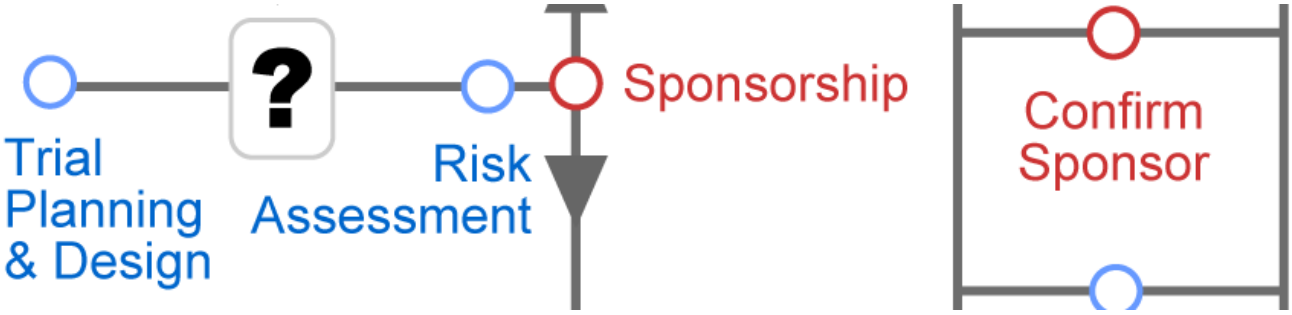
Routemap

Trial Planning & Design



Trial Planning Phase

Trial planning and design is the first station on this routemap and precedes confirming whether a trial falls within the scope of the Clinical Trial Regulations, and the Risk Assessment station. Trial Planning & Design is good practice and is relevant to all trials. This station is part of the 'trial planning phase' group of stations.

A robust trial design is essential to ensure a successful outcome. The trial design should be considered before developing the protocol. This will help ensure that all necessary practical requirements are identified early so that adequate funds are requested.

A well-documented study plan will facilitate the process of developing funding applications, ethics committee and R&D approvals / NHS permissions, and any necessary regulatory approvals.

Successful trials often share similar characteristics. They are:

- Conceptually simple and tailored to the patient group
- Address questions of clinical relevance where genuine uncertainties exist
- Avoid unnecessarily complex/restrictive entry criteria to ensure generalisability, where appropriate
- Avoid unnecessarily complex data requirements (resulting from a careful justification of each data point to be collected)
- Ensure the most appropriate choice of control arm (where appropriate)

- Ensure robust allocation concealment (where possible)
- Ensure robust blinding of intervention or appropriately blinded outcome assessments (where appropriate).

It is important to collaborate with a statistician who can help with:

- Designing your trial
- Choosing an appropriate outcome
- Providing justification of the sample size
- Advising on appropriate randomisation methodology
- Drawing up a statistical analysis plan
- Handling and structuring collected data
- Preparing and presenting interim reports to Data Monitoring Committees (DMCs), if applicable.

Patient and public involvement (PPI) is important to ensure that the question proposed is important and relevant to the people it directly affects and that the trial is practical and feasible. There is now a growing evidence base to support the positive impact that PPI can have on participation recruitment and retention in clinical trials. Many funders will require evidence of genuine involvement as a condition of funding.

The Health Research Authority have launched Best Practice Principles for Public Involvement that describes four key principles.

The National Context:

When initiating a trial, researchers should familiarise themselves with the framework in place for conducting trials. In particular:

1) The role of the National Institute of Health Research (NIHR), the process and criteria for inclusion of research on the NIHR Research Delivery Network Portfolio and the importance of public and patient involvement when conducting research.

The NIHR Research Support Service (RSS) supports researchers in England to develop and design high quality research proposals for submission to NIHR and other national, peer-reviewed funding competitions for applied health or social care research (see Funding Proposal station).

2) The role of the UK Clinical Research Collaboration (UKCRC), which provides information on the infrastructure for research in the UK. Their web pages include information on Research Delivery Network and Clinical Trial Units (CTUs),

including the process for identifying CTUs that may have expertise in coordinating multi-site research in different disease areas or with different trial designs (see UKCRC Registered CTU Networks).

3) The critical path for undertaking a clinical trial can be complex. The positioning of the stations on the route maps within this Toolkit also indicate which activities can be conducted in parallel and which activities should be completed before moving on the to the next stage.

For those new to managing trials, the NIHR Trial Managers Network (TMN) is a source of practical support and guidance on the trial management process.

4) The MRC-NIHR Trials Methodology Research Partnership (TMRP) promotes and encourages collaborative methodological research relevant to trials, with the aim of accelerating implementation of the most effective and appropriate methods. It supports workshops, conference and training in trials methodology, in addition to acting as a resource to highlight events and courses across the UK.

The MRC HTMR Network also collates outputs from various projects and initiatives under their "Guidance Pack" for trials.

The Network and individual Hubs also offer assistance to colleagues based in Clinical Trials Units and the Research Support Service when they receive enquiries, through the Methodology Advisory Service for Trials.

Further reading:

- MRC Ethics Series: Good Research Practice: Information published by the MRC giving guidelines on conducting research with human participants and their tissues and data.
- Planning a Randomised Controlled Trial: Points to Consider : A paper summarising some of the trial activities that would need to be considered.
- The NHS Research & Development Forum: The NHS R&D Forum is a network for those involved in managing and supporting R&D in health and social care. Information on key activities and developments is regularly updated.
- Trainees Clinical Trial Guidance to support NIHR trainees interested in getting involved in clinical trials.
- DIRUM is an open-access Database of Instruments for Resource Use Measurement.
- Recommendations for the design of MAMS (multi-arm multi-stage) trials.

- Avery et al. (.PDF) (2017) outlines the key issues to consider in the optimal development and review of operational progression criteria for RCTs with an internal pilot phase. Ten top tips (.PDF) for developing and using progression criteria for internal pilot studies are proposed.
- Gamble et al. (2017) recommend a minimum set of items that should be addressed and included in Statistical Analysis Plans for clinical trials.

Lancet Series on Research Waste:

- Avoidable waste in the production and reporting of research evidence by I Chalmers & P Glasziou.
- Increasing value and reducing waste in research design, conduct, and analysis by J Ioannidis et al.

Medicinal Research Council (MRC) Resources:

The MRC hosts The Experimental Medicine Toolkit and resources supporting research using health data and human tissue samples.

Further resources on Patient and Public Involvement:

- The NIHR Centre for Engagement and Dissemination leads NIHR's work to make health and care research representative, relevant and ready for use. The centre brings together its activities in patient and public involvement (PPI), engagement and participation with its strengths in research dissemination. The NIHR also provides a range of resources for PPI and for the evaluation of PPI.
- Two papers from the EPIC study (Evidence base for Patient and Public Involvement in Clinical trials) provide evidence to inform trial teams in planning for PPI in trials and optimising the impact of PPI.
- The People in Research website can be used to help find public contributors to involve in research, or for public contributors to find opportunities to get involved in research.
- Healthtalk.org showcases a range of different experiences in healthcare including participation and involvement in health research.