**What happens in a clinical trial?**

**Genomics 101 explainer episode transcript**

**Florence: What happens in a clinical trial? I'm joined with Callum Morris, Pharmaceutical Research and Development Insights Manager for Genomics England, to find out more. So, Callum, first things first. What is a clinical trial?**

**Callum:** So, a clinical trial is a study that looks to people to answer a specific medical research question.

So, this involves gathering a group of participants that are willing to participate in providing evidence on how to improve clinical care. And so, the main purpose for a clinical trial is to evaluate health related outcomes between different groups of participants. If it's an interventional clinical trial, you change clinical care for one group and not another.

And evaluate whether the change you made improved health outcomes for that group, or if it's an observational clinical trial, you might focus on different groups but not change anything about their clinical care and collect real world data to understand how outcomes differ across the groups.

**Florence: Can you briefly explain what we mean by real world data?**

**Callum:** Sure. So real world data relates to data collected routinely as part of standard clinical care. So, it could be collected from your electronic health records, data from product or disease registries, or data gathered from other sources such as digital health technologies.

And all of this can inform on particular groups from the population you're interested in.

**Florence: And are there different types of clinical trials?**

**Callum:** Yes. Clinical trials can take many forms depending on the medical research question you're trying to answer. They could be related to understanding the risk of disease. So, evaluating a potential risk factor that you may be concerned with. They might evaluate preventing disease. So, what different approaches can you take to people who have never had the disease, and does this prevent its occurrence? You can have a clinical trial that looks at screening for disease. For cancer, that's really important.

Does a new screening approach mean more people with cancer can be identified earlier? And importantly, does this lead to an improvement in survival? You can have clinical trials that evaluate the different approaches to diagnosing a disease and can you diagnose a patient earlier and better?

And then the classical clinical trial is revolving therapeutics or different treatments, and you can have treatments that are addressing the disease itself. Or you'd have treatments that are controlling the symptoms of side effects you might get from another treatment you might be taking.

So even within a specific medical research question, you can have different clinical trials depending on how much evidence you already have regarding that question. For clinical trials involving the assessment of new treatments and therapies, these are broken down into three stages and we call these phases.

So, you have phase one, phase two, and phase three.

**Florence: Can you explain a bit more about these phases?**

**Callum:** Sure.So, the overarching medical research question might be, what is the safety profile of this new therapy, and does it work improving on the current standard of care? So, you'll break this down depending on the phase, and with each phase you expand your clinical trial to a larger population.

Phase ones are typically on a small group of people around, let's say 20 to 50, and are designed to check the safety of a new drug that's being entered into humans for the first time. Sometimes, especially in early phase cancer trials, you're trying to find the right dose for your patients.

So, you might take a small group, test them on a low dose, and if there are no severe reactions to the new drug, you start incrementally increasing your dose a little bit more. And this gives you a really good idea of the safety profile of your drug as you try it for the first time in a human population.

Next, you'll move on to a phase two. And these are typically larger than your phase one, around 50 to 200 people. And, usually you use the dose recommended by the phase one. So instead of slowly adjusting your dose and just focusing on the drug safety profile, the phase two will evaluate the safety of the medicine in a large population, but also have an additional focus on health-related outcomes.

Is the medicine causing the effect you want? Whether that's relief of symptoms or for cancer reduction in the size of your cancer. If the data is really promising from your phase two, it will move to a phase three. And the idea is the same, increasing the size of the population. typically phase threes can be from 300 to 3000 participants.

And the key thing here is that you will evaluate the potential benefit of your new treatment against the current standard of care. Normally, meaning the treatments that are already available in the clinic. Health regulators will need to look at all the data collected from all the trials before they approve it for the general population.

And typically, they need a phase three to do this. They need a phase three to confirm that the benefit provided by the treatment outweighs the potential risks associated with it, across a fairly large cohort of participants. And this is to ensure the therapy is appropriate to be given to the general patient population.

But also, a phase three is needed to see that if the new treatment is moving clinical care forward in the right direction and in providing improvements for patients against what is already available in the clinic. And this is the process by which we call it evidence-based changes, to make improvements to clinical care.

**Florence: So then how do people join clinical trials?**

**Callum:** So firstly, it's about becoming aware of the clinical trial. You might be referred to a clinical trial by your doctor who's been aware of it and where it is. Or you might be able to find a clinical trial using clinical trial databases or finding about them through patient advocacy groups.

And they should be able to tell you which hospitals are taking part in the clinical trial. So, the next step might be your doctor can contact someone on the research team, and there is always a principal investigator per research site that is always a medical professional.

The study team at the site have all undergone training from the people organising the trial to run through the protocols necessary to keep the trial consistent in different sites.

Once they've been contacted, you'll undergo a screening process, and what they'll determine is your eligibility for the trial. They might assess medical history or your health status. And if you're eligible for the trial, the next step is to provide informed consent. The healthcare team should provide detailed information about the trial, its risks and benefits, the aim of the trial, and who's funding it.

And what are the treatment options for participating and not participating in the trial? How long is the follow-up in the clinical trial? And what will happen if you leave the clinical trial? And then also what are the safety concerns for the clinical trials and the possible side effects if it's something to do with a new treatment. Once you've been informed of all these details and you agree to be part of the clinical trial, you'll sign a consent form, and that means you're officially enrolled in the clinical trial.

**Florence: And what happens once someone is enrolled in a clinical trial?**

**Callum:** Once you are in the trial, you'll follow the procedures outlined in the trial protocol. This can take many forms, but normally it involves more regular follow-ups and check-ins with the clinical care team. And this is to establish safety concerns and to enable lots of data collection.

There also may be additional checks related to health outcomes during the trial, and so the study team may want to take additional samples to understand what is happening physiologically during the study. There also may be additional questionnaires for you to fill out, to capture patient reported health outcomes.

And this is to understand the patient's quality of life whilst they're on the trial. So, depending on the protocol, you may be followed up for a set period of time, and that may get less frequent as time goes on. And of course, you may pull out of the trial at any point after which the follow up will stop.

So, following data collection, there may be a while before you see anything, but results should be published following analysis of the data.

**Florence: And finally, why might someone want to be involved in a clinical trial?**

**Callum:** Clinical trials are all about providing evidence to improve clinical care. At any time we want to make a change to healthcare, we want it to be evidence-based. And so, this requires lots of people all contributing in a group effort to generate a data set large enough to determine how to change our approach to healthcare and move the field forward for improving people's lives.

**Florence: That was Callum Morris explaining what happens in a clinical trial. If you'd like to hear more explainer episodes like this, you can find them on our website www.genomicsengland.co.uk. Thank you for listening.**