NIHR | Clinical Research Network North West London

Understanding Clinical Trials

Improving the Health & Wealth of the Nation through Research

Contents

Introduction

If you are being treated in the NHS or other setting such as a care home, hospice, school or prison you may be asked to take part in a clinical trial. Clinical trials are research studies that involve patients or healthy people and are designed to test new treatments.

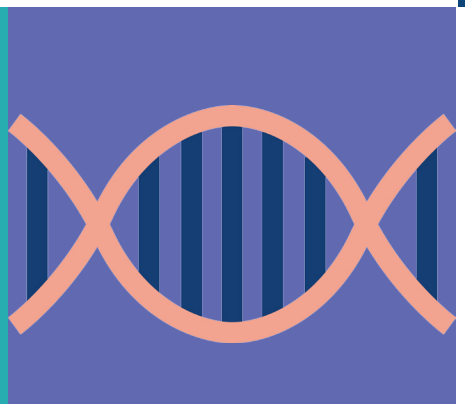
In this booklet we use the term 'treatments' to mean a wide range of health care approaches that can be tested in a clinical trial. These include drugs, vaccines, other approaches to disease prevention, surgery, radiotherapy, physical and psychological therapies, educational programmes and methods of diagnosing disease.

This booklet has been written to try to answer the many questions people ask about clinical trials. It explains what clinical trials are and why and how they are carried out. It is designed to give you the information to help you to decide whether to take part in a trial. It also includes some of the questions you may want to ask before you make a decision to join a trial.

Glossary

Controlled Trials

Controlled trials are designed to compare different treatments. Most controlled trials compare a new treatment with the standard or usual treatment by setting up two groups of people. One group, known as the trial group or intervention group, are given the new treatment. The other group is given the standard treatment and is known as the control group. In situations where there is no standard treatment the control group may not be given any treatment at all or may be given a placebo.



Placebo

A placebo treatment is designed to appear very similar to the treatment being tested. For example, in a drug trial the placebo looks exactly like the real drug, but in fact it is inactive. By comparing people's responses to the placebo and to the treatment being tested, researchers can tell whether the treatment is having any real benefit. The control group is very important. Comparing the results of the control group with those of the treatment group is the only way researchers can reliably find out whether any improvement seen with the new treatment is really due to that treatment and not just due to chance.

Blind Trials

In a blind trial, the participants are not told which group they are in.
This is because if they knew which treatment they were getting, it might influence how they felt or how they reported their symptoms. Some trials are double-blind, which means that neither the participants nor the doctors treating them know which people are getting which treatments. This also avoids the doctors' hopes and expectations influencing the results of the trial. To prevent people from guessing which treatment they are getting, all the treatments are made to look as similar as possible. For example, in a drug trial all the tablets will look the same whether they are the new treatment or the standard treatment.

Randomisation

Many trials are randomised. This means that people are allocated at random to the treatment groups in the trial, usually by using a computer programme. This is done so that each group has a similar mix of people of different ages, sex and state of health.

If it were left to the doctor or patient to decide who should get which treatment they might be influenced by what they know about their illness. Patients who are more or less likely to respond to a new treatment might all go into one particular group. In that situation, if one group did better that the other it would not be clear whether the difference was due to the treatment or because the groups were different.

If the people are allocated to the treatment groups at random, like will be compared with like. If one group does better than the other, it is likely to be because of the treatment, as the two groups are very similar in every other way.

What are clinical trials?

Clinical trials are medical research studies involving people. They aim to test whether different treatments are safe and how well they work. Some trials involve healthy members of the public. Others involve patients who may be offered the option of taking part in a trial during their care and treatment. Clinical trials are carried out to try to answer specific questions about health and illness.

