TRANSCRIPT

S5E9 – Clinical Trials

Dr Laxmi Iyengar: Welcome to *Spot Diagnosis.* My name is Dr Laxmi Iyengar, and I'm a GP and Research Fellow at the Skin Health Institute, a world-renowned center of skin excellence located in Melbourne, Australia.

I begin today by acknowledging the Wurundjeri people of the Eastern Kulin Nation, traditional custodians of the land on which we record this podcast and pay my respects to their elders past and present. I extend that respect to Aboriginal and Torres Strait Islander peoples listening today.

Today's podcast will be on a very important topic for those interested in research and leading-edge medicine, and it is on the groundbreaking subject of clinical trials. Some of our listeners may have a general idea what clinical trials are all about. They are research studies to test the effectiveness of new treatments to deliver the highest standard of care to patients.

But how can one be assured about the safety and efficacy of novel treatments? To discuss the topic in depth, as usual, *Spot Diagnosis* has brought together a panel of experts for you today. First up, we have Associate Professor Peter Foley, who needs no introduction. He is the Director of Research at the Skin Health Institute and Head of Dermatology Research at St. Vincent's Hospital, Melbourne, and holds the position of Associate Professor at the Department of Medicine at the University of Melbourne. He has been an investigator in over 160 clinical trials and has over 160 published manuscripts, so he is ideally suited to be a guest on today's podcast.

Associate Professor Peter Foley: Thanks, Laxmi. It's a pleasure to be here and to have the opportunity to discuss a topic that, as you know, is very near and dear to my heart. It is an area of medicine that has been a very major focus of my career, what I've spent the last couple of decades participating in, and it is an expanding field. It's very exciting to be part of this, and it is an area I'm quite passionate about, despite my usual monotone.

Laxmi: Next up, we have Dr Tam Nguyen. Tam is Deputy Director of Research at St. Vincent's Hospital, Melbourne, and is responsible for research strategy, development, and innovation. Tam is a regular invited speaker on a broad range of topics, including industry collaboration, research ethics, and governance, AI and machine learning, as well as clinical trials, so I'm fascinated to learn more from Dr Tam on this subject.

Associate Professor Tam Nguyen: Laxmi, thanks for having me on the show. It's great to be here, to be on the panel, and very much looking forward to the discussion, all things on clinical trials. Just to also add, I also teach at the Melbourne Medical School and sit on the investment committee for a fund, which is investing in, I guess, biotech and medtech, which is relevant to our discussion as well.

Laxmi: Thank you so much. It's a pleasure to have you here today. Our final guest for today is the person who keeps the show running at the Skin Health Institute, Mrs Sarah Chivers, and she's the Director of the Clinical Research Team and Advanced Targeted Therapeutics at the Skin Health Institute. She manages a large team to ensure the feasibility of clinical trials and oversees the delivery of specialised patient-centered care at the Skin Health Institute Advanced Therapy Clinics, a very important job indeed, so we will have many pearls to learn from Sarah.

Mrs Sarah Chivers: Thanks, Laxmi, and it's great to be here with you. I've worked at Skin Health Institute now for nearly five years, but all up in clinical trials for 20 years, and it's been a real privilege to have been a part of some real groundbreaking clinical trials. In that time, I've met countless trial participants that have made really valuable contributions to research, so I'm excited to talk about that. Thank you.

Laxmi: Thanks for being here, Sarah. Let's get stuck right into this episode on clinical trials without further ado. Peter, I might direct this first question to you. What are clinical trials?

Peter: Clinical trials are a very important part of the development of any new medicine or other intervention that may improve the health of an individual, may improve their wellbeing, but may also help prevent a disease state. A clinical trial is, if you like, a planned experiment. It's designed to assess the effectiveness of a treatment, which may be a medicine, a drug, or a device, so we'll call that an intervention by assessing the outcomes, and that's looking at both safety and effectiveness in a group of patients, which are often called participants, where they're treated with that test therapeutic.

By comparing this therapeutic either to a placebo group in a similar group of patients who receive a placebo or occasionally a competitive treatment, so it may be a comparison study or it may be a placebo-controlled study. There are a whole host of different phases of trials, but essentially, it's comparing whether a new therapy is safe and effective compared to placebo or another treatment.

Laxmi: Tam, could you please elaborate on what the difference is between clinical trials and research?

