TRANSCRIPT
Module 1: Introduction to Clinical Trials

- [Dr Burke] Hello and welcome to Module 1, which is our Introduction to Clinical Trials. Firstly, I am Dr Therese Burke, the Adaptive Clinical Trial Platform Coordinator at MS Australia. I will lead you through a series of nine modules designed to provide people living with MS and the wider MS community with information and knowledge about clinical trials. This will include what it's all about, some basic terminology, some practical logistics of clinical trials, and most importantly, we will hear about the lived experience of people with MS who have previously taken part in research and clinical trials. Each module covers an important aspect of clinical trials, and can be viewed at any time point, although we do recommend starting at Module 1 and working your way through in order, to gain the most out of the modules. There will be a discussion led by myself or another member of the MS Australia research team to take you through the key points of each module. Then, we will invite experts to talk with us about various aspects of each module as we progress our way through. We will have a full list of resources and references at the end of each module so that you can delve a little more deeply into the things that interest you. And finally, there will be a short quiz of four questions at the end of each module so that you can test your knowledge and understanding before moving on. Each module will have an outline. Today, our outline includes an introduction to clinical trials where we will talk about what clinical trials are, their purpose and potential benefits. We will then view an animation about the clinical trial process. And finally, a video interview will be presented at the end of the module with a person living with MS, talking about how participating in a clinical trial was a life-changing experience for them. So first up, what are clinical trials? So essentially, clinical trials are the tools that answer the question, does this intervention improve outcomes? Is this drug better for the patient? It may involve a drug, a device, a therapy, an action, a screening test, or even a diagnostic investigation. So I like to look at it that research is a very broad term at the top of the umbrella, and clinical trials are a type of research under that umbrella. Clinical trials help with developing our evidence base, which is essential for rigorous, science and medicine decision making. Clinical trials are designed to be robust, and can be followed by a direct process. And this means that they can be done simultaneously in different regions and different countries, but looking at the same sorts of outcomes. They ensure that our health system is based on outcomes which have validity and are based on evidence, not just on feelings or gut hunches. The randomised control clinical trial is considered to be the gold standard, and this is supported by the way that the clinical trial is performed. Often, allocation of patients are made into one or more treatment groups, and there would be a control or a placebo group. These sorts of trials are very robust and systematic. They use methodology to collect and analyse the data, but in very exciting news, in Module 9 we will also discuss a new type of clinical trial, the adaptive clinical trial. So in the meantime, what is the purpose of a clinical trial? Well, the clinical trial process helps us secure the evidence we need to make a change. To assess whether the impact of what we introduce to the patient can change practise, and are there better patient care outcomes? Clinical trials are vital as an option for patients, especially in diseases such as MS which do not have a cure. They may provide potential health benefits to these people. And thirdly, evidence, evidence, evidence. You've already heard me speak about evidence several times and we're only up to Module 1, but this develops the observations that we notice in medical practise or scientific practise into potential new treatments for patients. Essentially, we're

assessing if the things that have been noticed, are actually scientifically sound or otherwise. The following video developed by Roche Pharmaceuticals presents an overview of the clinical trial process.

