking for the latest news in your region, a guide to what to watch & find, that "video" or maybe you are interested in a structured online course?

You can also use the search box to look for specific words and keywords.

Why not try a few of the keywords listed in the box below?

PLEASE NOTE *** Some Chrome and Safari users have been experiencing issues with the database display, but in the meantime, if this occurs please try using another browser such as Firefox, Edge, or Internet Explorer.

Keywords:

- research ethics
- challenge studies
- research priorities
- research dissemination & publication
- clinical ethics
- resource allocation
- health systems & preparedness
- healthcare workers
- social distancing & isolation
- risk - justification & proportionality
- surveillance & apps & AI
- immunity passports & certificates
- data & sample sharing

PLEASE NOTE *** Some Chrome and Safari users have been experiencing issues with the database display, but in the meantime, if this occurs please try using another browser such as Firefox, Edge, or Internet Explorer.

ALL COVID-19 GUIDANCE AND POLICY BLOGS COURSES AND TOOLS TIPS AND AFFILIATES MULTI-MEDIA STATEMENTS REGION RESET SEARCH

Type: All Region: All Subject: All

CLICK below to explore each Working Group

Intervention Trials Diagnostics Disease Characterisation Social Science

Ethics & Community Engagement Vaccines Health Systems Grupo de Trabajo Lusófono

mesh
 community engagement network

Welcome About Resources Collaborate Discussions Mesh Events Learning & Training Themes

Groups

ALL GROUPS

Engagement at a Distance 14 Members - 9 Topics

In September 2020 Mesh hosted an interactive webinar exploring the possibilities for community engagement with health research when we cannot meet in person. What does it take to develop meaningful and valuable experiences online? What are the important lessons we have all learnt about continuing discussion on this topic and to answer questions from the webinar will

Tools and Resources

DAC Assessment Tool (DAT)

Clinical Trial Simulation

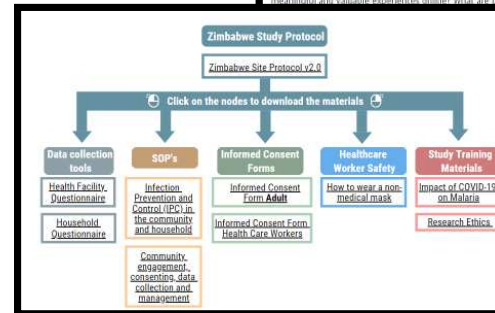
Integrating Sex & Gender

Target Policy Profile

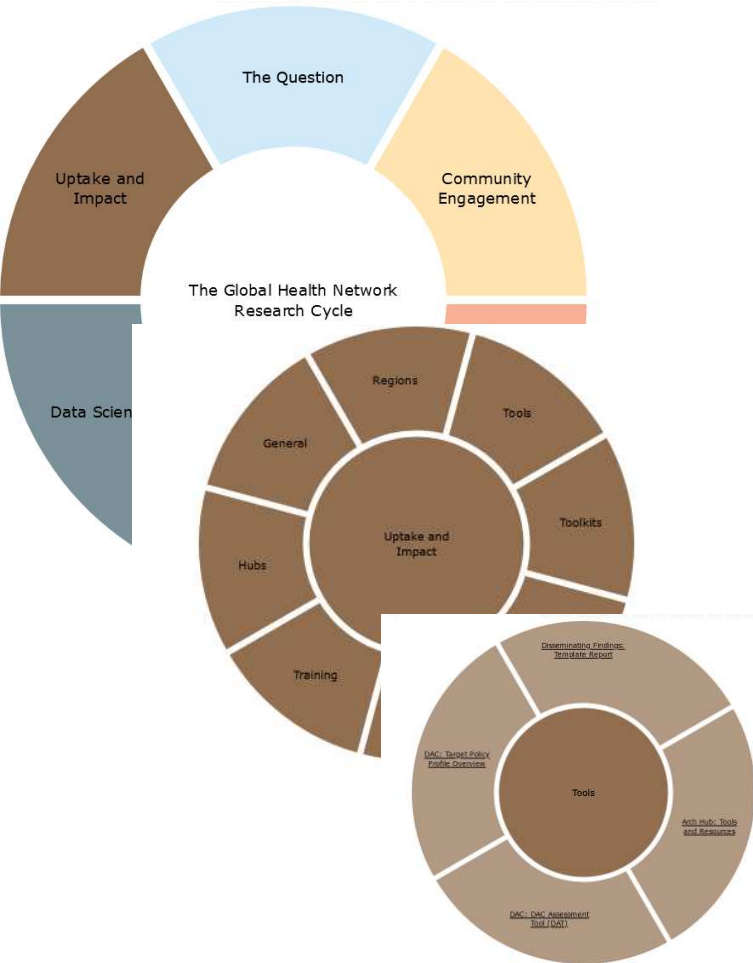
Publications

Search results table:

Title	Type	Region	Subject	Keywords
With Greek hopes Come Great Expectations: Vaccines & therapeutics	Articles	Multi-region	COVID-19	Vaccines & therapeutics
Science and humanism in the time of COVID-19	Articles	Europe	COVID-19	health systems & preparedness
Health research ethics, The Ethiopian Journal	Blogs	Multi-region	COVID-19	epidemics & emergencies
Jiménez, M, et al. (2020) La eficiencia no basta. Resource allocation, asignación de recursos escasos en situación de crisis y recomendaciones para la asignación de recursos escasos en situación de crisis	Articles	Europe	COVID-19	Resource allocation, asignación de recursos
Spain's pandemic moving into the unknown, BUS	Blogs	Europe	COVID-19	health systems & preparedness
Case COVID-19 vaccines when they're	Blogs	Americas	COVID-19	Research ethics