Tam: Sure. I guess clinical research can be looking at research, looking at, say, program evaluation, looking at aspects of disease like symptoms, risk factor, pathophysiology, or even, as I mentioned, clinical program evaluation or public health in general. Clinical trials actually assess the potential of therapeutic drugs, devices, and I would also add, I guess, as well as diagnostics and digital as well, in the management and control of prevention of disease.

Laxmi: Peter and Tam, could you tell us a bit about why clinical trials are important? Maybe I'll start with Peter first and then you, Tam.

Peter: Thanks for the question. I think the first thing that clinical trials do is try to address an unmet medical need. That may be where there are no therapies currently available or what treatments we do have available are either not as effective as we would like or they have safety concerns. Perhaps not as an aim of clinical trials, but a result is that we often find insights into the

pathomechanisms of diseases. Often, after a trial has been conducted, new information becomes available as to what actually causes a disease.

Clinical trials are also a means of introducing new therapies that are hopefully safer, ideally more effective, and may prove to be more convenient either by the dosing regimen or by the mode of delivery. What we hope is to improve patient care by advancing research into their disease state.

Laxmi: Tam, would you like to elaborate on that?

Tam: I think the importance of clinical trials is that the way we address some of the unmet needs or that health equity of access where, for example, typically in the trials or, Peter, as a clinician, would prescribe a medication and it's very general, whereas you can look at a bit more, you could call it precision medicine, specifically to a certain group.

I think certainly in the rare disease case, clinical trial is important because often what we call the orphan disease or the rare disease that's been neglected, the importance of clinical trial is actually getting access. Certainly, from the Australian perspective, it's a big health and medical research industry, and where the government is supporting that, and I think ultimately, it's getting a better patient outcome where we're able to prescribe the latest treatment options for our patients.

Laxmi: Could you please briefly discuss some of the different types of clinical trials?

Tam: Yes. I won't go into the clinical trials 101 with different trial design because it's actually getting fairly complicated where, as I mentioned, if you think of the four Ds, it's the drugs, devices, digital, and diagnostic. Diagnostics being you diagnose something and potentially come with the companion therapeutic for that. Digital is, for example, where a digital tool is actually helping with patients to monitor their conditions.

Your gold-standard randomise the RCT, as Peter mentioned before, you've got a treatment, you've got a placebo arm. As I discussed before, the trial design is actually getting more complicated in a way that is actually more precise and more personalised.

Peter: One example of a device trial that we're undertaking at the Skin Health Institute is the ACEMID study, which is using the Vectra machine, which is two banks of 46 digital cameras, to undertake melanoma surveillance or melanoma prevention. The idea is to see if over the course of five years, it's at least equivalent to today's gold standard, which is patient face-to-face examination. The idea is that patients, particularly in rural and remote areas, will be able to have this 3D imaging and a distant clinician will be able to evaluate that to save patients hours of driving without compromising their care.

Laxmi: That's a really nice example of how clinical trials can serve to improve patient care, so that's really good to know. Tam, you mentioned the words randomised control trials and placebo earlier. I've heard about double-blind randomised placebo control trials having the highest levels of evidence. Why is that?

Tam: Laxmi, randomised double-blind placebo control trials or studies, it's a mouthful, but consider it as a gold standard level one evidence where studies, when you've got a group of individuals, patients, participants, they've been randomised, blinding to avoid bias. Neither the patient or the clinician know who is in the treatment arm or who is in the control arm. This could be in the treatment trials or prevention trial, but essentially, that's at the highest level to reduce bias.

Laxmi: Now let's switch gears, and Sarah, I might direct this question to you. From a patient point of view, what is the benefit of being involved in a clinical trial?

Sarah: Thanks, Laxmi. I guess the most important and probably most obvious benefit is the potential access to a new therapeutic that might otherwise take some time to enter the market, especially if a conventional treatment hasn't worked for the patient. Whilst it's not always a given that the participant will receive active therapy in a trial, their participation allows researchers to collect really valuable data that helps support the use of these treatments in the real world.

For the participant, that feeling of being part of something that can have such an impact on healthcare can be a real benefit to them. I guess being a trial participant, as Tam alluded to earlier, can provide easier and quicker access to quality care because they are usually followed very closely when in a clinical trial. Most clinical trials also provide some type of reimbursement to cover costs for travel. If you look at it from the perspective of the participant, it's not just that potential of having some improvement in their condition, but also those other points that can actually benefit the patient as well.

Laxmi: Following on from that, Peter, from a clinical point of view, what are some of the advantages of enrolling your patients in clinical trials?

Peter: We've already heard from both Sarah and Tam that one of the benefits of being enrolled as a patient is early access to therapies. A lot of therapies are trying to address unmet needs. It may be that the patient has failed to respond to traditional therapies, and they need something new, or it may be what we have available is just far from ideal because of the treatment either being not that effective or having safety concerns. It's early access to therapy.

There is, of course, a risk that the patient may end up in the placebo arm. What it means is that because we have a placebo arm, we actually have a valuable information in terms of whether a drug is effective or not, rather than just, if you like, a placebo effect. It's having that comparison.

I remember one of the first trials we did where a patient didn't respond all that well, but his comment was, my grandchild may end up with this disease. If it provides information for when he is older, then it's worth my while, even if I don't get better. Patients are also looking at family members, descendants, how it may help. A lot of people do it for altruistic reasons, being fully aware that they may be on a placebo. Of course, I'd love to be on a treatment that works for them without any side effects.

I think it's also very exciting for a patient to know that they're on a new therapy, particularly if it works for them. Knowing that they're part of the developments of medicine and surgery, and intervention into health care. It also means that by being engaged with centres who are participating in research, they come into contact with other patients, with the condition, even to a patient support groups. It provides those additional benefits that aren't immediately addressed by the therapy they may be receiving.

Laxmi: I'm curious to discuss with all of you some of the commonly held misconceptions about clinical trials. Tam, I might start with you for this question. Would you like to elaborate on that?

Tam: Yes. The myth that we hear is, participating won't help me, as Peter mentioned, but in terms of the patient saying, well, it might not help me. I think it's important to recognise that it's actually building the body of knowledge. The providers or the PI treat me like a guinea pig. The trial will only give me a placebo. Clinical trials are only for really sick people. I think these sort of things come back to, I guess, some awareness.

I think, even the word itself, the first thing that we think about, trials evoke the sense of experiment, risk, and so on so forth.

Laxmi: I think you've raised some really excellent points there. Changing that psyche that trials are experimentation on vulnerable subjects. I think it's important as clinicians that we do that effectively and just reassure our patients that clinical trials are safe, and we have their best interests in mind always as clinicians. Sarah, would you like to comment on any misconceptions that you've heard?

Sarah: Yes, absolutely. I guess, probably, from my experience in 20 years, I've really seen the change in how clinical trials are designed. Certainly, more recently, you can see the efforts that government and advocacy groups are going towards, and certainly, the sponsors that also develop these clinical trials, in order to include the participant in how trials are designed and having the participants be more involved in the development of questionnaires, and the way in which we deliver clinical trials to make it easier for them to access.

I think that's well established now with the National Clinical Trials Governance Framework that's been introduced in Australia, where clinical trial sites are now accredited to be running clinical trials in a way in which we're partnering with our consumers, which is really important.

Laxmi: Peter, would you like to elaborate on any of these myths?

Peter: It'd be great to comment on a couple of myths, the first being that trials are only for really sick people. All of the vaccines that we have, be they the new shingles vaccine or COVID vaccines or influenza vaccines, had to go through clinical trials to show that they were safe, as well as effective. You didn't have to be sick; it's trying to prevent illness. If you want to be disparaging, you could suggest that people with acne are not sick. If we have a new treatment for acne, which really impacts on teenagers' quality of life, you have to do a trial. You have to see whether it's safe and whether it's going to work. You don't have to be bedridden or hospitalised to be in a clinical trial.

The other comment often is that if you're in a clinical trial, you're going to be a guinea pig. I think if anyone saw the regularity of visits in a clinical trial, they'd really be aware that safety monitoring is paramount in the minds of both the investigators and whoever is developing the therapy. There's an awful lot of safety monitoring going on. People may not appreciate before they start the fact that they have to have regular blood tests, but it's all about safety.

All trials, all therapeutic trials, have drug safety monitoring committees which are third-party committees looking at all the safety aspects. It's not we'll give you something to see how sick we can make you, it's we want to really detect early if there are any safety concerns, and programs get stopped if there are safety concerns.

Laxmi: I think what I'm collectively hearing from all of you is that clinical trials are important really so that we practice the highest attainable standard of medicine, and it's really important to continually work on improving patient care and giving them the most effective treatments that are available for their condition. We can only learn that from doing clinical trials. Sarah, how can patients be assured about their safety in clinical trials?

Sarah: All clinical trials are designed really to prioritise the safety and the wellbeing of the participant, and certainly in Australia, all clinical trials undergo very rigorous review by human research and ethics committees that have experts on their panels but also have consumers as well on their panels. All of these drugs are also listed with the Therapeutic Goods Administration, so they are regularly monitored, and all clinical trials are reviewed thoroughly.

Participants, as Peter suggested, are monitored really closely as well. Some studies require participants to be monitored every two to four weeks with blood tests and other assessments to ensure that there's nothing untoward going on. Then if anything is seen in the test results, then they're followed up straight away. All participants are provided with a really detailed participant information and consent form and are provided plenty of time to review the consent form with their family and perhaps their local GP to ensure that they're making the right decision for themselves.

Also, all trials are voluntary, and so participants can withdraw their consent at any time. If they change their mind, then they can withdraw. There's no effect on their ongoing care by their decision of removing themselves from a clinical trial. Obviously, we would talk to the patient prior to that decision, but there's plenty of opportunity for the patients and certainly the researchers to discuss the safety options and to keep safety as the top priority while the patient is in a clinical trial.

Laxmi: It's great to be reassured that patients have complete autonomy because sometimes there is this notion out there that patients are coerced by doctors to sign on to clinical trials in the interest of advancing research, but it is about the patient and we do have the patient's best interests at all times, so that's really good to know. Peter let's talk about the different phases of clinical trials.

Peter: There are four phases of clinical trials. Each phase has a different intention. Prior to being approved for use in the public space, all new medicines have to be tested in phase 1, phase 2, and phase 3. Prior to any human being exposed, there are pre-clinical studies. If the medication is shown to have in the laboratory the effect that it's expected, the first thing that happens is a phase one trial. That may be with a group of healthy volunteers, or it may be a small group of people with the disease state that's being investigated.

It's a small number, not a whole lot of patients being tested at one time, and it's really looking at safety to make sure it is safe to give to larger numbers for longer periods of time. It might be single doses that the dose goes up over time or multiple doses with the concentration going up over time. Single ascending dose or multiple ascending dose trials, small numbers, healthy volunteers, or people with the disease state.

If the medication passes through phase 1, it then enters phase 2. Still relatively small numbers, but it's looking at the effectiveness at a range of different doses. The trial might be in dermatological conditions, often for 12 or 16 weeks, and there'll be different arms. There'll be a placebo arm, and then patients randomised to receive a dose below what's expected to be used later on, above what's expected to be used, and the dose that's proposed. That's a short-term study.

Again, if the drug passes the safety checkpoints and is shown to be effective and better than placebo, then it moves into phase 3. Phase 3 studies are usually large trials with international participation with large numbers of patients for longer periods of time. The primary endpoint, so the target that's being aimed for may be relatively short term, maybe three months, four months, six months, but often with longer term extension.

It's looking at the effectiveness compared to placebo or to an active comparator, and looking at the safety to see if the safety profile differs from drugs that are currently available or from placebo. If a drug is shown to be effective and safe in phase 3 trials, the developer will then apply for the opportunity to market that medication to the general public. Phase 4 trials are so-called post-marketing trials, so that's after a drug has been approved for use in the public space.

It may look at different delivery systems, so going from a pre-filled syringe to an auto-injector. It may look at different dosing schedules or different concentrations of drug. It may look at the drug that's been approved in new conditions, so looking at different disease states. Obviously, if it's shown to be effective there in that disease state, that then go back to phase 2 and phase 3 trials, but it may be done post-marketing once the drug is available in a country.

Laxmi: Clearly, drugs are very rigorously tested before they enter the market. Tam, are all clinical trials sponsored by the pharmaceutical industry?

Tam: No, not all clinical trials are sponsored by pharmaceutical industry despite what we hear, and I guess linking to that is the potential bias in terms of pharmaceutical making gain from the sales of the drugs and so on and so forth.

There's different types in terms of sponsorship. You've got the commercially sponsored by the pharmaceutical companies. You've got what we call investigator-initiated studies where clinicians like Peter and others who would be looking at the hospital or the trial site actually supporting that. Then there's a collaborative research group where there might be funding from different foundations to support the trials. It also depends on the therapeutics area, the split between commercial and non-commercial sponsored studies.

Laxmi: Following on from that, Tam, why are there some medications that are available overseas but not here?

