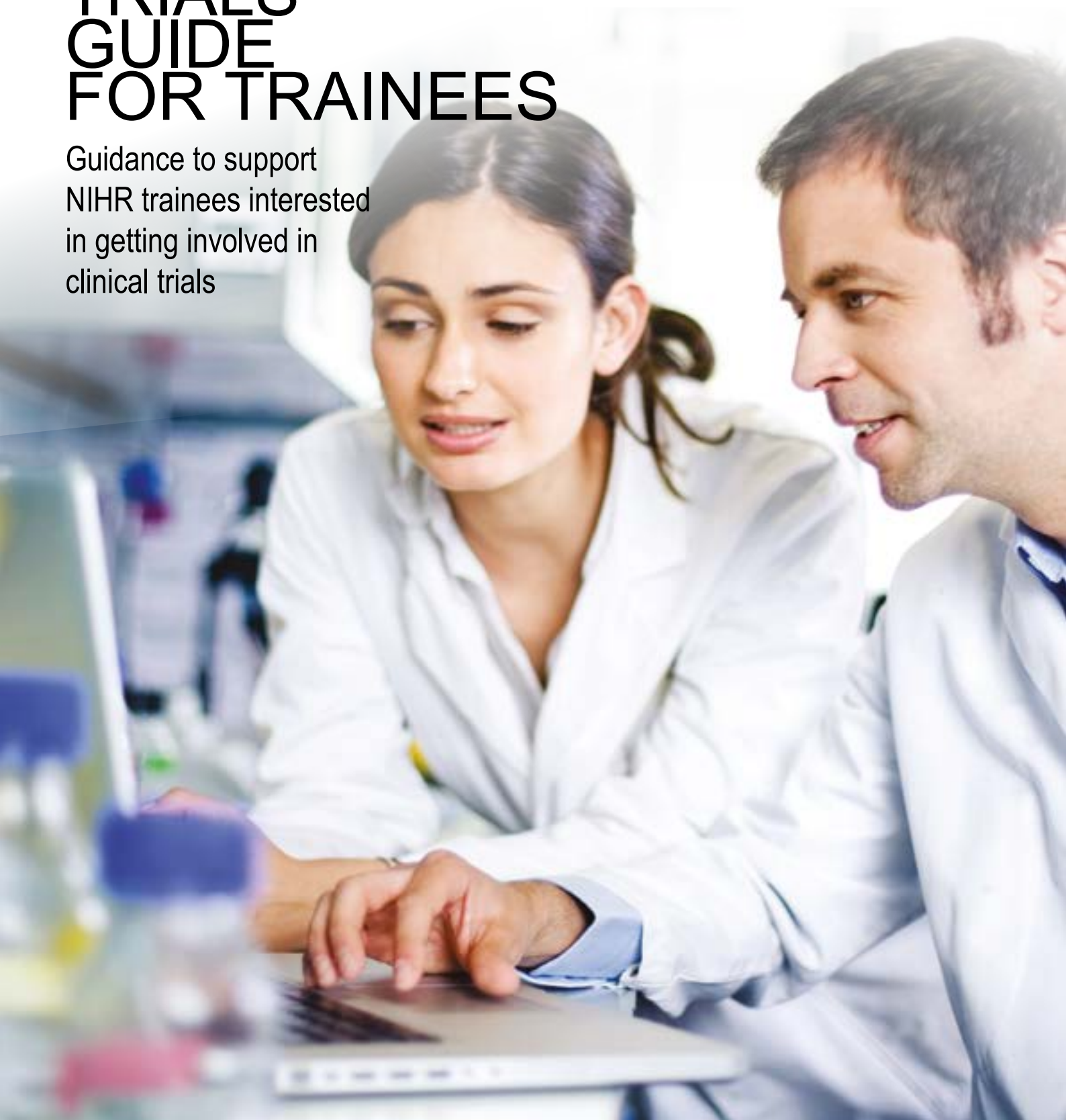


# CLINICAL TRIALS GUIDE FOR TRAINEES

Guidance to support  
NIHR trainees interested  
in getting involved in  
clinical trials



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# INTRODUCTION

Clinical trials contribute significantly to relevant research evidence developed by the National Institute for Health Research (NIHR) to support the NHS in England and are considered by many to be the gold standard method for evaluation of healthcare interventions. However, clinical trials are complex and many researchers, particularly those in the early stages of their career, find it challenging to know where to start, either to contribute to or lead a trial.

After conducting an internal report on trainee engagement in clinical trials, the NIHR Trainees Coordinating Centre began a project to develop a source of information to support individuals interested in pursuing a research career that involves the delivery of clinical trials.

This booklet is the outcome of the first stage of the project which was to determine which questions aspiring trialists need answering ahead of starting their journeys into clinical trials. Through collaboration with experts across the NIHR and conversations with existing trainees we have put together a list of questions (and answers!) that we hope trainees will find useful, as well a list of useful links to resources for further information.

We are pleased to release the first version of this booklet to mark International Clinical Trials Day 2015. As our project continues we will update this guide so that it includes the most useful and up-to-date information on clinical trials for trainees.

If you have any suggestions or feedback then please email [tcc@nihr.ac.uk](mailto:tcc@nihr.ac.uk) or tweet us [@NIHR\\_trainees](https://twitter.com/NIHR_trainees).

