Crystal Mark 20039
Clarity approved by Plain English Campaign

NHS
National Institute for Health Research

Understanding clinical trials

Contents

Introduction

If you are receiving NHS treatment you may be asked to take part in a clinical trial. Clinical trials are research studies that involve patients or healthy people. They 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 clinical trials including drugs, vaccines, new approaches to preventing disease, surgery, radiotherapy, physical and psychological therapies, educational programmes and methods of diagnosing disease.

We have produced this booklet to answer 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 you need 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 about taking part a trial.

What are clinical trials?

Clinical trials are medical research studies to test whether different treatments are safe and how well they work. Some trials involve healthy members of the public, and others involve patients who may be offered the option of taking part in a trial during their care and treatment.

Clinical trials aim to find the best ways to:

- prevent disease and reduce the number of people who become ill
- treat illness to improve survival rates or increase the number of people cured
- improve the quality of life for people living with illness, including reducing symptoms or the side effects of treatments, such as chemotherapy, and
- diagnose diseases and health problems

Clinical trials cover a wide range of different types of research. For example, trials are often used to test new medicines or vaccines, but they 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 ways to help people change their behaviour or lifestyle. This could include an educational programme designed to improve a person's understanding of their medical condition so they can manage it more effectively, or a psychological treatment, such as cognitive behavioural therapy, to treat 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 could be harmful. Many treatments that are now commonly used 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 gathered from the trial and decide whether it is safe and appropriate to continue the developing the treatment. If the treatment has no benefit, or has serious side effects, it may not be developed further.

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

How are trials set up?

Clinical trials are designed by doctors and other specialists, with input from a wide range of people, increasingly including patients. They work together to decide what questions need to be answered. First of all they look carefully at the results of any trials that have already been carried out to find out what is already known. This is called a systematic review. A systematic review provides more accurate answers than individual trials, and also helps to identify important questions that still need to be answered through further research.

Doctors, nurses, patients and researchers work together with statisticians, trial managers and representatives from pharmaceutical companies, if relevant, to design the best possible trial. The design for the trial forms the basis of the trial protocol.

When the trial protocol is ready it is sent to a research ethics committee, an independent group of people that includes doctors, nurses, other medical staff, members of the public and sometimes lawyers.

The research ethics committee decides whether:

- the potential benefits of a new treatment are likely to outweigh the side effects
- the information provided to help people decide whether they want to take part in a trial is clear and satisfactory
- the way people will be asked to take part in a trial is appropriate
- there will be compensation for people in the trial if something goes wrong, and
- travel expenses should be offered to people who take part in the trial.

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

Who can take part in clinical trials?

All trials have guidelines about who can take part. These are called eligibility criteria. The eligibility criteria make sure that trials include the sort of people who may benefit from the treatment, and to make sure that people who take part are not put at risk.

This means that there may not always be an appropriate or suitable clinical trial for you to take part in.

There are also 'inclusion criteria'. These help the researchers to decide who can take part in the trial. Some trials only include people in a certain age group, or of one sex, or at a particular stage of their illness.

There are 'exclusion criteria' which state who cannot take part in the trial. For example, many drug trials do not allow pregnant women to take part as there may be a risk to the unborn baby. People who are already taking particular medicines may also not be able to take part as these may affect the treatment being tested.

Before you start a trial you may have to have some extra tests to see if you are eligible or to make sure that you are not likely to be at risk of being harmed by the treatments being tested. For example, if a potential side effect of a new drug is that it increases blood pressure, you may have your blood pressure checked.

How are people asked to take part in a trial?

A clinical trial is often run in a number of different hospitals or health centres. The doctor or nurse who asks you to take part in a clinical trial may not be the person who designed and set it up, especially if the trial is very large.

However, they will have been given full details on the study before agreeing to become involved. They can give you all the information you need and will be able to answer your questions.

What are the risks and benefits of trials?

Clinical trials are carefully designed to reduce any risks and get the most benefits for everyone taking 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 tested for safety on 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 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 to 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.

Sometimes this means going to your hospital or GP more often than you would normally, so bear this in mind before you agree to take part. Ask how many extra visits will be needed and consider how convenient this will be for you. Usually you will be able to claim back any extra costs you have.

You may also be asked to fill in questionnaires or keep a diary.

This extra attention means that any changes in your health, whether or not they are related to the treatment you are having, are frequently picked up and acted upon earlier than if you were not in a trial. However, some people find that the extra attention makes them worry more about their condition and prevents them from 'getting on with their life'.

It is important to remember that not everyone receives a new treatment in a clinical trial. A clinical trial needs to compare a new treatment with the current treatment, if there is one. So some people in a trial will receive the standard treatment. Nobody will know which treatment is better until the results of the trial are analysed. New treatments may not always be better and you may not be worse off if you do not receive a new treatment.

People who take part in trials often feel that they are taking an active part in their health care. They are also helping others, by helping to identify the best treatments.

How are trials supported?

Many different types of organisation support clinical trials. These include:

- the NHS
- the Medical Research Council and government departments or agencies
- charities, and
- pharmaceutical companies.