- [Narrator] If you're interested in healthcare, you've probably heard of clinical studies, and you might know they're done to find out if experimental treatments are safe and effective. When experts talk about clinical studies, you'll hear expressions like double-blind, comparative, multi-centre or adaptive, and maybe also, study arms, statistical significance, bias, interim analysis, and above all, outcomes. Complicated stuff, what's it all about? Clinical studies are designed to answer specific scientific questions. For example, what side effects does a new drug have? Does it reverse or stop the disease it's designed to treat? Is it more effective than existing treatments? Can it be given alongside other drugs that are used for the same disease? In each case, the answer must come in the form of scientific data, not the impressions or opinions of the doctors or patients involved. These can be influenced by many factors which could bias the results. Studies are set up so as to make sure this doesn't happen. For a start, most studies are comparative. Half the patients get the experimental drug, the others get a standard treatment or a placebo, a mock-up that has no medicinal action. Most comparative studies are performed under double-blind conditions. Neither the patients nor the doctors know who's getting which drug or the placebo. So the two treatments must look exactly alike. And the patients entering the study are randomised, assigned on a purely random basis to one of the groups or arms of the study. The answers to most study questions lie in the statistical differences between the results obtained for each patient group. To ensure that enough data is gathered to answer the questions properly, a study must include the appropriate number of patients. How many of this is depends on the questions being asked. This is why many studies involve several hospitals. These multicentre trials ensure adequate data, as well as helping to safeguard objectivity. Even before a study is completed, enough data may have been collected to allow an interim analysis of its progress. This may lead to changes in the study, such as modifications to the dosage, number of patients or patient selection criteria. Studies set up to allow such changes are called adaptive studies. A well-designed study always provides an answer to the initial question. That's the study outcome. The answer may be positive or negative. The drug may or may not achieve its intended therapeutic effect. Either way, if the answer is clear and has a solid foundation in data, the study has been successful. Both positive and negative studies give researchers ideas about which direction to try next. A negative study is not a failed study. It's a reminder that there's more work to do.

- Now we're going to talk about the benefits of clinical trials. As I already mentioned, potential benefits are particularly important in diseases without a cure, which is MS, and particularly progressive MS. It allows us to make comparisons. We can't have dozens of treatments because financially that's just not possible for most countries. We just need the best treatments that are the most effective and the safest, and clinical trials allow us to make those comparisons to answer the question, is this better? Clinical trials must be supported by solid evidence, as we've talked about, not just we think we noticed this or we saw this, or we wonder this. and it helps develop that evidence base. And another big benefit of clinical trials is that it enables us to work together scientifically and medically towards a common goal. And many strong partnerships in MS research have come about because of clinical trials. We need as many smart people working on this goal of curing MS

as possible, and this can often lead to important work compounding the previous work, building upon it. And this is now very apparent in MS across the globe. And in Module 9, we'll talk about this in action in the form of adaptive clinical trials. Now we're going to look at the various phases of clinical trials. So first up, you may have heard about phase one. These are very small studies, and they're usually the first in humans. And they really look at the safety, the toxicity of the drug or intervention, and how to best deliver it. Phase two is a bigger study, which can involve up to a hundred or 200 people, and it really establishes the safety and efficacy of the drug, and gives a clear signal that it should move forward. Phase three, this is when things get quite serious because we're looking at hundreds and up to sometimes thousands of patients in a phase three study, and that's really looking to prove the clinical effectiveness. So it usually compares the new intervention or the new drug with the current standard of care treatment to see if it's better. Now, phase four is after the drug is marketed. So new findings can still emerge because obviously we're giving that medication to a very wide group of people in the community. And we can also see this in action as real world evidence trials, or real world evidence studies, where we continue to monitor how a drug goes after it's already put on the market. Now we're going to look at a video where we're going to be talking to Suzanne Kay, who was a person living with MS, and about how participating in the clinical trial was a life-changing experience for Suzanne. Today we're going to be talking about how a clinical trial actually changed someone's life. And joining me is the beautiful Suzanne Kay, who's a person living with MS. I first met Suzanne when we were working in a clinical trial together. I was the clinical trial coordinator and nurse, and Suzanne was one of the patients in that trial. Now, Suzanne's going to tell us a little bit about her story and her experience in that clinical trial. I'm just going to say upfront that not everyone has the experience that Suzanne's going to talk to us about today. We wanted to tell Suzanne's story first up, in the first module, because being part of a clinical trial had such a huge impact on Suzanne's life and that isn't the same for everyone. But I think it's important to consider, because years ago when Suzanne did participate in the clinical trial, we had very few options in relapsing remitting MS, and Suzanne will talk about that, which is why she considered the trial. But the situation is pretty much the same for people with progressive MS today, in that we don't have near the treatment options that we do for relapsing remitting MS. And it was because of people just like Suzanne that we do have that today, which is quite incredible on its own. So firstly, Suzanne, on behalf of people in the MS community, thank you for everything that you did in that clinical trial to get this product to market where it's helping people today. So yeah, my pleasure. So firstly, Suzanne, just tell us a little bit about yourself and what brought you to considering a clinical trial as your treatment for MS.

