

Introduction to Clinical Trials and Key Terms

It is difficult to compare scientifically people's experiences of MS. Extensive placebo-controlled clinical trials are required to research disease patterns and the effectiveness of new treatments.

What is a clinical trial?

Clinical trials are research studies that test the effects of "health interventions" on people. Such health interventions are most commonly new drugs or treatments, though clinical trials may also examine the effects of other health interventions such as diagnostic methods, surgeries or procedures, technological devices, and educational methods.

Clinical trials usually only begin once pre-clinical laboratory studies have already shown promising results. These initial studies typically involve human cells or animals.

The most reliable way of showing whether a new intervention is safe, effective or better than what is already available is through clinical trials.

What is a protocol?

A protocol is a set of rules on which the clinical trial is based. The protocol will describe who may participate, the length of the study, and give details of the schedule, procedures, medications and dosages.

What are the clinical trial phases?

If the pre-clinical laboratory based studies have shown promising results the health intervention may go to trial stage. The trials themselves have to progress through a set sequence of four "phases" to ensure the data collected is reliable and all those taking part are protected. Phase I must be successfully completed prior to moving on to Phase II and so on for all remaining Phases. Testing can be stopped at any time in any phase in order to ensure the safety of participants.

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What is informed consent?

Informed consent aims to protect those taking part in the clinical trial by providing them with all the key facts. These facts are included within informed consent documents that are distributed to potential participants by those managing the trial. Information includes:

- Why the research is being done
- What the researcher wish to accomplish
- What will be done during the trial and the timescale
- What risks are involved in the trial
- What benefits can be expected from the trial
- What other treatments are available

- The fact that study patients (subjects) have the right to leave the trial at any time
- These documents should be studied carefully, and any questions should ask before a decision is made. If a person decides to join a clinical trial they will be asked to sign a consent form. Under informed consent, participants may ask questions or withdraw at any time before, during or after the trial.

Who can participate?

All clinical trials will have guidelines regarding who may participate. The type of factors that are outlined within these guidelines may include: age, type of MS and degree of disability.

These factors are divided into "inclusion factors" which allow a person to participate, and "exclusion factors" which prevent a person from participating. Such inclusion and exclusion factors are used to identify appropriate participants and enhance safety. These criteria also help to ensure that the research will provide answers to the questions being studied.

Who sponsors clinical trials?

Clinical trials are sponsored by a variety of organizations including: government bodies (such as national health institutes); pharmaceutical and biotech companies; academic institutions; health care institutions, and companies that develop medical equipment. Those sponsoring the trial will hire medical researchers who will work in a wide variety of settings to conduct the clinical trial. Typical locations include: hospitals, medical centers, universities, and community clinics.

Typically the costs of the trial are paid on a per patient basis. The medical care to the participants is often provided free, though sometimes participants are asked to pay a small fee.

What happens during a clinical trial?

The clinical trial process will vary according to the type of research being completed. The team will include doctors, nurses, social workers and other health care professionals. Participant's health will be checked at the beginning of the clinical trial, monitored throughout and the researchers will remain in contact once the trial is completed. All participants will be given specific instructions that will outline the process.

Often clinical trials will require more tests and visits to doctors than would be required with standard treatment. For example, participants may be required to have regular MRI's or blood tests.

What is a placebo?

A placebo is a pharmacologically inactive substance (or inactive medical procedure) designed to mimic the experimental drug (or procedure) being

tested. In a placebo controlled study, participants may be randomised to receive either the active or the inactive form of treatment, but participants are unaware which is which (see "What is a blinded or double blinded study").

In clinical trials the treatment under trial is often compared to a placebo to assess its effectiveness and eliminate effects due to purely psychological causes.

What is the placebo effect?

The alteration in a patient's condition following treatment with a placebo (see above). The inactive nature of placebo treatment means such effects are due to the patient's expectations or to other unexplained psychological effects, rather than to any direct physiological or pharmacological action.

What is a control or control group?

A control group is a standard by which experimental observations are measured. In phase II and III clinical trials, patients are randomly divided into at least two groups. One or more receive the experimental treatment (sometimes different doses are tested in more than one "active" groups) while the other, the control group, receives the standard treatment available or the placebo.

Many medical researchers consider placebo controls to be the most efficient, cost effective and decisive way to determine safety and efficacy of experimental treatments. However, questions remain over the ethics of utilising placebo controls when partially effective treatment is available on the market.

What is a blinded or double blinded study?

A "blinded study" (sometimes known as a "masked study") is one in which the participants do not know whether they are in the experimental group receiving the experimental treatment, or are in the control group receiving the standard treatment or placebo.

A "double blinded study" (or "double masked study") is one in which neither those participating nor the research staff know which participants are in the experimental group receiving the experimental treatment, or the control group receiving the standard treatment or placebo. The aim is that neither the participant nor the doctor expectations can influence the results.

What are side effects?

Side effects or adverse reactions are unwanted, unpleasant or harmful consequences of treatment. In clinical trials all experimental medical interventions must be evaluated for short, medium and long term side effects.

What are the benefits and risks associated with clinical trials?

Joining a clinical trial has both benefits and risks. The benefits include:

- Having an active role in your medical care

- Gaining access to treatments that are not publicly available
- Having expert medical care at leading health establishments throughout the trial
- Contributing to the advancement of medical research
- In some cases a beneficial "placebo effect" is seen where patients experience medical benefit as a result of receiving the inactive placebo treatment

The **risks** include:

- Having adverse side effects for the experimental medical intervention.
- Experiencing ineffective treatment and possibly one that turns out to be worse than not being treated
- The protocol may require a lot of your time for tasks associated with the trial, eg trips to clinics, treatments and hospital stays

What should I know before I join a clinical trial?

It is important for anyone considering participating in a clinical trial to know as much as possible about the study prior to joining. Participants should feel comfortable asking questions and researchers should answer in a manner that participants can understand.

What questions should I ask? ■

Should I continue with my primary healthcare provider while participating in a clinical trial?

Clinical trials tend to provide short term treatment for the medical condition under examination and do not cover all health care issues of participants. It is therefore essential that participants continue with their primary healthcare provider. In addition, this enables the research team to work with participants' primary healthcare providers and ensure other medications do not conflict with that being researched.

Can I leave the clinical trial once it has begun?

Participants may leave a clinical trial at any time. Should participants decide to leave, they should inform the research team of the reason for this decision.

Do I get paid for participating in a clinical trial?

Though some clinical trials pay participants, this should not be assumed as many do not. Most clinical trials will reimburse participants expenses that are associated with the research, for example travel and accommodation.

Consumer Involvement

There is increasing awareness of the importance of involving the consumer (person with MS) and their partner, career and family, in all aspects of clinical trials. This could include playing a role in selecting the drug or intervention to be tested, planning the trial design, the outcomes to be measured, the way in which the data would be analysed and how the results should be interpreted

(Hanley et al). The consumer's role in outcome measurement is particularly important. Although there is a wide range of measures from clinical scales to counting abnormalities on MRI scans it is important that some measure incorporating the consumer's perspective is included in the study. In other words some measure of the impact of the disease as experienced by the person should be included. A further role of the consumer is in the scientific development of such scales as they must, by in definition be based on in-depth interviews with them.

Steps to increase consumer involvement clinical trials are already underway in many countries and are likely to continue until it becomes a reality.