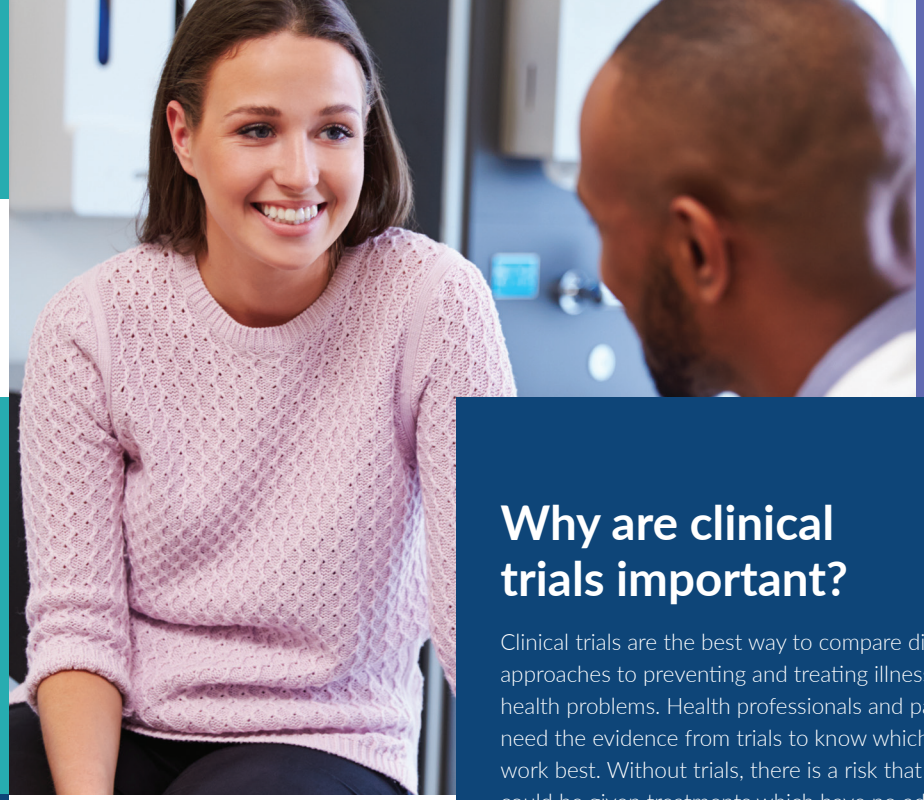
They aim to find the best ways to:

- Prevent disease and reduce the number of people who become ill
- Treat illness to improve survival or increase the number of people cured
- Improve the quality of life for people living with illness, including reducing symptoms of disease or the side effects of other treatments, such as cancer chemotherapy
- Diagnose diseases and health problems

Clinical trials cover a broad range of different types of research. For example, trials are often used to test new medicines or vaccines but can also be used to look at new combinations of existing medicines. They can also be used to test whether giving a treatment in a different way will make it more effective or reduce any side effects. Some trials are designed to try out ways to prevent a particular disease in people who have never had the disease, or to prevent a disease from returning.

The treatments being tested in these types of studies can include vaccines, but may also involve drugs or dietary supplements such as vitamins and minerals.

Clinical trials are not always about testing medicines, they can be used to test 'interventions' aimed at modifying a person's behaviour or lifestyle. This could include an educational programme designed to improve a person's understanding of their medical condition and help them to manage it more effectively, or a psychological treatment, such as the use of cognitive behavioural therapy for the treatment of anxiety or depression.



Why are clinical trials important?

Clinical trials are the best way to compare different approaches to preventing and treating illness and health problems. Health professionals and patients need the evidence from trials to know which treatments work best. Without trials, there is a risk that people could be given treatments which have no advantage, waste resources and might even be harmful.
Many treatments that are now in common use in health care were tested in clinical trials.

Some types of clinical trial are designed to look at a treatment at an early stage of its development. Researchers and regulators will look at the information they have gathered and decide whether it is safe and appropriate to continue the development of that treatment. If the treatment has no benefit or has serious side effects, it may not be developed further.

During the later stages of development of a treatment researchers will report on the benefits and risks so that doctors can decide whether or how best to use it.
It is important that the results of clinical trials are published so that others can use the information to help them make decisions about treatment and health care. Clinical trial results also form an important part of the evidence used to decide whether a particular treatment will be provided through the NHS.

Who can take part in clinical trials?

All trials have guidelines about who can take part. These are called **eligibility criteria**. Eligibility criteria are used to ensure that trials include the sort of people who may benefit from the treatment, and to make sure that people who take part are not exposed to avoidable risks.

How are people recruited to a trial?

The trial can only go ahead when it has been approved by an ethics committee.