- Well, I was living a dream life. I'd bought a house and married my husband and we had a beautiful baby boy. And six weeks after he was born, I started getting tingling in my hand, and my hand became sort of ineffective really. I couldn't hold things or anything like that. And it travelled up my arm, and I went to the doctor and the doctor said, "You might have carpal tunnel, but I'll refer you to a neurologist." And I went to a neurologist and we did an MRI, and the MRI that I went back to the neurologist and she said, "Well, the good news is you don't have carpal tunnel, but you do have MS." And I went, "Wow, okay." And within a 12 month period, I had four attacks. I had everything from obviously losing movement in my arm to constant double vision to extreme tiredness and loss of balance and that sort of thing as well. So nothing was working for me at all. And it was very, very frightening having a

newborn baby. And my husband had to give up work and we had to sell our home and move in with my mum. And it was a terrible, terrible time. I was taking the standard injections at the time but they just weren't working for me. I started off with once a week and went to every second day, but it wasn't changing. I was still having attacks quite rapidly.

- So then how did the clinical trial, how did you find out about the clinical trial?

- It was truly, truly one of those accidents, I guess. My mom was working with a lady whose husband went to university with a neurologist who was conducting this trial in the Gold Coast. So it was totally random. And I met with the neurologist and he said, "You are a perfect candidate, so how would you like to give it a go?"

- Wow, did you know that you were the perfect candidate before you went to see him? No, so you were going with hope, but you didn't know if you'd be accepted?

- Absolutely, we had everything I guess crossed but we didn't know if I would be ideal for it. So, it was very lucky.

- Yes, with the story you've told me, you didn't have a lot of choice at that time. So, the options that were available weren't working for you and you were clearly getting worse, and so that...

- Absolutely, it wasn't, yeah. The standard medication wasn't working for me and I needed something different. And it was a tough choice to make, but one that ultimately was the best one.

- The best one for you, because clear to see you now, what are we about 14 years later?

- It will be 15.

- I'd say 15.

- 15 years later, and look at you. You've got just such a beautiful full life. So, how did the clinical trial change your life?

- It changed everything. We were obviously, we were struggling. It was very difficult to look after my, he was one at that stage, toddler. And so it changed everything really, it did. It took some time to really get me back to my peak, I guess. But I was able to return to work. We were able to buy a home again. We were able to expand our family, which was absolutely incredible and something that we never ever thought we'd be able to do. And it all went beautifully. And yeah, it's totally changed everything.

- But I mean, we say it went beautifully, but it was still with a lot of effort from you because I know that clinical trial went for a number of years. And there were lots of assessments involved in that and a lot of time commitment for you, but for you, certainly it paid off, didn't it?

- Oh, certainly yes, absolutely it did. It was every month I had to go and give blood tests and that sort of thing, and that meant dragging a toddler to the hospital or all that, but it was worth it. And we had to delay having another baby for I think, six years. So hence why we've got a seven year gap. But I was very, very fortunate and it all worked, and the nurses made it very, very easy for me. I mean, they would welcome my little boy with open arms when I needed to give blood, and it was great.

- Yeah, thank you Suzanne. Thanks for sharing your story, we really appreciate it.

- My pleasure, thank you, thank you.

- [Dr Burke] Thank you for completing this module. A list of resources and references is also available if you would like to explore these concepts in more detail. I encourage you to please take the quiz to check your level of understanding before moving on to Module 2, where we will talk about regulations in clinical trials, the ethical guidelines and the governance framework around clinical trials. These all aim to protect clinical trial participants and keep them as safe and well-informed as possible.

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