All trials, no matter who funds them, are checked and monitored in similar ways to make sure that the people who take part are protected. Each trial also has a sponsor who is responsible for running the trial. The sponsor may be the organisation funding the trial or the institution hosting the research (for example, a university).

Many of these organisations involve patients to help decide what will be researched in the future. It is essential that research takes account of the needs and interests of the people it is trying to help. Specialists often know what needs to be found out about diagnosis and treatment, but patients and their families may think other aspects of care need further research.

How are trials designed and run?

Are there different types of trial?

Clinical trials are carried out in two stages - an 'early stage' and a 'later stage'.

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 on a large group of people. For trials of medicines and other treatments, early stage studies are carried out on 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' (see page 17).

A good example of how the clinical trial process helps to answer important questions is the way new drugs are developed. These are first developed in the laboratory to see whether they may be helpful in preventing or treating a particular illness. They are then tested on 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 reasonably safe, they will then be tested through different stages of clinical trials. For drugs, the different stages of clinical trials are known as phases:

Early stage trials:

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 of a trial aims to:

- test the new drug in a larger group of people to better measure the safety and side effects, and
- see if the drug has a positive effect in patients.

Later stage trials:

Phase 3

Phase 3 of a trial is large. It may include hundreds, or sometimes several thousands, of patients from all over the UK, and often from several countries.

Phase 3 of a trial aims to:

- compare the effects of newer drugs with the current treatment, if there is one
- find out how well the drug works, and how long the effects last, and
- 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 is carried out after a new drug has been shown to work and has been licenced to be used.

Phase 4 of a trial aims to find out:

- how well the drug works when it is used more widely
- the long-term risks and benefits, and
- more about the possible rare side effects.

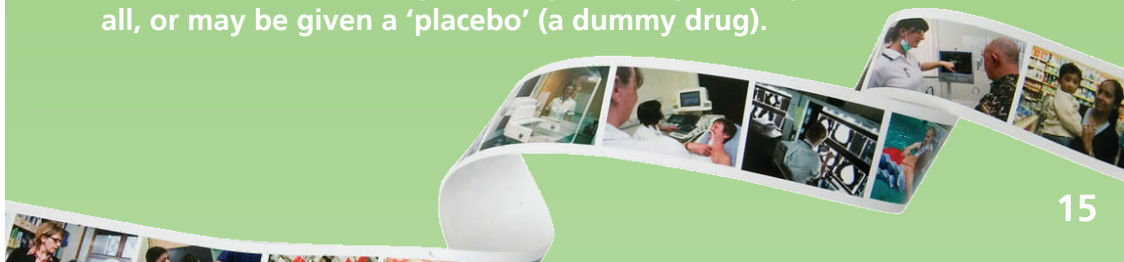
So:

- **phase 1 picks up very common side effects**
- **phase 2 helps to pick up less common side effects, and**
- **phases 3 and 4 properly assess safety and risks.**

There are three terms used to describe trials - controlled trials, blind trials and randomised trials. These different trials, and some of the words and terms you will hear used, are explained below:

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 known as the control group, is given the standard treatment. 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' (a dummy drug).



A placebo is designed to look very similar to the treatment being tested. So, in a drug trial the placebo looks exactly like the real drug, but does not do anything. 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 people taking part 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 the people taking part and the doctors treating them do not know who is getting the new treatment. This 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. So in a drug trial, all the tablets will look the same, whether they are the new treatment or the standard treatment.

Randomised trials

Many trials are 'randomised'. This means that people are put in the trials treatment groups at random, usually by using a computer programme. This is done so that each group has a similar mix of people of different ages, sexes and states 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 than 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 put into 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 similar in every other way.

Why do some trials need a lot of people?

Some clinical trials need thousands of people to take part. This is because sometimes the difference between the effects of two treatments is sometimes small. So large numbers of people are needed to find out reliably whether one treatment is better than another. Statisticians give expert guidance to help the researchers make sure a trial includes enough people to give reliable results.

Why do trials sometimes take many years?

It can sometimes take a long time to get the results of a particular trial. This could be because:

- it takes a long time to recruit enough people to take part in the trial
- the trial involves giving a treatment over a long period of time, or
- it is important to follow up patients over a long period of time to get a reliable picture of the long-term effects of a treatment.

Are you thinking about joining a trial?

What is 'informed consent'?

A doctor, nurse or other researcher should get your permission (your 'informed consent') before entering you into a clinical trial. They cannot enter you into the trial if you do not give your informed consent.

However, there are a few exceptional circumstances when people might be entered into a trial without their informed consent (for example, in a trial of the treatment of head injuries or dementia, an individual may not be able to give their informed consent). In these cases the informed consent may given by a relative or other legal representative.

If a clinical trial involves children, the process of getting informed consent is different and will be fully explained.

To help you decide whether you want to take part in a trial, the researcher or doctor 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, and
- what the possible risks and benefits are.

It is important that you are satisfied that you have enough information to make an informed decision and so give your informed consent.

You should feel free to ask any questions that are important to help you make 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.