We would also like to thank the following people for assisting the NIHR Trainees Coordinating Centre in bringing this guide together:

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*We hope you find this  
information helpful and we wish  
you luck in your future trials!  
- The NIHR Trainees  
Coordinating Centre*

# GENERAL

## What exactly is meant by the term ‘clinical trial’?

A clinical trial is a research project that compares two or more treatments in patients with a particular condition or at risk of a condition to help generate high quality evidence about which is the more effective treatment or preventative strategy. The treatment being investigated in a clinical trial can be a medicinal product, a procedure, a device or another type of therapeutic intervention. Clinical trials are an essential part of the process of evidenced based practice and can help guide treatment decisions for both health care professionals and patients. Clinical trials are an important part of the pathway by which new medicinal products can obtain a licence from MHRA and become available for use as a new treatment in patients.

**I like the idea of becoming involved in clinical trials, but don't know how to go about this. Where do I start?**

Clinical trials are performed widely across the NHS and the Research and Development Department in your local NHS Trust will have a record of all the clinical trials active in your hospital. Many trials are also registered on national and international databases that are searchable and can identify trials in specific diseases or using specific treatments. These include the NIHR research network databases, [ClinicalTrials.gov](https://www.clinicaltrials.gov) and [EudraCT](https://www.eudraCT.eu).

Many clinical trials, especially those involving a new medicinal product or involving multiple sites, are supervised by a Clinical Trials Unit (CTU) or a Clinical Research Organisation. Your

local registered CTU will also be a good point of contact about clinical trials being performed in your area.

**What is generally involved in conducting a clinical trial?**

A clinical trial should be considered when there is uncertainty as to which of a range of treatment options or preventative strategies is more effective. A team of investigators are responsible for conducting a clinical trial and this requires meticulous planning.

Once the case for a new clinical trial has been made on medical, ethical and financial grounds then the trial needs to be designed so that it will provide the highest possible quality of evidence to guide future decision making. Trial design is a multi-disciplinary activity involving input from clinicians, trial methodologists, pharmacists, statisticians and health economists among others.

After the clinical trial is designed, the funding to pay for the trial to be conducted must be identified either from industry, who may fund a clinical trial as part of the development pathway for a new medicinal product, or from a research funding body such as NIHR or Medical Research Council or from a charity such as Cancer Research UK or the British Heart Foundation. After funding is secured, then all the necessary permissions such as research ethics approval and NHS research governance approval must be sought.

Training on the legal responsibilities when conducting a trial can be provided locally as a Good Clinical Practice (GCP) course which is offered by your local NIHR Clinical Research Network.

**How will I know whether or not a clinical trial is appropriate for my research?**

Before embarking on a clinical trial it is important to establish whether a new trial is indeed needed. You should check what research has already been done. Are there existing trials that may provide enough evidence to answer the question that you wish to address?

NIHR is committed to avoiding waste in

research and unjustified duplication of a trial is unlikely to be funded. NIHR and other research funders recommend that all clinical trials should start with a systematic review of the existing research evidence. This may reveal that there is already sufficient high-quality research evidence to answer your research question (in which case you will need to think of a new trial or project) or provide sound information to justify your research, and potentially help with your trial design.

**If a clinical trial isn't appropriate, what are my other options?**

Clinical trials are not always the most appropriate option to further your research and to support the development and evaluation of new treatments. A pilot study to assess the feasibility of conducting a clinical trial is often needed. The pilot study will allow the team of investigators to determine the likely difficulties in performing a full clinical trial and also inform the calculations on sample sizes in a full clinical trial to be done.

An observational study may be a more appropriate option if there is uncertainty about the most robust endpoints to use in a clinical trial, or if the mechanism of a potential new treatment has not been established.

**What would be a realistic timescale for a clinical trial and does this differ at all?**

The time required to design a clinical trial, produce the detailed trial protocol and secure all permissions is substantial and can take 6-12 months to complete.

The time required to perform the clinical trial will vary widely and will depend on the sample sizes needed, the frequency by which participants are recruited and the follow up period for each participant in the study.

**How many projects should I become involved in?**

If new to clinical trials, it is best to get involved in one clinical trial initially and fully understand the processes involved in more detail.

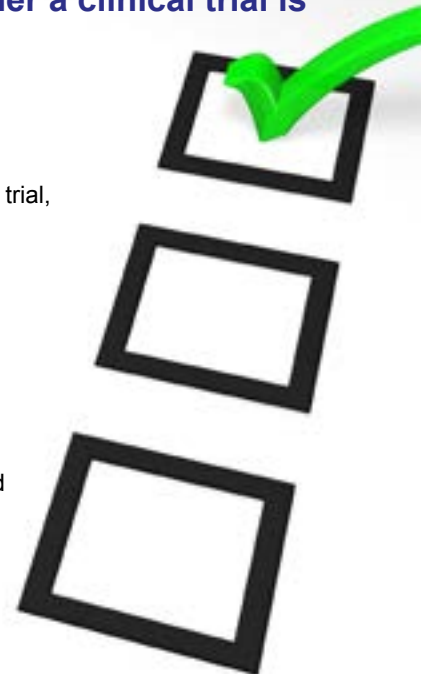
## The following simple checklist may help you decide whether a clinical trial is appropriate for your research:

### Step 1 – establish whether a relevant systematic review already exists

- ▶ If yes, and this resolves the clinical uncertainty – stop;
- ▶ If yes, and it demonstrates continued uncertainty – continue to design and justify your trial, using information from the systematic review as part of your justification;
- ▶ If yes, but the review is out of date, or of poor quality – consider updating the review;
- ▶ If no – consider doing a systematic review.