Myriad types of resources



Courses



= Training, strengthen skills base

Webinars



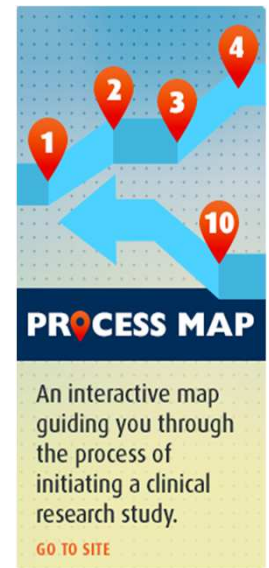
= Deliver, debate & share, lessons learnt, wider dissemination

Project materials



= Download, modify & re-use

Apps & toolkits



= Adapt & replicate

Certified open access eLearning: 130+ courses with 80+ translations



Welcome to the Global Health Training Centre



Online training

Free eLearning courses in global health research for staff of all roles, in all regions and covering all disease areas, developed by The Global Health Network in collaboration with respected partners such as the World Health Organization



Webinars

Online workshops and seminars in global health research, spanning research disciplines, regions, and therapeutic areas, aiming to foster collaboration, facilitate discussion, and celebrate advances and achievements towards faster and better research for health



Professional development

Build your professional profile, create your CV and track your career in global health research as it develops. This flexible framework covers all the competencies that should be demonstrated by a research team to carry out a successful study

RESEARCH PROCESSES & METHODS | SOCIAL SCIENCE, ETHICS & COMMUNITIES

| INFECTION, IMMUNITY & RESISTANCE | WOMEN & CHILD HEALTH

| LABORATORY, VECTORS & DIAGNOSTICS

Essential Research Skills Training Curriculum

This study was developed as a collaboration between the Special Programme for Research and Training in Tropical Diseases (TDR) and the Global Health Network (GHN).

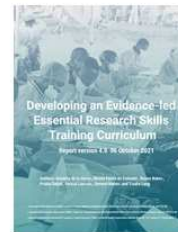
The aim of the Essential Research Skills Training Curriculum study is to identify the minimum set of skills, knowledge and key principles that would enable those with limited or no previous experience to undertake high-quality research for health. The study design was underpinned by a three-stage mixed methods consensus methodology to ensure an evidence-led approach for establishing this curriculum.

[Download Final report \(PDF\)](#)

[The Study Chart ->](#)

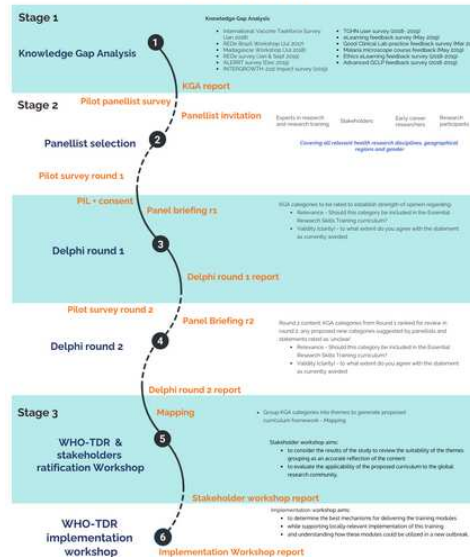
[The Research Methodology and Findings ->](#)

[Conclusion and Recommendations ->](#)

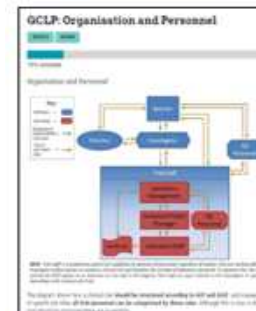


Developing an Evidence-led Essential Research Skills Training Curriculum

Delphi Study



Good Clinical Laboratory Practice



Introduction to Clinical Research

1 module

An overview of the basic concepts of clinical research, focusing on the main areas of why and how clinical research is carried out, the importance of ethics in research, and an outline of the five main clinical study designs.

[English](#) | [Español](#) | [Français](#) | [Português](#) | [Swahili](#) | [Viêt](#) | [中文](#)

Research Ethics Online Training



- Many different collaborators
- Open access, globally applicable
- Peer reviewed, regularly updated
- Certificate issued > 80% in quizzes
- > 500,000 people taken courses

Sharing expertise through webinars



Workshops

Workshops are a valuable and engaging way to learn, providing a fantastic opportunity for collective training sessions, skills transfer, networking and information sharing.

The range of workshops and format for delivering these sessions can be creatively designed to best serve the context of the learning. Initiatives such as these help to support and strengthen capacity at both an individual and institutional level. We set-up and facilitate a wide range of practical workshops in close collaboration with coordinators and study teams in diverse settings. Please do review the variety of workshops hosted across the regions that cover a breadth of topics, which have generated rich outputs from these sessions to benefit researchers globally.

AFRICA

Research in Global Health Emergencies	Africa CDC One Health workshops	Research Ethics during Epidemics
Laboratory Quality Control	Infection Prevention and Control AMR	Grant Writing Workshop
Introduction To Scientific Writing	Laboratory Quality Control	PC-NTDs Workshop
Nigeria Workshop 2021	Treatment protocols and approaches from different countries: The African Story	Africa's capacity for real-time polymerase chain reaction (RT-PCR) diagnosis of infectious diseases
Implementation of Novel Diagnostics	Improving clinical trial conduct in Africa	



Migrant Communities and the COVID-19 Pandemic: Ethical considerations

Mon 6th Jun 1:00pm – 2:00pm (BST)

During the COVID-19 pandemic, migrants have often been denied rights and placed in situations which put them at heightened risk of disease. This webinar looks at migrant communities' explicit and implicit ...