The person asking you to take part in the trial should first discuss the study with you and answer any questions you have at the time. They should also give you an information leaflet for you to take away and read in your own time. You may want to discuss it with your family or friends, to 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 consent to confirm that you agree to join the trial and have decided to do so of your own free will. You will be given a copy of the signed form to keep. If English is not your first language, the trial should be explained to you in the language you prefer. You should also be given a consent form that has been written in a language of your choice.

The researchers should continue to give you information and answer your questions throughout the trial. They should let you know if any new information comes up during the trial so that you can re think your decision, and withdraw from the trial 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.

And remember, if you give your consent you can leave the trial at any time without giving a reason.

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 ask about any new symptoms you have.

Researchers will also look at the effects a treatment has on your life as a whole, not just its effects on your symptoms. There are also detailed tests and questionnaires to measure your quality of life, so you may be asked if you:

- can carry out your usual day to day activities
- need any extra help around the home or to look after your family, or
- feel happy or sad, anxious or depressed.

Some clinical trials will also look how cost effective treatment is and it's effects on other aspects of care. So you may also be asked how the treatment affects other areas of your life such as:

- whether you can work during the treatment
- the number of times you visit your doctor and nurse, and
- how you travel.

What happens at the end of a trial?

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 available to everyone who took part. They will also be published so that others can use the information to help them make decisions about treatment and health care. The researchers must publish the results, regardless of what they show, and state 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 the records of your trial 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 taking part in the trial without asking you first. If your doctor or consultant is not the person who recruited you onto the trial, it would be helpful for them to know you are in a trial, but they can only be told with your permission.

Once the trial has finished, the results are often presented at conferences. No name or any information that can identify you will be used in any reports about the 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 to allow a trial if it has no insurance or other compensation arrangement.

Pharmaceutical companies are insured so that if a patient is harmed 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 harm caused by their own studies.

Before agreeing to take part in a clinical trial you may want to find out exactly what arrangements there are 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 lists of different trials or organisations that can help you, and some of these are set out 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 about 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.

What should I ask before I join a trial?

These are some of the questions you may like to ask before deciding whether to take part in a clinical trial.

General questions:

- What is the aim of the trial and how will it help people?

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- Who is funding the trial?

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- What treatment will I get if I don't take part in the trial?

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- **How long is the trial expected to last and how long will I have to take part?**

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- **How long will it be before the results of the trial are known?**

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- **What will happen if I stop the trial treatment or leave the trial before it ends?**

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Practical questions:

- **How much of my time will I have to give?**

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- **What extra tests or appointments will I have?**

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- **Will I need to take time off work?**

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- Will I need extra help from family and friends?

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- Will you cover the costs of my travel to take part in the trial?

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- 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 from my doctor?

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- Will I have to fill in questionnaires or keep a diary?

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- What are the possible side effects of my treatment?

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- How could the treatment affect me physically and emotionally?

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- **Who can I contact if I have a problem? and will someone be available 24 hours a day?**

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- **How do I find out the results at the end of the trial?**

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Where can I find more information?

Links

Information from the NHS about clinical trials
www.library.nhs.uk/trials

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

Database of ongoing and completed clinical trials in the UK
www.controlled-trials.com/mrct

UK Clinical Trials Gateway:
www.controlled-trials.com/ukctr

Directory of clinical trials funded by the pharmaceutical industry
www.ifpma.org/clinicaltrials

The U.S. National Institutes of Health ClinicalTrials.gov
www.clinicaltrials.gov

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

Organisations

UK Clinical Research Collaboration (UKCRC)
www.ukcrc.org
The UKCRC is a partnership of organisations working to establish the UK as a world leader in clinical research. Improving the public's understanding of clinical research, and increasing patient and public involvement in clinical research, is an important aim of the UKCRC.

NIHR Clinical Research Network Coordinating Centre
www.crncc.nihr.ac.uk
The NIHR Clinical Research Network Coordinating Centre (NIHR CRN CC) supports clinical research and helps to support clinical trials and other well-designed studies across the UK.

Medical Research Council
www.mrc.ac.uk
For over 50 years the Medical Research Council (MRC) has been performing clinical trials to find the answers to important questions about public health and improve clinical care. MRC trials evaluate options across health care including diagnostic screening, assessing new treatments against existing treatments, the effect of advice to change behaviour and prevent disease, managing long-term conditions, and rehabilitation. Many of these studies also help us understand how the body's processes work to influence health.

INVOLVE
www.invo.org.uk
INVOLVE is funded by the National Institute for Health Research to promote public involvement in NHS research, and research relation to public health and social care. INVOLVE believes 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.

Association of Medical Research Charities
www.amrc.org.uk
The Association of Medical Research Charities (AMRC) is a membership organisation of the leading medical research and health research charities in the UK. AMRC aims to help the charities be more effective and to advance medical research. It does this by developing best practice, providing information and guidance, improving public information about research and science, and influencing the Government.

The James Lind Library
www.jameslindlibrary.org
The James Lind Library is a web based resource created to help people understand clinical trials. It contains short essays explaining the principles of trials, and illustrates these with key passages and images from books and journal articles, commentaries, biographies, portraits, and other material showing how tests have developed over the centuries.

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