### Step 2 – establish whether relevant clinical trials exist

- ▶ Are there already clinical trials that address your research question;
- ▶ If no, continue to design and justify your trial;
- ▶ If yes, but there is clearly insufficient evidence to answer the clinical question robustly e.g. a single trial with uncertain results - use this information to justify the need for and inform the design of your trial;
- ▶ If yes, consider carrying out the systematic review as a first step.



Even if similar reviews or trials exist, if these are in a different context or setting, or address a slightly different question, your trial may still be relevant – but it will be important to be clear why it is different and still needed.

When searching for systematic reviews or clinical trials it is helpful to enlist the help or advice of a trained information specialist or medical librarian.

### Useful places to search:

- ▶ completed systematic reviews: [www.cochranelibrary.com/](http://www.cochranelibrary.com/) and <http://www.crd.york.ac.uk/CRDWeb>
- ▶ ongoing systematic reviews: [www.crd.york.ac.uk/PROSPERO/](http://www.crd.york.ac.uk/PROSPERO/)
- ▶ ongoing clinical trials: [www.ukctg.nihr.ac.uk/default.aspx](http://www.ukctg.nihr.ac.uk/default.aspx), [www.isrctn.com/](http://www.isrctn.com/), <https://clinicaltrials.gov/>, <http://apps.who.int/trialsearch/>



### What pitfalls should I be aware of in general?

By working with an experienced CTU and experienced trial methodologists then the risk of pitfalls can be reduced. However, common pitfalls include underestimating the time it takes to develop the trial protocol and secure all the permissions before starting.

Failing to recruit participants in an appropriate time-frame is also a significant pitfall. There is a risk in over predicting the ease by which specific groups of patients will be willing to participate and this can lead to unrealistic milestones being set.

Careful monitoring for serious adverse events is essential when conducting a clinical trial. If these events occur they will be reviewed by the research ethics committee and by an independent data monitoring committee who have the power to terminate a study early if there is potential that the intervention being assessed is causing harm.

◀ Photo: NIHR/Wellcome Trust's Kings Clinical Research Facility

# FELLOWSHIPS AND CLINICAL TRIALS

## Do clinical trials fit within the remit of the NIHR Integrated Academic Training Pathway and the NIHR Fellowships Programme?

NIHR spends a large proportion of its research programme budget on clinical trials. The importance of clinical trials to the NIHR means that it is very keen to attract and develop future clinical trial leaders. The NIHR Fellowships programme supports outstanding individuals to become health research leaders of the future and supporting people who will lead NIHR funded trials is very much within this remit.

**What aspects of a clinical trial can realistically be included within a Fellowship application to NIHR? Does this change depending on the level of award I apply for?**

Applicants do need to consider:

- the type (e.g. clinical trial of investigational medicinal product (CTIMP), trial of surgical intervention or trial of complex intervention);

- the scope (single or multi-centre);
- feasibility / pilot trial ([http://www.nets.nihr.ac.uk/glossary?result\\_1655\\_result\\_page=F](http://www.nets.nihr.ac.uk/glossary?result_1655_result_page=F));
- phase of trial (I to IV), and
- risk level of the trial (see <http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Submittinganotificationforatrial/index.htm> in respect of CTIMPs)

Applicants should also ensure it is commensurate with the level of award and experience of the applicant. For example, we would not normally expect a doctoral level applicant to propose leading a multi-centre randomised controlled trial of an investigational medicinal product. Fellowship applications, especially at doctoral and early post-doctoral level, will tend to focus on feasibility and pilot trials or may form a distinct add-on to an existing trial (in this case it must be clear the trial is a distinct, standalone piece of work and the role of the applicant must be clear).

**What is the difference between running a clinical trial in an NIHR Fellowship and an NIHR project grant?**

It is very important that applicants keep in mind that the proposed research project in a Fellowship application is a vehicle for training and this needs to be clearly demonstrated as part of the application.

Applications for a fellowship can't just look like a project grant application. Applicants should also consider the feasibility of the trial within the scope of a

fellowship award. NIHR research training awards are personal fellowships and not project or programme grants; therefore awards will not be extended to allow completion of a trial. Please bear in mind the lead in time for clinical trial set-up vis-à-vis the time available within the course of a fellowship.

Run-in time for drug and placebo procurement, manufacture and packaging for CTIMPs and the fact these activities must be completed, before regulatory approval can be sought, must be taken into account when planning the fellowship schedule and completing the application form. Regulatory, ethical and R&D approval can take several months and appropriate advice on the processes and timelines should be sought from the outset.

**How do I move from hypothesis-generating to clinical trials hypothesis-testing under an NIHR funded career pathway?**

There are a number of pathways, depending on a person's experience and the sort of trial needed. This might be a doctoral fellowship, for a hypothesis answered within a small single centre trial, or the doctoral/postdoctoral fellowship might be a pilot/feasibility study, then a later fellowship might support a full trial. If in doubt, please contact your local Clinical Trials Unit, Research Design Service or the NIHR Trainees Coordinating Centre.

# APPROVALS

## What parts do I need to seek approvals for in my research? Where do I obtain approval from?

There are two distinct types of approval that are required on a clinical trial:

- 1. Regulatory body approval:** This occurs at a study wide level by regulatory bodies who have a legal responsibility to approve, license or inspect particular research activities. This is the responsibility of the Chief Investigators and sponsors of a clinical trial. Please see: [www.hra.nhs.uk/research-community/applying-for-approvals/](http://www.hra.nhs.uk/research-community/applying-for-approvals/) for overall guidance and resource links to other regulatory bodies, and [www.mhra.gov.uk/Howweregulate/index.htm](http://www.mhra.gov.uk/Howweregulate/index.htm) for medicines (CTIMPs) and medical devices specifically.
- 2. NHS permission** (also referred to as Site Specific Approval): This occurs at a site level by an NHS organisation that has a duty of care to their patients or staff that will be recruited to the study at that site. This is the responsibility of the Principal Investigator at that site. In England, for NIHR Clinical Research Network Portfolio studies, these would go through the NIHR coordinated system for gaining NHS Permission (CSP), [www.crn.nihr.ac.uk/can-help/funders-academics/gaining-nhs-permissions/](http://www.crn.nihr.ac.uk/can-help/funders-academics/gaining-nhs-permissions/). The first step in the application process, the Portfolio Application Form, within NIHR CSP is the entry point for non-commercial studies applying for Clinical Research Network support: [www.crn.nihr.ac.uk/can-help/funders-academics/nihrcrn-portfolio/](http://www.crn.nihr.ac.uk/can-help/funders-academics/nihrcrn-portfolio/).

**Is there a pathway I can follow in order to obtain regulatory approval? Where can I find out information on trial governance?**

Comprehensive guidance on the support that the NIHR Clinical Research Network (CRN) can give to non-commercial researchers can be found here [www.crn.nihr.ac.uk/can-help/funders-academics/](http://www.crn.nihr.ac.uk/can-help/funders-academics/).

The NIHR CRN workforce development team have developed Good Clinical Practice training which is free to researchers which may be useful for trainees. You can find out more at the following link:

- ▶ [www.crn.nihr.ac.uk/learning-development/good-clinical-practice/](http://www.crn.nihr.ac.uk/learning-development/good-clinical-practice/)

**How much monitoring should I be doing?**

Monitoring and governance information can be found within the HRA research community website: [www.hra.nhs.uk/research-community/during-your-research-project/](http://www.hra.nhs.uk/research-community/during-your-research-project/). The monitoring of a clinical trial is usually done by the Clinical Trials Unit and/or the Sponsor institution.

**How do I, and can I, publish the protocol for a clinical trial?**

It is a condition of Research Ethic Committee (REC) favourable opinion that trials are registered: [www.hra.nhs.uk/resources/during-and-after-your-study/transparency-registration-and-publication/](http://www.hra.nhs.uk/resources/during-and-after-your-study/transparency-registration-and-publication/).

In addition, many trial protocols are published in journals, such as the online BioMed Central (BMC) series.

Please note that trial registration is not quite the same as publication of the protocol. Open access journals will often publish trial protocols and they can also be made available on a study or unit website.

Further information on approvals and when they will be required can be found by using the Clinical Trials Toolkit route map:

- ▶ [www.ct-toolkit.ac.uk/routemap](http://www.ct-toolkit.ac.uk/routemap)



# DESIGNS, TYPES AND PLANNING

## What are the different types of trials?

There are many clinical trial designs and the exact type depends on your research question. The optimum design is the one that is least likely to incur bias and will have the best chance of answering your research question. For example, if the intervention under investigation is delivered in groups, it might be most appropriate to choose a cluster randomised trial. Alternatively, if you are testing a drug to treat a chronic disease, you are more likely to consider an individually randomised design. When considering trial 'phase', the most common phases in clinical trials are phase II trials, feasibility trials, pilot trials and phase III trials of effectiveness/efficacy.

The term 'phase' usually refers to I-V:

- I = first in man
- II = proof of concept/efficacy
- III-V = effectiveness

Pilot or feasibility studies could be done for any phase of trial.

For further information, please see the following:

- ▶ [www.nihr.ac.uk/CCF/RfPB/FAQs/Feasibility\\_and\\_pilot\\_studies.pdf](http://www.nihr.ac.uk/CCF/RfPB/FAQs/Feasibility_and_pilot_studies.pdf)
- ▶ What is a pilot or feasibility study? A review of current practice and editorial policy. Arain M, Campbell MJ, Cooper CL, Lancaster GA. BMC Medical Research Methodology 2010, 10:67. doi:10.1186/1471-2288-10-67

### I've heard other trainees talk about trial designs, what does this mean?

Trial designs incorporate many aspects to optimise the ability for teams to answer their research questions. The term can refer to all aspects of the study design and how it is implemented, including all methodological aspects and the patient pathway.

Commonly used designs in trials include:

- **Parallel group trials** – groups or individuals randomised to one of two interventions (A or B) with outcomes compared at the final endpoint (either by comparing differences in a pre-specified primary outcome at a pre-specified time point, or by comparing the disease severity between baseline and follow-up).
- **Factorial trials** – groups or individuals randomised to single treatments (A or B), or a combination of treatments (A and B). This design allows you to answer two or three questions at once (e.g. is treatment A more effective than treatment B / Is the combination of treatments better than a single treatment A etc.) and enables you to consider potential interactions.
- **Cross over trials** – groups or individuals randomised to one of two treatments (A or B), followed

by a wash-out period (not always needed) then switching of treatments (B or A). These are only possible in trials of chronic conditions; they are also carried out for other conditions; however whether or not this is useful is a different question.

Whilst the above gives a brief overview, it should not be taken that this is all that needs to be considered in study design.

For more information please go to

- ▶ [www.ct-toolkit.ac.uk/routemap/trial-planning-and-design](http://www.ct-toolkit.ac.uk/routemap/trial-planning-and-design)

### How would I know which design to choose? What do I need to consider when choosing my design?

It is important to talk to people with expertise and experience in trial design and methods to help you design your study.