A clinical trial is often run in a number of different locations. The person who asks you to take part in a clinical trial may not be the same person who designed and set up the study, especially if it is very large.

Social media

Sometimes studies recruit via social media if large numbers of participants are required. This method of recruitment will have been approved when the trial was first set up.

What are the benefits and risks of trials?

Clinical trials are carefully designed to minimise the risks and maximise the benefits to all who take part, whatever treatment they receive. Some trials will have very little risk involved. However, the risks of a trial may be greater when less is known about the treatment being tested. Before any drugs are first given to people, they will have been developed in a laboratory and checked for safety in animals.

In all trials the treatment may cause side effects that doctors cannot predict and that you may not be expecting. These may be unpleasant and very rarely can be life-threatening. You should be told everything that the researchers know about any possible risks and side effects and why the trial is necessary so that you can make an informed choice about whether you should take part.

If you take part in a trial you will be monitored regularly during and after the study. You will have regular tests and you may be asked some extra questions about how you are feeling. You may also be asked to fill out questionnaires or to keep a diary.

As a result of participating you will be receiving extra attention which may pick up any changes in your health, whether related to the trial or not. Not everyone receives a new treatment in a clinical trial, as any new treatments need to be compared with standard treatments (or no treatment at all, depending on the trial - this is known as a placebo). If you are asked to take part in a trial, you will be given full details to help you decide.

How are trials designed and run?

Are there different types of trial?

Clinical trials are carried out in several stages. Early stage trials usually involve a small number of patients or healthy people. When psychological treatments or educational programmes are being tested, these early stage studies can be used to fine tune the treatment before it is tested in a large group of people.
For trials of medicines and other treatments, early stage studies are carried out in a small group of people to assess safety by looking for unwanted side effects. Later stage clinical trials usually involve larger numbers of participants and are usually **randomised trials**. The process of **randomisation** is explained later in this section.

What are the Phases of a clinical trial?

A good example of how the clinical trial process helps to answer important questions is the development of new drugs. These are first developed in the laboratory to see whether they may be helpful in the prevention or treatment of a particular illness. They are then tested in animals to check their safety and to find out how they affect the body. If they look like they may be of benefit and are likely to be acceptably safe they will then be tested through different stages of clinical trials. For drugs, the different stages of clinical trials are known as phases:

Phase 1

Phase 1 is the first stage and usually involves small groups of healthy people or sometimes patients. Phase 1 trials are mainly aimed at finding out how safe a drug is.

Phase 2

By the time a drug reaches Phase 2, researchers will know quite a lot about it.

Phase 2 trials aim to:

- Test the new drug in a larger group of people to better measure the safety and side effects
- See if the drug has a positive effect in patients

Phase 3

Phase 3 trials are large and may include hundreds, or sometimes many thousands of patients from all over the UK, and often from several countries.

Phase 3 trials aim to:

- Compare the effects of newer drugs with the standard treatment, if there is one
- Find out how well the drug works and how long the effects last
- Find out more about how common and serious any side effects or risks are and about any possible longer-term problems that could develop

Phase 4

Phase 4 trials are carried out after a new drug has been shown to work and has been given a licence.

Phase 4 trials aim to find out:

- How well the drug works when it is used more widely
- The long-term risks and benefits
- More about the possible rare side effects

Phase 1 trials only pick up very common side effects. Phase 2 trials help to pick up less common side effects, but Phase 3 or 4 trials are needed to properly assess safety and risks.

Are you thinking about joining a trial?

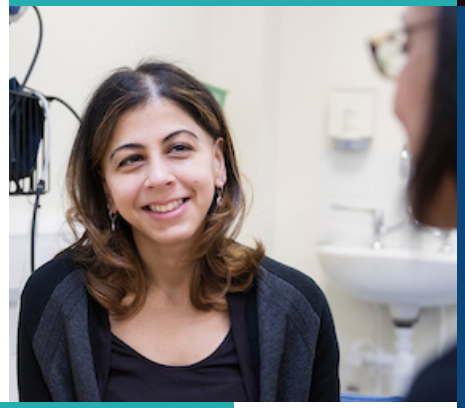
What is informed consent?