Tam: Great question. I'll probably need another podcast on this, but just to try to summarise that, essentially, we Australian, the ecosystem involved in clinical trials tend to be in the very early phase. The later phase, as Peter mentioned, in the phase three, requires a larger number, and with a small population base, we tend to be involved in a smaller scale. It takes time for the process to go through having running the trials, having the medication being approved, and then listed on the PBS, the Pharmaceutical Benefit Scheme, it takes a lot of time and effort.

Whilst Australia, some of the recent stats to demonstrate that I think we run about 11% of the overall worldwide clinical trial, which is massive for the size of our population. What it tends to demonstrate is that we run trials in the earlier phase, which might not be a bad thing because in the early phase, they come back to us in the later phase, even though we have a smaller population. Then back to some of our discussion point earlier, what it means for us is that we are leading the group in terms of doing clinical research and trials that bring better treatment for our patients.

Associate Professor Alvin Chong: *Ever wondered what the Skin Health Institute does? At the Skin Health Institute based in Melbourne, we aim to improve skin health for all our patients, and the research we conduct shapes clinical treatment and practice. We provide over 30,000 patient treatments each year and also deliver exceptional education programmes for dermatologists, registrars, and healthcare workers. We provide specialist training for visiting international medical graduates, workshops to upskill GPs and medical students, and public education programmes aimed at improving skin health in the community.*

The Institute also conducts clinical trials and research projects that are published and presented internationally. We make substantial contributions to the worldwide clinical care and management of skin diseases, skin cancer, and melanoma, and are recognised globally for our medical research. We have multiple clinics for GPs to directly refer patients to. GPs can complete our online referral form available on our website at skinhealthinstitute.org.au/patientreferrals or email referrals to referrals@skinhealthinstitute.org.au.

Laxmi: Now, let's chat about some of the logistics of being involved in a trial.

Sarah: I guess that's the most important question that a patient would normally ask their doctor if the doctor is speaking to them about the opportunity of participating in a trial. Generally, the first thing that will happen once we receive a referral from a clinician or through safe advertising,

because we do some advertising for clinical trials, we would establish over the phone whether the patient is eligible just based on some simple questions that we would ask them over the phone.

If we establish that they looked like they were eligible based on their answers, then we provide them with a consent form. In that consent form, it's usually anywhere from a 14 to 20-page document, depending upon the complexity of the clinical trial. We would provide them with the opportunity to read through the consent form, discuss it with their family, with their local doctor and to make a decision about whether they wanted to proceed with screening.

Once they make that decision to come in, then we book them in for a screening visit. At that particular point in time, the researcher, someone like Peter or one of our sub-investigators would then meticulously go through the consent process with the patient, ensuring that they understand what their responsibilities are as a participant, what the possible side effects are, understanding their rights, and also confidentiality, which is really important as well with regards to the collection of their data.

Once the patient is actually happy with all the details in regards to the clinical trial, then the consent form is signed with the researcher by the participant, or if they have a parent, if it's a young person entering into a clinical trial. Then from that point on, we start the process of assessing whether or not they're eligible to go into what we call the active part of the study.

In screening period, they would meet their study coordinator or study nurse, and that nurse or study coordinator would liaise with them and the researcher in completing all of the necessary assessments. That would include things like blood tests, ECGs, assessing their condition for severity, and also establishing any of their past medical history that may potentially make them ineligible for clinical trial.

At each visit, various assessments will be completed by the doctor and the study nurse. Once they're established as being eligible for the study, they're randomised, and sometimes we know what drug they're on, and sometimes we don't. Usually, the first visit once they're finished screening we will require them to get the treatment or the placebo. Then we continue monitoring them over the period of time that the study runs for.

Laxmi: It's good to hear that patients are well supported during their journey in a clinical trial. Peter, from a clinician perspective, what is generally involved during each visit for a clinical trial?

Peter: The initial visit or screening visits are a little bit different to the follow-up visits. At the initial visit, as Sarah's touched upon, patients are given the consent form, they consented, a lot of background information is collected that we only need to do once. What's the history of their disease? What prior treatments have they been experienced with?

Once the patient's been randomised, so once they're in the trial and they return for follow-up visits, usually after the patient's greeted and pleasantries have been exchanged, patient reported outcomes are recorded. Before there's any discussion, the patients are asked to complete

questionnaires on quality of life. There might be questionnaires on their mood or their mental health so that the rest of the visit can influence how they respond.

Then once that's been completed, often the patient's vital signs are taken, and the clinician, the investigator, or sub-investigator will sit down with the patient and ask about any illnesses or injuries, so-called adverse events that have happened since the last visit or that are continuing from the last visit. Patients will be asked about whether they're taking any other medication, so-called concomitant medications, and they'll be asked about their disease state.

Then what happens is a very critical part of the trial, so that's really looking at the safety part, but then the patient will be examined. Whatever disease state we're trialing the new therapy in, there will be a disease severity measure that is objective, so the patient will be examined and assessed and that will be recorded. The patient may then undergo an ECG, have any blood tests performed. Part of the role of the investigator is to look at those blood test results, look at ECGs or the interpretation. If the ECGs are being interpreted centrally, then the investigator just needs to be across what's being reported.

Sometimes outside investigations may need to be done, chest X-rays, CT scans, audiology, ophthalmology, respiratory. This is in dermatology trials, but areas where we don't have expertise but we will outsource those investigations, we need to be across what the results are and we need to explain any blood test results to the participant. Then once all that has been undertaken, the patient can be dispensed therapy, and that might be a tablet that they take home or an injection they take home, or they may receive treatment at the trial site. Quite a bit involved, really looking at safety, patient welfare, but also effectiveness.

Laxmi: What are adverse events and serious adverse events and why are they so carefully documented?

Sarah: I guess, firstly, in regards to what those terms mean, an adverse event is anything that's untoward or unfavourable that may happen medically while a patient is participating in a study, and this might include abnormal signs or symptoms. It might also be something that is expected, but it needs to be documented. A serious adverse event is any event that might result in death or is life-threatening or places the participant at immediate risk from death and requires prolonged hospitalisation and causes perhaps a persistent or significant disability or incapacity.

The results may also cause congenital abnormalities or birth defects, and usually the adverse event and the serious adverse events are judged by the researcher. If anyone is admitted to hospital for longer than a 24-hour period, regardless of whether it's associated with the clinical trial that the patient is participating in, then it is automatically considered a serious adverse event. The reason why we document them and why we follow them is really the most important thing is to protect the participant from any harm in participating in the study. That really is the most important reason. Many clinical trials are designed to document any pattern to an adverse event and how serious they are. Collecting this information is important to confirm and validate the use of medication in the general population.

Tam: Just to chime in, from Sarah's perspective about adverse events and reporting the importance of, I guess, from my perspective, as someone who managed the Ethics Committee, looking at having that oversight in terms of reporting and ongoing monitoring, whether the trial is being commercially sponsored, investigated, initiated, collaborative research group has the same standard. That is the importance of reporting of outcomes or any adverse events as they come along.

The Ethics Committee regularly monitor the trials through various means. Commercially sponsored study, the sponsor would have their monitoring team, the Data Safety Monitoring Review Board, same as investigator-initiated study, where a site, a hospital, acting as a sponsor has the responsibility to make sure the trials is conducting with the highest level of oversight and risk management and risk mitigation as well.

Laxmi: That is great to be reassured that patient safety is paramount and all steps are taken to minimise adverse effects. I've heard of the Good Clinical Practice Code of Conduct in relation to clinical trials. Could we elaborate on the Good Clinical Practice Code and why it is so important in relation to clinical trials?

Sarah: Good clinical practice is an international ethical and scientific quality standard for the design, conduct, performance, and monitoring, including auditing and recording, and analysing the data that we collect in clinical trials. It's also about how we protect the participant when they are in a clinical trial. It really does serve to protect the rights and the integrity and the confidentiality of anyone that does participate in a clinical trial.

Really the short answer about why it's important is the fact that we need to have a Bible. A long time ago, when we were conducting clinical trials, we weren't necessarily doing it for the benefit of the patient or the participant. Post the war, these good clinical practice guidelines to help us ensure quality data is collected and ensure that patients are safe whilst they participate in a clinical trial.

Peter: I'd just like to echo Sarah's comments on good clinical practice, which is the result of an international conference harmonising what's required. It's all about protecting the participant, their rights, their confidentiality. It's important to realise that every person that's involved with a clinical trial, be they the doctor, the nurse, the trials coordinator, anyone involved has to undergo GCP training, and now it's really required to be done every year. It's not just a matter of you tick the box, but every year we are reminded of the importance of protecting the participant in the clinical trials.

Laxmi: Our GP listeners and derm trainees out there can feel a lot more confident about referring patients to clinical trials now. This leads me to my next questions. GPs, for example, manage patients with a wide variety of concerns, so chronic disease such as diabetes, rare disease such as alpha-1 antitrypsin deficiency, but also patients with terminal illness such as cancer. How can GPs find further information about specific clinical trials and can GPs directly refer patients for consideration for clinical trials?

Tam: Certainly, there's various way, actually, for GP to refer their patient to clinical trials. One is actually that there are trials been listed on, I guess, hospital website, but also, it's a clinical trial registry called ANZCTR, which is Australian and New Zealand Clinical Trial Registry website.

In terms of using technology, there are different apps available out there listing trials, Importantly, we have campaigns where we're actually asking patient to really ask their GP or their specialist about opportunity to involve in clinical trials.

Sarah: There's been a lot done to raise awareness of clinical trials out in social media. I think you'd find a lot of, not necessarily public hospitals, but certainly private clinical trial sites like Skin Health Institute do a lot of social media advertising. We have a clinical trial Facebook page where we post a lot of our new clinical trials. It's important to say that all of the advertising that we actually publish onto social media is all ethically approved. We have minimal information about the actual study and prefer patients to follow links to register their interests where we then call them up and ask them about the study.

Tam was talking about some of the platforms where you can find information. There's another really great clinical trial site, which is an international clinical trial site called clinicaltrials.gov, which has a lot of information about trials that are running right throughout the whole world, not just in Australia. There are some really great apps. One I can think of at the moment is ClinTrial Refer, which is one that a lot of doctors are using now to find the right trial for their patient. It's something that's easily accessible on their phone, which is really good. That's generally how we get a lot of our referrals, through social media and through referrals from our clinicians.

Tam: If I could add to Sarah's point about advertising as well, as someone who managed the Ethics Committee at St. Vincent, we definitely have a very tight, strict advertising guideline in terms of what the trial site or the sponsor can say and can't say in terms of talking about the current ongoing study without really coercing or over-promising the potential benefits. Certainly, there are, and we've seen that during the pandemic where the TGA actually really clamped down on providers who really step over the line of promoting or advertising guideline of clinical trials

Laxmi: Yes, you've raised an excellent point about advertising and clinical trials. I think with social media now, that's a big concern because any message out there can just spread rapidly and exponentially and it could be the wrong message or a really exaggerated message to a vulnerable patient on Instagram or something like that.

Sarah: Can I add also the importance of patient advocacy groups as well? We have a number of advocacy groups that we do actually use, not necessarily to advertise clinical trials blatantly, but we will advise them of what we're doing so they can then inform their readers or their members about what is actually out there because I think that is the most important thing that we really want to try and do is increase awareness and knowledge about clinical trials because there are lots of people out there that could really benefit from participating in a clinical trial, but just don't quite know how to get there.

Laxmi: Peter, what are some of the different trials that are offered at the Skin Health Institute?

Peter: As you touched upon at the start, we've been involved with a lot of clinical trials over the last couple of decades at the Skin Health Institute. The big ones at the moment tend to be particularly psoriasis, atopic dermatitis or eczema, vitiligo, alopecia areata, and hidradenitis suppurativa. Over the years, we've been involved with new therapies that are routine practice now for treating basal cell carcinoma, for treating actinic keratoses or sunspots, acne, rosacea, even seborrheic dermatitis. There's a whole host of dermatological conditions that we've been involved with and there are more studies coming through.

We've even been involved with a generic version of Botox for frown lines. Again, even though it's for cosmetic purposes, a head-to-head comparison trial approved by an ethics committee was required in order for that drug to be licensed in Australia.

Sarah: We're also running investigator led and collaborative studies as well that a lot of our clinicians at the Skin Health Institute are participating in. Whilst sponsored clinical trials are generally our bread and butter with regards to what we provide, we do have a number of clinical trials or research projects that we are running at Skin Health Institute, which have been developed by our own doctors. We also look at quality assurance projects as well, which are generally considered to be low risk, but we are looking at collecting data of what we are doing with standard of care and working out whether or not there's a better way of managing patient health just through what we can see through our general care of participants or patients.

Laxmi: Tam, would you like to discuss some of the trials being offered at St. Vincent's Hospital?

Tam: Yes, sure. At St. Vincent Melbourne, we're part of St. Vincent Health Network, fairly active in clinical research and trials. We would have something like just under 500 clinical trials spanning, drugs, devices, digital, and diagnostics as I mentioned before. Specifically, in Melbourne, we as a tertiary teaching center, we cover really broad therapeutics areas. Oncology, hematology, gastroenterology, neuro, of course, dermatology as well. If the listener wish to refer their patient to some of our trials, you can certainly look up our website for further details.

Laxmi: That's great that there's such a broad range of trials. Sarah mentioned earlier that there are many patients wanting to get onto clinical trials and they just don't know about it. Can patients self-refer to get on a clinical trial, or do they require a medical referral?

Tam: There needs to be a referral and the screening part which Sarah touched on as well. I think if I could add to that is actually supporting our clinicians. Not everyone is involved in clinical trials. To actually support our clinician to make sure that they are aware of trials available rather than the patients and the family constantly asking for trials. That could be a bit challenging.

Sarah: I would have to agree with Tam there. I think obviously, one of the biggest challenges is getting the information out there for patients and families, but it's also providing succinct information that clinicians can use when they're seeing a patient because they're often very busy, there's lots of things that they're running through with the patient while they're in the clinic and so a clinical trial is not necessarily the thing that they want to talk about.

Laxmi: Finally, what do you enjoy most about being involved in clinical trials? I might start with you, Peter.

Peter: Thanks for putting me on the spot. I think being part of clinical trials as a clinician means being at the cutting edge, being at the forefront of innovation. Unfortunately, in almost every disease state that we as medical practitioners address, no therapy is universally effective or universally without side effects. We're always trying to find new ways to treat patients more effective, safer, more convenient, more cost-effective. By being involved with clinical trials, it means we are, hopefully, positively changing patients' lives by bringing those new therapies to the participants, but also to the general public should those trials show that the investigational product is both safe and effective. It's being at the cutting edge and offering therapies that others can't offer.

Laxmi: Tam yourself?

Tam: I wholeheartedly agree with Peter on the aspects of being involved in the latest cutting-edge, not only in Australia but on the global stage as well. Perhaps maybe we could zoom out a little bit at a macro level where the cost of healthcare is always increasing and so we're talking about 14% to 15% of GDP spent on healthcare. Now to make sure it's been effective, there's a fair bit of research and innovation, and clinical trials will address some of that, address some of the burdens of disease, address some of the inefficiency, and so and so forth in our healthcare system.

To a certain extent, in some therapeutic areas, it's actually cost saving for the government, for the hospital if patients are on clinical trials. I think importantly, the point that Peter raised that really important, that I think everyone recognises that getting the latest treatment option for the patient and addressing that health equity is important.

Laxmi: Clearly, you both find it very rewarding to be part of clinical trials. Sarah, what about yourself?

Sarah: Well, for me, obviously, with my boss here in the room, I would say that working with Peter Foley, one of the key opinion leaders in dermatology in Australia is a real highlight. I guess really at the end of the day, for me, it's about working with my team, the clinical trial coordinators, the nurses, and also our advanced therapeutic nurses, our team that work on our dermatology registry. That brings me a lot of satisfaction, but most importantly it's working with the participants.

Having worked in clinical trials for 20 years, I've been privileged to have been a part of a lot of clinical trials that have brought some really important therapies to the market. Certainly, in dermatology, but also with hepatitis C and HCC or hepatocellular carcinoma have been really important for me and seeing a positive outcome for these patients and certainly for people in the future that really rely on us running clinical trials to make their lives much better.

Laxmi: Thanks for that, Sarah. We couldn't run our clinical trials without you, so thank you.

Laxmi: That concludes today's episode and what a fantastic discussion that has been about clinical trials. I hope some of our listeners that are interested in research have enjoyed this discussion just as much as I have. Sarah, Peter, and Tam, I would really like to thank you for being here today and sharing your pearls of wisdom. We would like to thank the education team at the Skin Health Institute and Balloon Tree Productions.

Remember these podcasts are not meant to replace medical advice. If you have a skin condition that requires attention, we strongly encourage you to see your medical practitioner. For listeners who want more information on this subject, a transcript of this episode and links to other resources can be found on our website spotdiagnosis.org.au. That's spotdiagnosis.org.au. Please share *Spot Diagnosis* with your friends and colleagues. Rate us and review us. Let us know what you think. We would really appreciate your feedback and any suggestions. Also, please note that *Spot Diagnosis* is eligible for RACGP and ACRRM CPD.

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