If you are involving a CTU, there will be experts here to support you. Otherwise, your supervisory or mentoring team should include someone with experience and/or expertise in trial design, and the your local Research Design Service will be able to provide additional advice. Trial statisticians are very important collaborators that can help with planning and designing your study.

Once you think you have chosen the best design, consider all of the ways that bias might be introduced in that design: [www.ct-toolkit.ac.uk/routemap/trial-planning-and-design](http://www.ct-toolkit.ac.uk/routemap/trial-planning-and-design).

### How can I minimise the potential for bias in my clinical trial design?

Each type of possible bias should be considered and appropriate approaches/designs implemented, such as participation bias reduced by the recruitment methods (e.g. recruited by independent researchers/clinicians).

The following is a resource commonly used for systematic reviewers and may be useful for trialists.

- ▶ [http://handbook.cochrane.org/chapter\\_8/8\\_4\\_introduction\\_to\\_sources\\_of\\_bias\\_in\\_clinical\\_trials.htm](http://handbook.cochrane.org/chapter_8/8_4_introduction_to_sources_of_bias_in_clinical_trials.htm)

### Are there any study designs that can be used in situations where it wouldn't be appropriate/feasible to conduct a clinical trial?

There should be a design that would suit a trial and issues such as ethics can be considered in the trial design. Trials are no longer restrictive and many innovative approaches are possible, even with the most complex of interventions.



## When should a pilot study be performed before a clinical trial and what methods should be used in a pilot study?

For further information on what pilot and feasibility studies should include and what the definitions are for both, please see the following links:

- ▶ [www.themedcalls.nihr.ac.uk/\\_data/assets/pdf\\_file/0019/114175/LTC-CYP-Pilot-and-Feasibility-studies.pdf](http://www.themedcalls.nihr.ac.uk/_data/assets/pdf_file/0019/114175/LTC-CYP-Pilot-and-Feasibility-studies.pdf)
- ▶ [www.nihr.ac.uk/CCF/RfPB/FAQs/Feasibility\\_and\\_pilot\\_studies.pdf](http://www.nihr.ac.uk/CCF/RfPB/FAQs/Feasibility_and_pilot_studies.pdf)
- ▶ What is a pilot or feasibility study? A review of current practice and editorial policy. Arain M, Campbell MJ, Cooper CL, Lancaster GA. BMC Medical Research Methodology 2010, 10:67. doi:10.1186/1471-2288-10-67

## How do I go about developing my research question into a clinical trial proposal?

The following is a useful document for this issue:

- ▶ [www.hra.nhs.uk/documents/2014/05/guidance-questions-considerations-clinical-trials.pdf](http://www.hra.nhs.uk/documents/2014/05/guidance-questions-considerations-clinical-trials.pdf)

## What are the advantages and disadvantages of a multi-centred trial?

Multi-site make results more generalizable to the population. They also increase the ability to recruit. Multi-centred trials require a different set of skills and expertise to single site studies and are often more challenging to conduct, e.g. more work getting sites to agree, set-up, approvals and monitoring.

## Can NIHR trainees or fellows lead a multi-centred trial?

From the point of view of the NIHR a trainee can lead a multi-centre study and it may be very beneficial for their training and development to do so, provided they have appropriate experience of clinical trials and the right support around them. Please be aware that there are both large multi-centre and small multi-centre studies; this is not a single entity. Any decision about the role a trainee will have on a clinical trial and the size and scope of that trial should be taken in discussion with supervisors and/or mentors bearing in mind the scope of the research training award in which the trial will be included and the experience and expertise of the individual. For instance, a senior fellowship holder with significant clinical trials experience may well be very suitable to lead a multi-centred trial, whereas a doctoral level fellow with limited trial experienced would be more likely to focus on smaller scale/feasibility studies.



# METHODOLOGIES

## Where would I go to find help with analysing data produced by the trial?

Analysis plans are usually written by trial statisticians with input from the study team, and the data analysis is likewise conducted by the trial statistician. This is in part to ensure robust blinding to the study intervention throughout the trial. However, where a clinical trial forms part of a higher degree, especially where a pilot or feasibility study is conducted, it would be very suitable for the PhD student to be involved in the data analysis.

The level of input will depend on the level of the fellowship that you're applying for and what can be requested in terms of the scheme. It is not recommended that fellows seek to do this on their own unless they have expertise in this area. Given that most applications will be for pilot or feasibility studies, most trainees will only be looking at descriptive analysis; however most will also involve sample size calculations, which will require input from an expert.

**Where can I get statistical assistance, such as how to do a power calculation?**

At the pre-funding application stage, this support can be sought either from the trials unit that you are collaborating with or from the Research Design Service.

**What should I be looking out for when interpreting data from clinical trials?**

The analysis plan (which should be written during the set-up period) should clearly indicate how data will be analysed and will state what the measure of efficacy/effectiveness will be. Collaboration with a statistician is essential for writing the analysis plan. Once the analysis is complete, interpretation of the data should involve the full trial team including all stakeholders. Involving patient and public involvement groups will help ensure a patient perspective in interpretation of the data.

# TEAMS AND MANAGEMENT

## Are there any managerial and/or structural frameworks available for managing a clinical trials team?

Things to bear in mind when managing a team are:

- make sure you choose the right people (provision of expertise and those conducting the research);
- ensure accountability (e.g. contracts);
- schedule meetings in advance;
- standing agenda items related to co-applicant involvement;
- publication strategy and plan in advance (linked to protocol) etc.