A doctor, nurse or other researcher should always ask your permission to enter you into a clinical trial. They cannot enter you into the trial if you do not give your consent. Except in some circumstances - for example in A&E or if you are being treated by paramedics and can't consent at the time. Your permission will always be sought as soon as possible.

There are a few exceptional circumstances where the consent process is different, and people might be entered into a trial without their consent. For example, in a trial of the treatment of head injuries or dementia an individual may not be able to give their consent. In these cases, consent may be obtained from a relative or other legal representative and there will be additional safeguards to protect the participants.

Where clinical trials involve children the consent process is also different and will be fully explained by the person recruiting to the trial.

It is important that you are satisfied that you have enough information to make a decision and to give your informed consent. You should feel free to ask any questions that are important to you in helping you to reach a decision. You should also feel satisfied that you have been given enough time to think about the trial and what it will mean to you.



To help you decide whether you want to take part in a trial, the researcher should explain:

- The aim of the study - what it is trying to find out
- How you will be treated and what you will need to do
- What the possible risks and benefits are

The person inviting you to take part in the trial should first discuss the study with you and answer your immediate questions. They should also give you an information leaflet about the trial that you can take away and read in your own time. You may want to discuss it with your family or friends and consider any practical issues, such as extra appointments and tests.

If you decide that you do want to take part, you will be asked to sign a form that says that you agree to join the trial and that you have decided to do so of your own free will. You will be given a copy of the signed consent form to keep. All reasonable accommodation should be made to provide information in your preferred language, in braille etc.

The process of informed consent should continue throughout the trial. The researchers should continue to give you information and answer your questions. They should let you know if any new relevant information comes up during the trial so that you can re-think your decision and withdraw if you want to.

If you decide not to take part in the trial your decision will be respected, and you do not have to give a reason. You will continue to receive the appropriate medical treatment that any other person would receive. Remember that even after you have given your consent you can leave the trial at any time without giving a reason. If you are asked, you should be given time to consider.

What happens during a trial?

As well as carrying out tests to find out how well a treatment is working, researchers will also look out for any side effects and you may be asked questions about any new symptoms you have.

Researchers will also look at the wider effects of a treatment on your life as a whole, not just its effects on symptoms. There are also detailed tests and questionnaires that are used to measure people's quality of life.

Some clinical trials will also look at the cost-effectiveness of treatments and their effects on other aspects of care, so you may also be asked about how the treatment affects other areas of your life such as:

- **Whether you are able to work during the treatment**
- **The number of times you visit your doctor and nurse**
- **Travel**

What happens at the end?

Some trials can run for many years, so it may be some time before the results of a trial are known. At the end of a trial the results will be made available to everyone who took part if they want them. They will also be published so that others can use the information to help them make decisions about treatment and health care. The researchers have a duty to publish the results, regardless of what they show, and also to show how the results add to available knowledge.

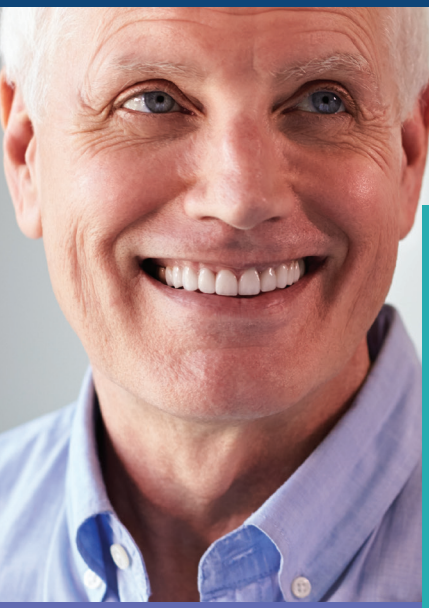
If you are having a new treatment as part of a trial you may not always be able to continue on this treatment when the trial ends. It may be some time before a new treatment is provided by the NHS. In this case you will be given the standard treatment. In some circumstances you may be able to buy the new treatment.

Will my information be confidential?

If you agree to take part in a clinical trial, all your trial records and any information that is collected about you will be kept confidential, in the same way as your medical records. The researchers cannot tell anyone that you are in the trial without asking you first. If your doctor or consultant is not the person who recruited you onto the trial, it can be helpful for them to be told you are in a trial as they will be responsible for your day-to-day health care; but they can only be told with your permission.