Richard T Johnson Lecture | Neurologic morbidities from pediatric cerebral malaria—Looking Beyond the Body Count

Tue 14th Jun 2:00pm (BST)

Neurological infectious diseases pose some of the greatest challenges to clinicians. The presenting clinical syndromes are often elusive, determining the causative organisms can be problematic, and th ...



Indigenous communities, 'vulnerability', and the COVID-19 pandemic

Mon 20th Jun 1:00pm (BST)

Indigenous populations around the world have historically experienced—and continue to experience—both social and economic marginalization, and as a result are at disproportionate risk during public



Introduction to Research for nurses and midwives

Thu 23rd Jun 12:00pm – 1:00pm (BST)

Global Research Nurses mission is to empower nurses and midwives to get involved in research, no matter where they work or the role they undertake. This webinar will inspire you to get started in rese ...



Global Brain Health Clinical Exchange Platform – Critical Care of the Neurologic System in COVID-19

Fri 24th Jun 2:00pm – 3:00pm (BST)

In this interactive workshop, Dr. Ayush Batra will cover critical care of the neurologic system during acute COVID-19. Chair: Ass Prof (Dr) Sherry H-Y Chou Associate Professor of Neurology (Neurocritic ...



Communicating Science to Facilitate the Uptake of Research Findings into Policy and Practice

Tue 28th Jun 1:00pm – 3:00pm (BST)

Part 2: How to write a policy brief Speaker: Dr Sohana Shafique A stakeholder mapping exercise conducted in March 2020 by the Applying Research to Policy and Practice for Health (ARCH) programme at th ...

Supporting career development

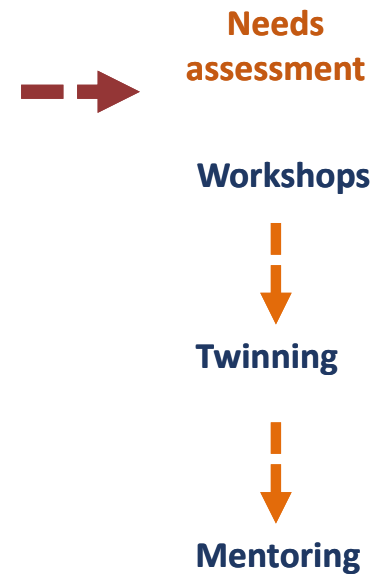
- Professional Development Scheme (PDS) created by The Global Health Network & WHO-TDR
- Records, tracks and guides professional development using *core competencies*
- Can aggregate data across teams = track and measure development over time



Core competencies

Ethics, Quality & Risk management Area

Competency	1	2	3	4	5
Ethics and Human Subject Protection	1	2	3	4	5
Design & planning of research	1	2	3	4	5
Professional skills	1	2	3	4	5
Study & site(s) management	1	2	3	4	5
Research operations	1	2	3	4	5



Increasing findability & attributing effort



THE
GLOBAL
HEALTH
NETWORK
AFRICA



Home Events Workshops Your Career Toolkits Resources Topics eLearning Country Projects Translate

Resources

Resources actively guide, teach and train researchers in setting up and running high-quality studies

A range of resources exist to truly provide active and detailed support for implementing health research studies. This includes the provision of openly accessible study documentation presented in **study profiles**, which can be downloaded and adapted to suit various study designs and settings. Structured guidance is available through the **process map** to methodically walk researchers through the various steps in the design and operational set-up of a study. Free **eLearning** courses afford the opportunity to engage in wider skills-based training, including the fundamental basics, and more specialist modules.



Study Profiles



Process Map



eLearning Courses

Digital Object Identifiers

The Global Health Network is a member of Crossref and can assign DOIs to content published on the platform. This not only improves discoverability of your content but strengthens it by ensuring it meets international standards as citable material, improves recognition for your work and also enhances collaboration within the global research community.



1 A Digital Object Identifier (DOI)

2 The benefits of DOIs include:

3 How it works:

Methodology research: mixed methods → data from 7000+ individuals in 153 countries



Open Access

Research

BMJ Open Understanding the barriers and enablers to the implementation of investigator-initiated clinical research in Ethiopia

Strategies for developing sustainable health research capacity in low and middle-income countries: a prospective, qualitative study investigating the barriers and enablers to locally led clinical trial conduct in Ethiopia, Cameroon and Sri Lanka.

Using The Global Health Network Community and Data to Assess Capacity for Regulatory Standard Clinical Research in LMICs

The Global Health Network
February 2018

Samuel R P Franzen,¹ Cleo Julius Atashili,⁵ Brian Angus,

Abstract
OBJECTIVES: In 2013, the WHO stated that unless low-income and middle-income countries have evidence-based guidance for the development of locally led clinical research, their health goals would be hard to achieve. Among the capacities needed to develop locally led clinical research are enablers to locally led clinical research.

SETTING: ...
PARTICIPANTS: ...
PRIMARY

of research, health
is important.
e barriers and
s mapping
purposively
using thematic coding anal...

Clinical trials: foundational & core,



DESIGN

1. Prioritize disease burden/target epidemiology as criteria for trial site selection
2. Use accepted and validated endpoints whenever possible
3. Map study outcome to immediate or ultimate policy impact
4. Justify effect estimates and prevalence assumptions
5. Simulate trial to ensure right sample size and optimal design
6. When feasible and relevant, apply adaptive, pragmatic, platform, or other innovative clinical trial designs

Designed to guide, teach, support, and train you and your team in setting up and running high-quality studies

ANALYZE

7. Analyze real world evidence to optimize study investments, objectives, and feasibility
8. Prioritize complete studies
9. Design decision success or reduce the subject
10. Willingness to develop
11. Adherence to standards of good clinical practice, including a focus on monitoring participant safety and study integrity
12. Use staff with experience in the therapeutic area being studied
13. Implement a real-time data analysis capability, toward improved monitoring of recruitment targets, data quality, and other metrics

Read the experiences of African, Asian and Latin American institutions working with TGHN

COMMUNICATE

14. Engage local regulators, ethics committees and policymakers before, during, and after the trial

The DAC Assessment Tool (DAT)

The DAT is a questionnaire which may be used or completed by the study PI and her/his team covering design, analyze, and communicate topics important to consider when designing informative studies. While not all points are relevant to all studies, in general they are intended to promote sound and proven scientific methodology combined with the use of recent innovations in trial design.

For example, in addition to supporting PI teams as they plan their study, fully completed DATs can serve as diagnostic guides to help study stakeholders assess whether a proposed study is likely to provide definitive answers and lead to implementable results. Completed DATs help identify gaps in study planning that need to be addressed with

[Click on General](#)

Clinical Trial Simulation

Efficient power and sample size calculations for late-phase clinical trials .

Target Policy Profile Overview

A tool to facilitate dialogue around evidence needed to effect a change in policy.

TARGET POLICY PROFILE TEMPLATE - AVAILABLE IN 6 LANGUAGES

Clinical Trial Simulation
Clinical trial simulations play a central role in the design of modern clinical trials. Simulation-based...
Mediana

Integrating Sex & Gender
Developed in partnership with the Global Center for Gender Equality at Stanford University, this overview of best practices includes links to tools & references to support sex-gender integration.

- Evidence-based catalogue of best practices, open-source simulation software, & other tools
- Now publicly available, translatable across trials, implementation research

The next five years



NEW
The Global Health Network Africa

THE GLOBAL HEALTH NETWORK AFRICA



The Global Health Network - Africa regional hub. Embedding research skills and expertise for lasting capability is important for the future of Africa-led research.

[VISIT SITE >](#)

NEW
The Global Health Network Asia

THE GLOBAL HEALTH NETWORK ASIA



The Global Health Network - Asia regional hub. Embedding research skills and expertise for lasting capability is important for the future of Asian-led research.

[VISIT SITE >](#)

NEW
The Global Health Network LAC

THE GLOBAL HEALTH NETWORK LATIN AMERICA AND THE CARIBBEAN



The Global Health Network - Latin America and the Caribbean (LAC) regional hub. Embedding research skills and expertise for lasting capability is important for the future of LMIC-led research.

[VISIT SITE >](#)



1. Shift leadership to the Global South through three regional leadership centres
2. Take mechanisms for knowledge mobilisation, capacity building & connecting excellence to scale with out partners
3. Support the whole ecosystem for health research: embedding research everywhere

WHO Collaborating Center for research information sharing, e-learning and capacity development

Thank you!

Elizabeth Allen

Co-Lead Global Health WG TMRP

TGHN Strategic Partnerships Lead

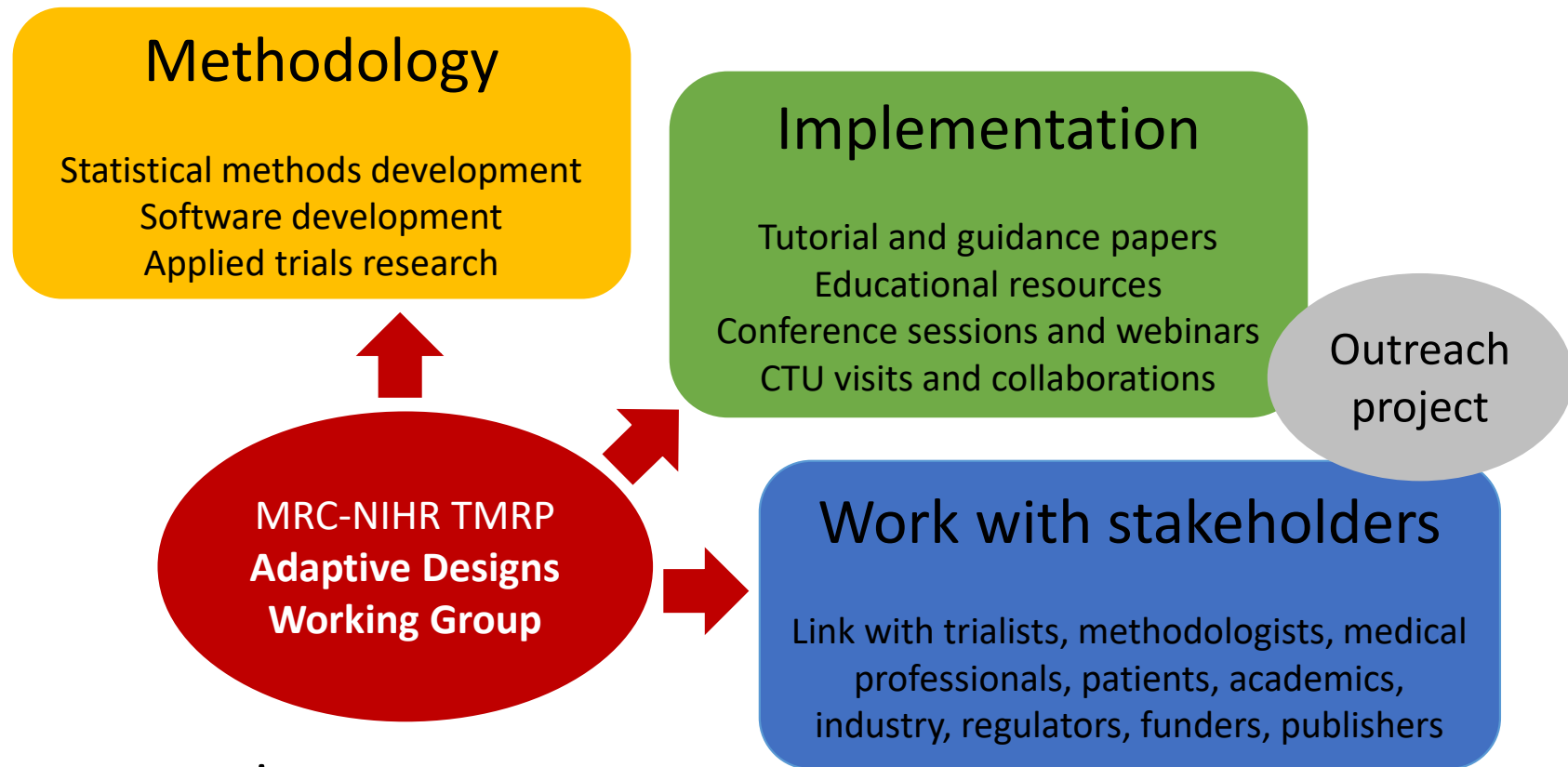
elizabeth.allen2@ndm.ox.ac.uk

www.methodologyhubs.mrc.ac.uk

<https://tghn.org/>

<https://dac-trials.tghn.org/>





Selected current projects:

- sample size simulation
- patient information sheets
- estimands
- bias-adjusted point and confidence intervals estimation
- early phase reporting guidance

>30 active members from across the UK and Ireland



Dimairo et al. *BMC Medicine* (2018) 16:210
<https://doi.org/10.1186/s12916-018-1196-2>

BMC Medicine

Dimairo et al. *Trials* (2020) 21:528
<https://doi.org/10.1186/s13063-020-04334-x>

Trials

GUIDELINE

Open Access

Development process of a consensus-driven CONSORT extension for randomised trials using an adaptive design



Munyaradzi Dimairo^{1*}, Elizabeth Coates¹, Philip Pallmann², Susan Todd³, Steven A. Julious¹, Thomas Jaki⁴, James Wason^{5,14}, Adrian P. Mander⁶, Christopher J. Weir⁶, Franz Koenig⁷, Marc K. Walton⁸, Katie Biggs¹, Jon Nicholl¹, Toshimitsu Hamasaki⁹, Michael A. Proschan¹⁰, John A. Scott¹¹, Yuki Ando¹², Daniel Hind¹ and Douglas G. Altman¹³

METHODOLOGY

Open Access

The adaptive designs CONSORT extension (ACE) statement: a checklist with explanation and elaboration guideline for reporting randomised trials that use an adaptive design



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Wilson et al. *BMC Medicine* (2021) 19:251
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Wason et al. *BMC Medicine* (2022) 20:254
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RESEARCH ARTICLE

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



Nina Wilson¹, Katie Biggs², Sarah Bowden³, Julia Brown⁴, Munyaradzi Dimairo⁵, Laura Flight⁶, Jamie Hall⁶, Anna Hockaday⁶, Thomas Jaki⁶, Rachel Lowe⁶, Caroline Murphy⁶, Philip Pallmann⁷, Mark A. Pilling⁶, Claire Snowdon¹⁰, Matthew R. Sydes¹¹, Sofia S. Villar⁸, Christopher J. Weir¹², Jessica Welburn², Christina Yap¹⁰, Rebecca Maier¹¹, Helen Hancock¹³ and James M. S. Wason¹⁴

CORRESPONDENCE

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Practical guidance for planning resources required to support publicly-funded adaptive clinical trials



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<https://doi.org/10.1186/s12916-018-1017-7>

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Burnett et al. *BMC Medicine* (2020) 18:352
<https://doi.org/10.1186/s12916-020-01808-2>

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CORRESPONDENCE

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Adaptive designs in clinical trials: why use them, and how to run and report them



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Adding flexibility to clinical trial designs: an example-based guide to the practical use of adaptive designs



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Find out more

<http://www.methodologyhubs.mrc.ac.uk/about/working-groups/>

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PANDA: A Practical Adaptive & Novel Designs and Analysis toolkit

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TMRP series - Global Health/Adaptive Designs Working Groups, 27th Sept 2022



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Outline

- Brief background and the birth of PANDA
- Intended purpose and target audience
- PANDA platform features
- Wishes and the future
- Take a few questions



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Where we are coming from ...