For further information on clinical trials management, please follow these links:

- ▶ [www.nets.nihr.ac.uk/\\_data/assets/pdf\\_file/0020/117047/tmn-guidelines-web.pdf](http://www.nets.nihr.ac.uk/_data/assets/pdf_file/0020/117047/tmn-guidelines-web.pdf)
- ▶ [www.ncbi.nlm.nih.gov/pmc/articles/PMC2917433/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2917433/)

**How do I maintain the involvement of co-applicants, particularly those over large geographical distances and who may be involved in multiple studies?**

Keeping in touch with co-applicants based in other centres is very important for the success of a clinical trial and can be difficult, especially where large geographical distances are involved. Face-to-face meetings are important to ensure a shared clear vision and plan for the conduct of the trial, especially right at the start but also through Trial Steering Committee meetings during the trial. In between, regular teleconferences are often a very effective tool of communication.

# PATIENT AND PUBLIC INVOLVEMENT



## What is public involvement in research?

INVOLVE defines public involvement in research as research being carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them.

When using the term 'public' we include patients, potential patients, carers and people who use health and social care services as well as people from organisations that represent people who use services. Whilst all of us are actual, former or indeed potential users of health and social care services, there is an important distinction to be made between the perspectives of the public and the perspectives of people who have a professional role in health and social care services.

For further information, please see Briefing Note 2 here:

- ▶ [www.invo.org.uk/wp-content/uploads/2012/04/INVOLVEBriefingNotesApr2012.pdf](http://www.invo.org.uk/wp-content/uploads/2012/04/INVOLVEBriefingNotesApr2012.pdf)

## Where do I start with patient and public recruitment?

To help you plan and undertake public involvement in your research we suggest you consider the following points:

- involve people as early as possible;
- be clear with the people you want to involve about what their role will be;
- be accessible;

- resource public involvement in research;
- offer training and support;
- clarify organisational responsibilities;
- document and record public involvement in your research.

You can find out more patient and public involvement at:

- ▶ [www.invo.org.uk/wp-content/uploads/2012/04/INVOLVEBriefingNotesApr2012.pdf](http://www.invo.org.uk/wp-content/uploads/2012/04/INVOLVEBriefingNotesApr2012.pdf)

## What are the practical issues regarding selection? Who should I involve and how do I find them?

In deciding who best to involve it is important to think about the knowledge and perspective that you are looking for from members of the public, and what support you are able to give to people who you plan to involve.

Even if your research is about informing practitioners about approaches to practice, the end user of the research will be the person receiving the practice. In some research projects you will want to consider involving both practitioners and members of the public.

Once you have considered who you would like to involve, you then need to think about how to make contact with them. Speak with colleagues and members of the public and ask for their views on how to find the people you want to involve. Allow time to make contact with organisations and individuals as finding people will nearly always take longer than you think.

For further information, please see Briefing Note 6 at:

- ▶ [www.invo.org.uk/wp-content/uploads/2012/04/INVOLVEBriefingNotesApr2012.pdf](http://www.invo.org.uk/wp-content/uploads/2012/04/INVOLVEBriefingNotesApr2012.pdf)

## What do I do if things go wrong?

Problems can often be sorted out by informal discussions, but if you think that things are going wrong it is best to act quickly. If left unresolved, problems can affect other members of a team or organisation.

If you are unable to resolve issues or if either you or the member of the public feel a more independent review of the situation is required then a more formal approach should be considered. It is helpful to outline in your planning and preparation the procedure for complaints and resolving differences so that the information is clearly available from the beginning.

For further help on this topic, please see Briefing Note 9 at:

- ▶ [www.invo.org.uk/wp-content/uploads/2012/04/INVOLVEBriefingNotesApr2012.pdf](http://www.invo.org.uk/wp-content/uploads/2012/04/INVOLVEBriefingNotesApr2012.pdf)

For further information on PPI, including the full set of Briefing Notes for Researchers, please see the links below:

- ▶ [www.invo.org.uk/wp-content/uploads/2012/04/INVOLVEBriefingNotesApr2012.pdf](http://www.invo.org.uk/wp-content/uploads/2012/04/INVOLVEBriefingNotesApr2012.pdf)
- ▶ [www.invo.org.uk/posttypepublication/public-involvement-in-clinical-trials/](http://www.invo.org.uk/posttypepublication/public-involvement-in-clinical-trials/)

# CLINICAL TRIALS UNITS

## What does a Clinical Trials Unit (CTU) do?

CTUs are specialist units which have been set up with a specific remit to design, conduct, analyse and publish clinical trials and other well-designed studies. They have the capability to provide specialist expert statistical, epidemiological and other methodological advice and coordination to undertake successful clinical trials. In addition, most CTUs will have expertise in the coordination of trials involving investigational medicinal products which must be conducted in compliance with the UK Regulations governing the conduct of clinical trials resulting from the EU Directive for Clinical Trials.

Units awarded UKCRC Registration are required to provide evidence to an international panel of experts of their capability to centrally coordinate multi-centre clinical trials (i.e. having overall responsibility for the design, development, recruitment, data management, publicity and analysis of a portfolio of trials), and that they have established robust systems to ensure conduct and delivery of clinical trials to the highest quality standards. More information on the UKCRC CTU Network and unit registration can be found at [www.ukcrc-ctu.org.uk/](http://www.ukcrc-ctu.org.uk/).

### In what ways will a CTU help me with my clinical trial?

CTUs collaborate with you to play a key role in providing the dedicated expertise and support necessary for the design, development, management, analysis and publication of high quality clinical trials. Registered CTUs will usually work with the Chief Investigator on the following:

- Coordination and preparation of the grant application including;
  - Trial development (including the question identification and appropriate design)
  - Systematic reviews (when appropriate)
  - Trial costing and staff planning
  - Discussion with disciplines required for different trial components e.g. quality of life, health economics, associated translational research
  - Sub-study development. Communication with research networks regarding feasibility and levels of interest
- Conduct of the trial including;
  - Regulatory and governance issues
  - Negotiation with international collaborators and/or industry (if applicable)
  - Management of funded trials
  - Protocol development and Case Report Forms (CRFs) design
  - Liaising with potential centres and sites, identifying and initiating participating centres, and maintaining good communications throughout to deliver required patient identification and recruitment
  - Trial set-up and permissions (e.g. ethics, MHRA etc.)
  - Central coordination and management of essential trial documents and patient data
  - Data monitoring

- Analysis and publication including;
  - Interim and final analyses
  - Report preparation (e.g. for funding bodies, MHRA, Data Monitoring Committee, Trial Steering Committee)

### How do I gain access to a Clinical Trials Unit?

The UKCRC CTU Network contains a variety of information on registered units, including a resource finder to help identify the best unit for your area: [www.ukcrc-ctu.org.uk/](http://www.ukcrc-ctu.org.uk/).

The NIHR recognises the important and crucial role played by CTUs in helping the design, development and delivery of quality research projects, and provides NIHR CTU Support Funding to selected units in England to support their NIHR activity. A list of units receiving funding and interested in collaborating on NIHR research is available from [www.nets.nihr.ac.uk/programmes/ctu](http://www.nets.nihr.ac.uk/programmes/ctu).

If you are interested in working with a CTU, you should contact them as early as possible in the process. Ideally, this should be at least 3 months before a research grant deadline (although many units prefer longer than this for open calls) in order to provide adequate time to schedule the work required and ensure the CTU is able to offer the full benefit of its experience and knowledge from the initial stages of study development. You will need to provide the CTU with information about your study and your requirements. Some CTUs will have their own collaboration request form.



# FINANCES

## What are NHS Service Support Costs?

The Department of Health guidance 'Attributing the costs of health and social care Research and Development (AcoRD)' ([www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/140054/dh\\_133883.pdf](http://www.gov.uk/government/uploads/system/uploads/attachment_data/file/140054/dh_133883.pdf)), defines NHS support costs as 'the additional patient care costs associated with the research, which would end once the R&D study in question had stopped, even if the patient care involved continued to be provided.' For example, if during a clinical trial patients require additional tests to pick up any adverse effects to the new treatment which wouldn't need to be continued if the treatment later became standard care in the NHS, the costs of these additional tests would be classed as service support costs.

### What is classified as an Excess Treatment Cost?

AcoRD guidelines classify NHS treatment costs as 'the patient care costs, which would continue to be incurred if the patient care service in question continued to be provided after the R&D study had stopped.' So continuing the example from the above the NHS treatment costs would be the costs of treating the patients in the clinical trial that would continue if the new treatment later became standard care in the NHS. Excess treatment costs arise when the new treatment being trialled is more expensive than standard care.

The difference between the treatment costs of the new intervention and standard care is classed as the excess treatment costs. Of course the new intervention may be cheaper than standard care in which case a saving in treatment costs to the NHS will be observed.

### How do I cost a clinical trial for an NIHR Fellowship application?

All NIHR application forms are accompanied by extensive guidance notes which detail what costs can and cannot be included in a particular application. Again this is another area where expert advice must be sought.



## ADDITIONAL SUPPORT

### What additional support can the Research Design Service offer?

The Research Design Service (RDS) supports research teams to develop and submit high quality applied health and social care grant applications to NIHR and other national peer-reviewed funding programmes.

We offer specialist advice on all aspects of an application including:

- designing a research study
- research methods (qualitative and quantitative)
- identifying suitable sources of funding
- involving patients and public in research design
- identifying potential academic, clinical and lay collaborators

Their advice is confidential and free of charge. For more information visit:

- ▶ [www.rds.nihr.ac.uk](http://www.rds.nihr.ac.uk)

### Who can I contact for specific information about how to fit a clinical trial into an award?

For those in NIHR ACF and CL posts within the Integrated Academic Training (IAT) Programme for doctors and dentists, please email:

- ▶ [IAEnquiries@nihrfcc.org.uk](mailto:IAEnquiries@nihrfcc.org.uk)

For queries relating to the NIHR Clinician Scientist awards, please email:

- ▶ [NIHR.ClinicianScientists@nihrfcc.org.uk](mailto:NIHR.ClinicianScientists@nihrfcc.org.uk)

For trainees in the HEE/NIHR Integrated Clinical Academic (ICA) Programme for non-medical healthcare professions, please email:

- ▶ [ICA@nihrfcc.org.uk](mailto:ICA@nihrfcc.org.uk)

For Research Methods trainees, please email:

- ▶ [Research.Methods@nihrfcc.org.uk](mailto:Research.Methods@nihrfcc.org.uk)

Queries relating to the Fellowship awards, should be directed to:

- ▶ [NIHRFellowshipEnquiries@nihrfcc.org.uk](mailto:NIHRFellowshipEnquiries@nihrfcc.org.uk)

