Welcome to the What are Clinical Trials? section of the EBM Express course. EBM Express is designed to build your understanding of evidence-based practice in short manageable blocks of content.

In this section, we'll be looking more closely at clinical trials, defining the types of clinical trials and talking about clinical trial phases. Throughout we'll be using the definitions that are used by the National Library of Medicine, specifically as they define publication characteristics within the medical subject headings or MESH.

Let's start by reviewing the three primary types of clinical trials that were discussed previously in EBM Express. To begin let's look at NLM's definition of a clinical trial in general. They state that a clinical trial is a clinical study in which participants are assigned to receive one or more interventions so that researchers can evaluate the interventions on biomedical or health related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic or other types of interventions. In other words, a clinical trial is a study that can look at a variety of interventions, includes participants that are assigned in a predetermined and specific way and that evaluates the intervention.

The National Library of Medicine defines a controlled clinical trial as a clinical trial involving one or more test treatments, at least one control treatment, specified outcome measures for evaluating the studied intervention and a bias-free method for assigning patients to the test treatment. The treatment may be drugs, devices or procedures studied for diagnostic, therapeutic or prophylactic effectiveness. Control measures include placebos, active medicine, no treatment, dosage forms and regimens, historical comparisons, etc. Controlled clinical trials are different in that they must contain at least one control intervention and that participants must be assigned to the control or test group using a bias-free method.

A randomized control trial is defined by the National Library of Medicine as a clinical trial that involves at least one test treatment and one control treatment, concurrent enrollment and follow up of the test and control treated groups and in which the treatments to be administered are selected by a random process such, as the use of a random numbers table. The primary distinction in a randomized control trial is that participants are selected for the test or control group by a fully random process.

Besides the three main types of clinical trials, there are a few other ways to define them. For example, a clinical trial can be adaptive. This means that the study protocol includes the anticipated modification of the trial based on analyzing data as it is produced. An adaptive trial will also be categorized as a clinical, controlled clinical or randomized control trial. Clinical trials can also be pragmatic. This distinction is given to a trial that takes place in an actual clinical setting. Setting is not a defining characteristic of other types of clinical trials.

Now let's review the different phases of clinical trials. You can think of the phases as the scientific progression of an idea or hypothesis. The hypothesis and the significance of the results must get stronger as the idea moves through the phases. A treatment whether a drug, a medical device or something else typically has to make it through the first three phases before being approved for general public use. It is important to remember that a Phase I clinical trial is probably not the first test of the hypothesis. Before getting to a Phase I trial, the hypothesis may have been studied observationally or in a laboratory with animal subjects. A Phase I clinical trial means that the study is a pre-planned, usually controlled, clinical study of the safety and efficacy or effectiveness of an intervention. The study is based on a small number of people and typically conducted for about a year. When the intervention moves into a Phase II clinical trial it is also a pre-planned, usually controlled, clinical study of safety and effectiveness for an intervention, but in Phase II there are usually hundreds of participants or test subjects and the study will typically be conducted over about 2 years. So in short, Phase II has a lot more participants and lasts twice as long. As the intervention progresses into a Phase III clinical trial it will last even longer, typically 3 years so that long-term effects can be seen. In order to make it to a Phase III trial, the intervention being studied has already shown that it is effective and in this phase the participants are typically being monitored for adverse effects of the intervention. For example, the trial might be looking to see if a drug that reduces blood pressure has any serious side effects, like causing stomach ulcers which may take years to develop. Finally Phase IV clinical trials usually take place after an intervention has been approved and is in general use. These studies continue to monitor safety and effectiveness about the intervention over time and as an increasing number of patients use the intervention.

You can find more information about clinical trials at clinicaltrials.gov. This site gives basic information about understanding trials and has a searchable list of clinical trials. The list includes active trials, completed trials and trials that are currently recruiting participants. To find articles on the results of clinical trials we can check in PubMed. In this example, we can see from the abstract that the intervention required further assessment and that this is a Phase III multi-center randomized double-blind placebo controlled trial. Here's an example of a pragmatic randomized control trial. You can see in the abstract methods that it is a randomized control trial but they don't mention that it is pragmatic. However, the article was assigned the pragmatic clinical trial publication type. In this example, we need to read the article. When we do we can see right away in the methods that the trial was pragmatic, randomized and conducted at 687 sites. It may not always be in the abstract, but every reliable clinical trial article will either tell you explicitly in the methods what type of trial it is or it will provide you with enough detailed methods information that you can determine the trial type. As previously mentioned the definitions throughout this presentation are from the National Library of Medicine's publication types.