- Adaptive designs can be very efficient when used appropriately
- Their use in practice is steadily increasing
- Lack of practical knowledge among diverse stakeholders is still a persisting barrier
- A lot is being done and things are improving ... **but more still needs to be done!**



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Back then ... and the birth of PANDA

- Very limited practical training on adaptive designs
- Face-to-face tends to be expensive and inconvenient
- Training tends to target statisticians; other key stakeholders are left behind (clinicians, trial managers, proposal developers, etc)
- Extra burden on leading statisticians to educate trial teams throughout the trial cycle



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Purpose of PANDA and target audience

- To bridge the practical knowledge gap in adaptive trial designs
- Offers **self-paced practical learning**
- **Easily accessible** to **anyone** involved in clinical trials research interested in learning about issues around adaptive trials
- Less technical language
- One-stop shop repository (e.g., guidance on specific topics)

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Credit: <https://coldsunflowers.co.uk/baby-steps/>



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Accessing PANDA: <https://panda.shef.ac.uk/>

PANDA A Practical Adaptive & Novel Designs and Analysis toolkit

Home Types of Adaptive Designs Search About PANDA The Team Disclaimer Contact Us Admin sign in

Sample Size Re-estimation (SSR)
Group Sequential Design (GSD)
Multi-Arm Multi-Stage (MAMS)
Adaptive Population Enrichment (APE)
Response Adaptive Randomisation (RAR)

What is an adaptive design?

Adaptive trial designs aim to answer research questions efficiently while balancing ethical and scientific interests. They offer controlled flexibility to change certain aspects of an ongoing trial based on emerging trial data, such as removing ineffective therapies, stopping the trial early, changing the sample size, or targeting a specific group of patients who are likely to benefit most.

[Read more about adaptive designs](#)

General information

Adaptive designs allow researchers to make changes to certain parts of a clinical trial based on what they are learning from patient data. However, researchers need to ensure that the design is relevant to the research question and feasible; the trial is conducted and monitored correctly; data are analysed appropriately; the results are reported fully and transparently.

[Read more about general practical and statistical considerations when using adaptive designs](#)

Types of Adaptive Designs

Sample Size Re-estimation (SSR)	Group Sequential Design (GSD)
Changes to the initial sample size required to address research questions are made based on accrued information in response to incorrect assumptions or guesses made at the planning stage about study design parameters. Sample size can be increased or reduced accordingly.	Offers opportunities to stop the trial early as soon as there is sufficient evidence to make reliable conclusions about the effects of a treatment by analysing accumulating data at interim analyses. Researchers can stop a trial early because they found enough evidence of benefit or lack of benefit. The criteria for early stopping are pre-specified.
Read more	Read more

- Linear structure
- Linked content
- Easy of navigation and to find content
- Defined technical terms
- Key references for further reading
- Link to related resources (e.g., Mediana)



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I want to learn about an adaptive design

• • •

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Adaptive design

- Overview
- Traditional clinical trial design
- Can we do better?
- What is an adaptive design?
- How often are adaptive designs u...
- Opportunities and considerations...
- Resources

What is an adaptive design?

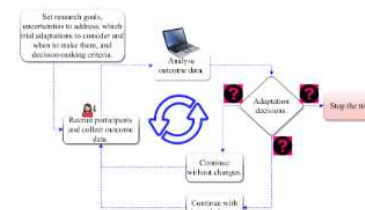
In an adaptive clinical trial design (see Figure 2), researchers start from the same place by making assumptions on design parameters. However, they cast their net wider by acknowledging uncertainties around these assumptions. This allows them to have flexibility to make necessary changes to parts of the trial once they gain more knowledge over the course of the study. These changes are informed by what they are learning from outcome data or information gathered from a group of patients already recruited as the trial progresses (interim data).

Thus, there are potentially multiple paths the trial can take depending on what the emerging data are telling them. *Similar to driving a car with your eyes open¹ using real-time travel information available to you (e.g., road signs and satellite navigation system) – you stop at a red traffic light, take the quickest route to reach your destination, change the route when there is a diversion on the current route, or abandon your journey when all routes are blocked.*

It is important to note that researchers do not make things up as they go along! Whilst flexibility has advantages, unplanned changes impact on both the validity of statistical inference and the practicalities of doing the trial and may undermine the credibility of the results. The type of changes (trial adaptations), and the criteria for making them need to be considered in advance. Changing a trial part-way through needs thought. More specifically, the criteria and timing of possible adaptations are decided at the design stage and specified in trial documents (e.g., the trial protocol and statistical analysis plans). Researchers should not compromise the scientific rigour in running the trial to produce reliable and valid results to influence practice.

In summary, the overall goal of an adaptive design is to address research questions that are relevant to clinical practice quickly and efficiently while balancing ethical and scientific interests.

Figure 2.



I want to learn about general considerations ...

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General considerations about adaptive trials

Overview Planning and design Conduct Measures to minimise operational... Data management considerations f... Considerations when writing an a... Analysis Reporting Resources

Data management considerations for adaptive trials

Adaptive designs need trial data before the trial ends to decide how it should proceed. Whilst this can provide a more efficient trial, it is imperative that the required interim data are accurate for reliable interim decisions and are available in a timely manner, which in turn needs appropriate resourcing. In addition, data or information should be accessed or shared in a controlled manner to avoid introducing [operational bias](#) in the conduct of the trial. Some key data management considerations are summarised here (see ^{1,2}).

- 1. Awareness of the trial adaptations and implications on database features**

It is essential to make the data management team aware of the potential [trial adaptations](#), their implications on the conduct of the trial, and what is expected from the data management team. This includes how the potential outcomes of the interim decisions will affect the trial's data management processes, case report forms, and any specific areas or features of the trial database. For instance, the decision to cease recruitment to a treatment arm for futility requires unblinded outcome data; likewise, adding or removing arms requires amending both data capture forms and the database. For some adaptive designs (such as adaptive population enrichment), case report forms must be updated or certain data fields blocked in the database if an interim decision is made to stop further recruitment of patients with certain characteristics. In response to a pre-planned change in eligibility criteria.
- 2. Key data for interim analyses and how they are captured**

The trial manager and data management team should be aware of the data that are required for each [interim analysis](#), where those data are obtained, and how they are recorded in the database. This will enable them to chase up missing data (e.g., from sites) or seek relevant approvals prior to the interim analysis. If some of the information is captured outside the database, there needs to be a plan for how it will be incorporated into the database or linked to other patient records, whether data will be timely obtained and whether access to these data will be timely granted by relevant external parties for adaptations to be smoothly implemented.
- 3. Real-time data capture and cleaning**

Once we know the data needed for interim analyses (which is decided at the design stage) and how they are captured in the database, priority should be given to ensure that these data are of suitable quality (i.e., no missing values, or reasons given as to why data are missing), and cleaned in a timely manner (to ensure they are accurately recorded) ready for analysis. This will ensure reliable [interim decisions](#) based on good quality data. The objective is to avoid a situation

- Specific topic (e.g., data management, costing in grant applications,
- Reporting guidance
- Resources (tutorial papers, easy-to-read books, etc)

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I want to learn more about a specific adaptive design ...

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Multi-Arm Multi-Stage (MAMS)

Overview ^

Motivation

Planning and design v

Conduct v

Analysis v

Resources v

Multi-Arm Multi-Stage (MAMS)

Overview

In summary:

- Multi-arm multi-stage (MAMS) trials evaluate several active treatments (e.g., different regimens or doses/schedules of the same treatment or completely different treatments) in a single trial;
- Treatment arms that show promise on the basis of accrued outcome data are retained for further testing, whilst those unlikely to show benefit are dropped;
- The criteria for selecting or dropping arms at interim analyses should be pre-specified;
- MAMS designs are useful where multiple competing treatments need to be reduced to a small number of most promising ones.

Video

0:00 / 3:38

Concept behind the MAMS design

- Motivation
- When is it appropriate
- Design concept
- Statistical methods
- Case studies
- Statistical software
- etc

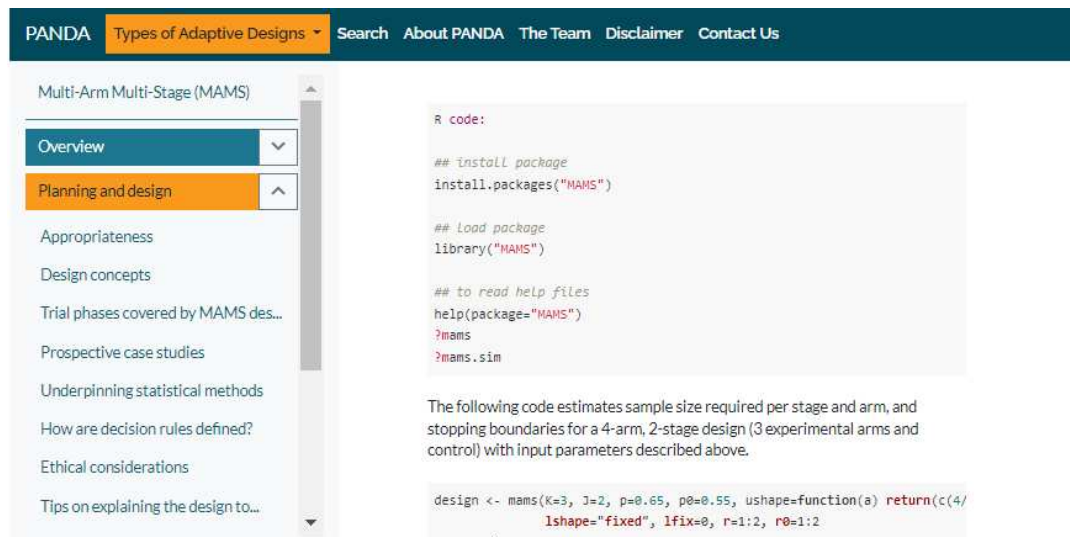
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Show me how to do it ...



```
R code:

## install package
install.packages("MAMS")

## load package
library("MAMS")

## to read help files
help(package="MAMS")
?mams
?mams.sim
```

The following code estimates sample size required per stage and arm, and stopping boundaries for a 4-arm, 2-stage design (3 experimental arms and control) with input parameters described above.

```
design <- mams(k=3, J=2, p=0.65, p0=0.55, ushape=function(a) return(c(4/
  lshape="fixed", lfix=0, r=1:2, r0=1:2
))
```

The following code simulates operating characteristics (type I error rate, expected sample size) under the null hypothesis. PANDA users may wish to increase the number of simulations and explore its impact on the precision of estimates.

```
mams.sim(nsim=10000, nMat=t(design$n * design$rMat), u=design$u, l=desig
```

The following code simulate operating characteristics (power, expected sample size) under the "least favourable configuration" of the alternative hypothesis.

```
mams.sim(nsim=10000, nMat=t(design$n * design$rMat), u=design$u, l=desig
```

- Snippets of statistical code



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Easy access to statistical implementation resources

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Multi-Arm Multi-Stage (MAMS)

- Overview
- Planning and design
- Conduct
- Analysis
- Resources

Statistical software

Statistical software

Some existing statistical software resources to support the implementation of MAMS (and platform trials) have been reviewed and functionalities summarised¹. Here, we summarise some of the statistical software resources to support the design, monitoring, or analysis of MAMS trials.

References

1. Meyer *et al.* Systematic review of available software for multi-arm multi-stage and platform clinical trial design. *Trials*. 2021;22(1):183.

Open-access software

MAMS (R package)

Supports implementation of MAMS design based on group-sequential methods for normally distributed, binary, ordinal, and time-to-event primary outcomes (see details). It accommodates:

- a number of statistical stopping boundaries;
- treatment selection rules (e.g., selecting all promising or only best performing);
- recalculation of stopping boundaries for dealing with unplanned changes (e.g., mistimed interim analysis) or after sample size re-estimation;
- simulation of operating characteristics.

rpact (R package)

Incorporates the design and analysis of MAMS trials with binary, continuous, and time-to-event outcomes based on combination test and conditional error functions (see details in this book especially chapter on "*Applications and Case studies*"). Decision rules/boundaries can automatically be recalculated during trial monitoring. Statistical inference is based on stagewise ordering approach to obtain adjusted treatment effect estimates, confidence intervals and p-values. Comprehensively covers step-by-step practical examples in the design and analysis of MAMS trials and other adaptive trials.

asd (R package)

Supports the simulation of a MAMS design that addresses phase 2 and 3 objectives simultaneously in a single trial (seamless 2/3 design) accommodating:

- treatment selection to be based on an adaptation outcome that is different



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costing

Tags: Sections: Topic:

Search results

General considerations about adaptive trials

Planning and design

All trials should be well-resourced and costed properly to deliver them successfully. Adaptive trials tend to require more resources to support them in comparison to non-adaptive t...

General considerations about adaptive trials

Planning and design

Researchers should never use adaptive designs as an excuse or remedy for poor planning. In general, adaptive designs require more planning time compared to non-adaptive designs (

- Subject of interest
- In specific sections or topics
- Tag specific



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Wishes and the future

- It is a community resource
- Work in progress (videos, content, ...)
- Help us to improve the content in PANDA
 - Feedback
 - Practical related content (e.g., lessons learned from implementing adaptive trials)
- The field is growing so we need to keep PANDA up to date
 - Content relating to new adaptive designs (e.g., adaptive platform designs, etc)
- Can this be expanded to early phase trials?

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Open-access clinical trial simulation software

Alex Dmitrienko | Sep 27, 2022

Outline

- Clinical trial simulation
- Software tool
 - R package (MedianaDesigner package)
 - Power/sample size calculations for adaptive and other trials
 - Documentation and case studies
 - Online training

Clinical Trial Simulation

Clinical trial simulation

- Clinical trial simulation
 - Only reliable approach for designing modern trials with complex designs and analysis strategies
 - Simulation-based approaches free trial sponsors from artificial restrictions
- Clinical trial optimization
 - Facilitates a disciplined simulation-based evaluation of candidate trial designs to transition from traditionally used designs to optimal designs
 - *Clinical Trial Optimization Using R* (Edited by Dmitrienko and Pulkstenis, 2017)

Open-source software tools

- Mediana package
 - R package released in 2015 to streamline the process of designing clinical trials and general research studies
 - It has become very popular in the clinical trial and general research community (downloaded over 35,000 times)
- MedianaDesigner package
 - Extended Mediana to adaptive trial designs and other trial designs

Software Tool

Software tool

- Open-source software tool
 - R package (MedianaDesigner package)
- Power/sample size calculations
 - Support for simulation-based power/sample size calculations in late-stage trials, including a broad class of adaptive trials
 - User-friendly interface with emphasis on most commonly used features and design parameters
 - Efficient clinical trial simulation engine

Two deployment options

- Desktop deployment
 - Software tool is deployed as an R package (aimed at expert users with R programming experience)
 - Available on CRAN web site
 - <https://cran.r-project.org/web/packages/MedianaDesigner/index.html>
- Cloud deployment
 - Software tool is available as a web application running in the cloud (aimed at beginners and casual users)
 - Web applications available on Mediana's cloud platform
 - <https://cloud.mediana.us>

Power/Sample Size Calculations

Supported trial designs

- Adaptive designs
 - Phase II (proof-of-concept) designs
 - Response-adaptive designs
 - Phase III (confirmatory) designs
 - Adaptive designs with sample size or event count re-estimation
 - Adaptive treatment selection designs
 - Adaptive population selection designs
- Related components
 - Optimal selection of a futility stopping rule
 - Blinded event prediction in event-driven trials

Supported trial designs

- Traditional designs
 - Traditional trials with multiple objectives
 - Support for all popular traditional multiplicity adjustments and advanced multiplicity adjustments (gatekeeping procedures)
 - Cluster-randomized trials

Documentation and Case Studies

Documentation

- Technical manuals
 - Detailed description of statistical methodology with examples
 - <https://mediana.us/medianadesigner/>
- Online user manual
 - Multiple case studies to help users come up to speed with the software tool
 - <https://medianasoft.github.io/MedianaDesigner>
- English and French versions

Online Training

Online training

- Ten-part training course
 - Adaptive designs and clinical trial simulation
 - Available on Mediana's YouTube channel
 - <https://medianasoft.github.io/AdaptiveDesignTraining>
- Introductory modules
 - First two videos (Parts 1 and 2) are aimed at a broad audience
- Technical modules
 - Remaining videos (Parts 3 through 10) are more technical and assume a statistical background

Online training

- Adaptive designs
 - Phase II (proof-of-concept) designs: Response-adaptive designs
 - Phase III (confirmatory) designs: Designs with sample size re-estimation, treatment selection and population selection
- Methodology and case studies
 - Two videos for each class of adaptive designs
 - Underlying statistical methodology and regulatory considerations
 - Case study with a detailed software demonstration

Summary

Open-access software

- Software tool
 - Open-source software tool to facilitate power/sample size calculations for traditional and adaptive trials
 - Documentation, case studies and online training
- Feedback
 - Feedback and suggestions are welcome
 - <https://github.com/medianasoft/MedianaDesigner/issues>

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Thank you!

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