# SUMMARY OF USEFUL LINKS

## Completed systematic reviews

- ▶ [www.cochranelibrary.com](http://www.cochranelibrary.com)
- ▶ [www.crd.york.ac.uk/CRDWeb](http://www.crd.york.ac.uk/CRDWeb)

## Ongoing systematic reviews

- ▶ [www.crd.york.ac.uk/PROSPERO](http://www.crd.york.ac.uk/PROSPERO)

## Ongoing clinical trials

- ▶ [www.ukctg.nihr.ac.uk/default.aspx](http://www.ukctg.nihr.ac.uk/default.aspx)
- ▶ [www.isrctn.com](http://www.isrctn.com)
- ▶ <https://clinicaltrials.gov>
- ▶ <http://apps.who.int/trialsearch>

## Feasibility and pilot studies

- ▶ [www.nets.nihr.ac.uk/glossary?result\\_1655\\_result\\_page=F](http://www.nets.nihr.ac.uk/glossary?result_1655_result_page=F)
- ▶ [www.themedcalls.nihr.ac.uk/\\_data/assets/pdf\\_file/0019/114175/LTC-CYP-Pilot-and-Feasibility-studies.pdf](http://www.themedcalls.nihr.ac.uk/_data/assets/pdf_file/0019/114175/LTC-CYP-Pilot-and-Feasibility-studies.pdf)
- ▶ [www.nihr.ac.uk/CCF/RfPB/FAQs/Feasibility\\_and\\_pilot\\_studies.pdf](http://www.nihr.ac.uk/CCF/RfPB/FAQs/Feasibility_and_pilot_studies.pdf)

## Trial risk levels

- ▶ [www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Submittinganotificationforatrial/index.htm](http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Submittinganotificationforatrial/index.htm)

## Regulatory body approval

- ▶ [www.hra.nhs.uk/research-community/applying-for-approvals](http://www.hra.nhs.uk/research-community/applying-for-approvals)
- ▶ [www.mhra.gov.uk/Howweregulate/index.htm](http://www.mhra.gov.uk/Howweregulate/index.htm)

## NHS permission

- ▶ [www.crn.nihr.ac.uk/can-help/funders-academics/gaining-nhs-permissions](http://www.crn.nihr.ac.uk/can-help/funders-academics/gaining-nhs-permissions)
- ▶ [www.crn.nihr.ac.uk/can-help/funders-academics/nihr-cr-n-portfolio](http://www.crn.nihr.ac.uk/can-help/funders-academics/nihr-cr-n-portfolio)

## Trial governance

- ▶ [www.crn.nihr.ac.uk/can-help/funders-academics/](http://www.crn.nihr.ac.uk/can-help/funders-academics/)
- ▶ [www.crn.nihr.ac.uk/learning-development/good-clinical-practice/](http://www.crn.nihr.ac.uk/learning-development/good-clinical-practice/)
- ▶ [www.hra.nhs.uk/research-community/during-your-research-project/](http://www.hra.nhs.uk/research-community/during-your-research-project/)

## Publishing the protocol of a clinical trial

- ▶ [www.hra.nhs.uk/resources/during-and-after-your-study/transparency-registration-and-publication/](http://www.hra.nhs.uk/resources/during-and-after-your-study/transparency-registration-and-publication/)
- ▶ [www.ct-toolkit.ac.uk/routemap](http://www.ct-toolkit.ac.uk/routemap)

## Types of trial

- ▶ [www.nihr.ac.uk/CCF/RfPB/FAQs/Feasibility\\_and\\_pilot\\_studies.pdf](http://www.nihr.ac.uk/CCF/RfPB/FAQs/Feasibility_and_pilot_studies.pdf)

## Study design

- ▶ [www.ct-toolkit.ac.uk/routemap/trial-planning-and-design](http://www.ct-toolkit.ac.uk/routemap/trial-planning-and-design)

## Minimising bias

- ▶ [http://handbook.cochrane.org/chapter\\_8/8\\_4\\_introduction\\_to\\_sources\\_of\\_bias\\_in\\_clinical\\_trials.htm](http://handbook.cochrane.org/chapter_8/8_4_introduction_to_sources_of_bias_in_clinical_trials.htm)

## Clinical trial proposals

- ▶ [www.hra.nhs.uk/documents/2014/05/guidance-questions-considerations-clinical-trials.pdf](http://www.hra.nhs.uk/documents/2014/05/guidance-questions-considerations-clinical-trials.pdf)

## Teams and management

- ▶ [www.nets.nihr.ac.uk/\\_data/assets/pdf\\_file/0020/117047/tmn-guidelines-web.pdf](http://www.nets.nihr.ac.uk/_data/assets/pdf_file/0020/117047/tmn-guidelines-web.pdf)
- ▶ [www.ncbi.nlm.nih.gov/pmc/articles/PMC2917433](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2917433)

## Patient and public involvement (PPI)

- ▶ [www.invo.org.uk/wp-content/uploads/2012/04/INVOLVEBriefingNotesApr2012.pdf](http://www.invo.org.uk/wp-content/uploads/2012/04/INVOLVEBriefingNotesApr2012.pdf)

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- ▶ [www.ukcrc-ctu.org.uk/](http://www.ukcrc-ctu.org.uk/)
- ▶ [www.nets.nihr.ac.uk/programmes/ctu](http://www.nets.nihr.ac.uk/programmes/ctu)

## NHS support costs

- ▶ [www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/140054/dh\\_133883.pdf](http://www.gov.uk/government/uploads/system/uploads/attachment_data/file/140054/dh_133883.pdf)







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