Once the trial has finished the results are usually published and often presented at conferences. No name or any information that can identify you will be used in any reports about the trial.

What happens during a trial?



What happens if something goes wrong?

Before any trial can start, arrangements have to be put in place in case something goes wrong and people are harmed. Research ethics committees can refuse approval for trials where there is no insurance or other provision for compensation.

Pharmaceutical companies are insured so that if a patient is damaged by their drug, compensation can be paid. However, it is rare for patients to be seriously harmed by trial treatments, although some may cause unpleasant side effects.

Trials funded by other organisations may not have this kind of insurance, but a payment may be made if something does go wrong. Individual NHS Trusts are responsible for insuring themselves against damage caused by their own studies.

Before giving your consent to take part in a clinical trial you may want to find out exactly what arrangements have been made for compensation.

How can I find out about trials that are happening now?

It can be difficult to find a suitable trial to take part in. There are a number of registers of different trials or organisations that can help you, and some of these are listed at the end of this booklet. If you would like to take part in a clinical trial but have not been asked, you should discuss it with your doctor or nurse as they will normally need to refer you. They may also know of a trial that would be suitable for you.

It is important to remember that there may not be a trial which is suitable for you.
For more information visit: www.bepartofresearch.nihr.ac.uk

What else should I know?

If I take part in a trial then what questions do I ask?

- What is the aim of the trial and how will it help people?
- What treatment will I get if I don't take part in the trial?
- How long is the trial expected to last and how long will I have to take part?
- How long will it be before the results of the trial are known?
- What will happen if I stop the trial treatment or leave the trial before it ends?

Some practical questions:

- How much of my time will be needed?
- What extra tests or appointments will I have?
- Will I need to take time off work?
- Will I need extra help from family & friends?
- Will you cover the cost of my travel and parking if I take part in the trial?
- If the trial is testing a drug, will I have to collect it from the hospital, will it be sent to me by post or will I get it through my doctor?

Some general questions:

- Will I have to fill in questionnaires or keep a diary?
- What are the possible side effects of my treatment?
- How may the treatment affect me physically and emotionally?
- Who can I contact if I have a problem? Will someone be available 24 hours a day?
- How do I find results at the end of the trial?

Where can I find more information?

Organisations

CRN North West London
www.local.nihr.ac.uk/lcrn/north-west-london

The NIHR Clinical Research Network North West London is the smallest of 15 Networks in England, by geography and population. The Network provides the infrastructure that allows high-quality clinical research to take place in the region, so that patients can benefit from new and better treatments. It helps to increase the opportunities for patients to take part in clinical research and ensure that studies are carried out efficiently.

Be Part of Research
www.bepartofresearch.nihr.ac.uk
Be Part of Research makes it easy for the public to learn about UK health and social care research. Anyone, whether they have a condition or not, can search for ethically-approved studies, and ask to take part. Every volunteer makes a difference.

DISCOVER
www.registerfordiscover.org.uk
Discover is a register of adults 18 and over living in North West London who are interested in health research and want to find out more about health research opportunities.

JDR
www.joindementiaresearch.nihr.ac.uk
A site where people with dementia, their carers or those without a diagnosis can sign up to be matched with suitable research trials.

INVOLVE
www.invo.org.uk

INVOLVE is funded by the National Institute for Health Research to promote and support active public involvement in NHS, public health and social care research. INVOLVE believe that involving members of the public leads to research that is more relevant to people's needs and concerns, more reliable and more likely to be used.

Links

Information from the NHS about clinical trials: **www.nhs.uk/conditions/clinical-trials**

MRC Clinical Trials Unit: **www.ctu.mrc.ac.uk/about_clinical_trials.aspx**

Opportunities for public involvement in clinical research: **www.peopleinresearch.org**

Acknowledgements

Understanding Clinical Trials has been adapted from the widely used booklet Understanding Cancer Research Trials, published by the UK Patient information charity Cancerbackup which has since merged with Macmillan Cancer Support.

www.macmillan.org.uk

We would like to thank the CRN West Midlands' Patient Research Ambassadors group for their contribution to updating this booklet.

Notes: