NATF North American Thrombosis Forum
Fighting blood clots through education

The Beat

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Clinical Trials 101: Your Guide to the Gold Standard of Research

Dr. Suresh Vedantham

The race is on to develop a COVID-19 vaccine, and several trials are underway to ensure that the vaccine is safe and effective. But what exactly happens in a clinical trial? We asked Dr. Suresh Vedantham, Assistant Dean for Clinical Research and Professor of Radiology and Surgery at Washington University School of Medicine, for answers to common questions about trial research.

Q: What does a clinical trial involve?

A: A clinical trial is a study that's designed to answer a question about a diagnostic method, a treatment, a vaccine, or about health care in general. Clinical trials are typically done in four phases. (See infographic on page 3.)

All trials are designed according to what's called a protocol, which is basically the plan for doing the study, and that plan must be approved by an independent body called an Institutional Review Board (IRB). The IRB, which includes healthcare providers and laypersons, reviews the ethics and safety of the trial from the perspective of a patient who might be in that study.

Once the IRB approves the trial, researchers start recruiting patients for the study. Common marketing techniques for clinical trials include social media, radio, TV, billboards, or signs/posters in hospitals. Researchers will also partner with providers. So, if I'm trying to enroll people with a certain condition, I'll reach out to doctors who see patients with that condition, I'll ask if I can put up ads in their clinics, and my team and I will educate the doctors and staff so they can pass along the information to their patients. We're also able to use electronic medical records to find participants for some studies – as long as adequate privacy protections are in place.

There are unique ways to find participants if you're studying an in-hospital population, too. For example, if you're looking at a condition that requires a CT scan for diagnosis, we may be able to obtain

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Inside

Get to Know Our COVID-19 and Thrombosis Grant Recipients!

We now know that some patients who get COVID-19 can develop serious blood clots. To address the need for more studies on COVID-19 and thrombosis, NATF awarded two $25,000 grants to support research and career development among clinicians and scientists in the early stage of their careers. We're thrilled to introduce the NATF community to our two awardees, Drs. Alec Schmaier and Shuchi Gulati!

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Upcoming Support Groups and Events

In-Person Blood Clot Support Groups

Temporarily moving online due to COVID-19

October 13, 2020

November 19, 2020

December 17, 2020

Please visit natfonline.org for more information. All support groups start at 7:00 PM EST.

World Thrombosis Day

Website: worldthrombosisday.org

October 13, 2020

Get in Rhythm. Stay in Rhythm.® Virtual Atrial Fibrillation Patient Conference

Hosted by our partners at StopAfib.org

October 30-November 1, 2020

For more information and to register, visit getinrhythm.com

For more information or to register for these events, please visit www.natfonline.org/events or email events@natfonline.org.

GET TO KNOW OUR COVID-19 AND THROMBOSIS GRANT RECIPIENTS!

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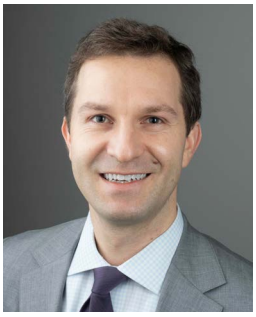

Dr. Alec Schmaier

MEET DR. SCHMAIER

Alec Schmaier received his medical degree and PhD at the University of Pennsylvania, where he studied platelet biology. "Platelets are the tiny blood cells that help us form clots. They can be activated in disease and cause heart attacks and strokes. I studied how they become activated on vessel wall collagen under conditions of blood flow," he explains.

After finishing his PhD, he completed his internal medicine residency at the Hospital of the University of Pennsylvania in Philadelphia. He then came to Boston to pursue a cardiology fellowship with an additional year of clinical training in vascular medicine. He also completed a postdoctoral research fellowship at Beth Israel Deaconess Medical Center, where he's now on staff in the Department of Cardiovascular Medicine. "I currently see patients in clinic every week and do vascular medicine consults as I try to grow my own laboratory program in basic science and translational research. I think of translational research as going from bench to bedside, meaning from the lab to the patient care setting or the reverse, from bedside to bench. Translational research exists right at that interface. It may involve measuring patient samples, looking for new biomarkers that could have value in making a diagnosis or providing treatment to a patient, or taking early therapies developed in the lab and examining how they function in a clinical trial."

Dr. Schmaier has been researching the body's response to inflammation for several years. "People who have severe infections get very sick, which is known as "sepsis." They have inflammation all over their body, their blood vessels become leaky, and they're prone to having blood clots. My colleagues and I have done research looking at patients with sepsis. Some of them had a predisposition to forming blood clots and some didn't, and we identified some key proteins and signaling pathways that were unique in the patients who had clotting

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information about that CT scan and identify the patient that way, and then we can approach the patient in person.

Importantly, all recruitment methods need to be approved by the IRB.

Q: What are the benefits of participating in a trial?

A: As a trial participant, you'll generally be part of a structured program and closely monitored. For some types of trials, you may have access to treatments that you wouldn't have otherwise; for example, investigational treatments that aren't FDA approved yet. And, of course, you'll get the satisfaction of knowing that what you're doing will ultimately benefit other people. I've also found that patients really like the concept of being actively involved in their own care. Oftentimes, trials enable you to ask more questions and learn a bit more about your condition.

That said, it's important to know that you won't get worse or inferior care if you don't participate in a trial. There are some inconveniences that come with trial participation as well. Typically, you'll have to devote some time to traveling to and from study visits, and patients do take on some risk when they join a trial since the risks and benefits of some treatments/therapies aren't fully understood yet.

Phases of a Clinical Trial

PHASE 1

New treatments or therapies are tested in a small group of people (fewer than 100) to determine safety and identify side effects.

PHASE 2

The same treatment or therapy is given to more people (100-300) to further assess safety and effectiveness.

PHASE 3

The treatment or therapy is given to much larger groups of people (typically more than 1,000) to confirm that it works. Researchers will continue to monitor side effects during this phase.

PHASE 4

Also called "post-marketing studies," these trials are conducted to obtain more information about the risks, benefits, and best use of a drug or therapy after the U.S. Food and Drug Administration (FDA) has approved it.

Q: What's the next step once I agree to participate in a trial?

A: A member of the research team will ask for your informed consent, which involves a discussion between you and the researcher or team member to review the study protocol, discuss what your participation would entail, and address the potential risks and benefits of participating in the trial. You'll also receive a written description that summarizes the goals of the study and what you'll be expected to do. Most trials include study visits, and the consent document will outline what will occur at these visits.

Local travel expenses and participant time (for example, coming for a study visit, parking, etc.) are typically covered as part of the study. Compensation is spelled out in the consent document upfront, along with how long the study will go on for.

Before giving your consent, you should feel free to ask any questions that come to mind so that you understand every component of the trial process. It's completely your choice to take part in the study. If you decide to provide informed consent, you'll be asked to sign a consent document, either in person or online.

After giving consent, you may be asked to participate in some baseline studies. These assessments can include a medical history, physical exam, imaging studies, blood draws, or just written questionnaires.

You can withdraw from the study at any time.

Q: What should I expect once the study starts?

A: Although every trial requires different levels of participation, you'll likely have regular contact with a member of the research team. We typically call that person a coordinator; they'll facilitate and guide you through your study visits.

During the study, there will be some type of routine assessment to determine what's happening now that we've changed a component of your care. So again, we may use blood tests, imaging studies,

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questionnaires, etc. to look at what's working or not working, or to monitor changes.

You'll be notified when the study is over and thanked for your participation. Once the study outcomes are known, you may also receive a letter detailing the results.

Q: Are clinical trials safe?

A: Some treatments being studied turn out to be more effective or safer than existing treatments, and and some don't. You only know that once the trial is over – but the IRB would not allow a trial protocol to proceed if there were obvious red flags upfront. In addition, the study plan needs to incorporate safeguards for patient safety, appropriate to the type of study being done.

For treatments that might carry some risk, an independent expert board called a Data and Safety Monitoring Committee will periodically review the ongoing results of the trial. This committee doesn't have any relationship to the researchers, so they don't have a stake in the trial continuing or not; they just want to ensure safety. If one treatment turns out to be conclusively better than another in the middle of the trial, the board would stop the study. Likewise, the trial would be suspended if one treatment clearly causes harm.

Q: How is patient data kept private?

A: The specifics around patient privacy must be provided upfront to the IRB, and they won't approve a trial protocol unless they're confident that adequate safeguards are in place. Beyond that, researchers generally store health information in a secure study database where participants are assigned an anonymous ID number.

Privacy is also outlined in the informed consent document that patients sign. There will be statements about what the research team would like to do with the information; in other words, who would have access to it down the road. Researchers often want the ability to share information with other researchers so we can obtain the most good from it, as long as privacy protections are appropriately maintained. You should always make sure that you understand the privacy statements in the informed consent document prior to signing it.

We can never say in the modern world that anything is 100% hackproof, but there are very strong efforts to prevent data breaches in research. Researchers think about privacy explicitly when designing protocols.

Q: Will my treatment outcome change if I participate in a trial?

A: A trial plan will always detail what parts of treatment you'd normally get and what new treatments you might get in the trial. If there are any standard treatments you'd have to give up in the trial, that should be made clear, too. It's not easy to predict outcomes upfront because the change in care is often what's being studied in the first place.

Q: How has the COVID-19 pandemic affected clinical trial research?

A: Outside of vaccine trials, COVID-19 has had a significant impact on study participation. Most researchers have been trying to find ways to make it easier for patients to participate in studies with a minimum of in-person visits to the study center. We're leveraging technology as much as we can so that patients can fill out questionnaires and sign informed consent documents from the comfort of their home. For visits that must be done in person, we're being proactive to help patients safely navigate research visits. We're ensuring that they have safe spaces for waiting, that they're distanced from other people, that they're wearing masks, and that everyone is doing their part to maintain a safe environment. The trial I'm currently working on, called C-TRACT, now allows some visits to be done remotely when needed and I think patients appreciate that. (For more information on C-TRACT, see below.) ■

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problems. We found that if we can activate these pathways, we can potentially help suppress blood clots in experimental models. The COVID-19 pandemic now gives us a natural opportunity to study some of these protein targets we've identified and learn more about how clotting is regulated in severe illness. We think that these signaling pathways that affect blood vessel integrity are going to be severely altered in COVID-19. That's the first thing I'm hoping to look at with NATF's generous grant."

A second aim of the project is to look at a new therapy in COVID-19 trials. "We have a novel therapy unrelated to this project and we're going to be taking patient samples and testing them on cells grown in our laboratory to see whether this drug can decrease the tendency of the endothelial (blood vessel lining) cells to form blood clots in COVID-19," says Dr. Schmaier.

"I think that we're going to learn a lot more about the biology of COVID-19 and what's going on with blood vessels and clotting. I think—and hope—that our research will give us information that we can apply to other diseases and to blood clotting in general. Sometimes, the silver lining of these extreme medical situations is that they give us really important insights that we can apply broadly to other issues."

Dr. Shuchi Gulati

MEET DR. GULATI

Shuchi Gulati attended medical school in India and completed her internal medicine residency in Reading, Pennsylvania. She completed her fellowship in hematology and oncology at the University of Cincinnati and recently obtained a master's degree in clinical and translational research. She specializes in genitourinary cancers—prostate, kidney, and bladder cancers—and also oversees clinical trials at the University of Cincinnati School of Medicine.

Dr. Gulati had an interest in treating cancer since childhood. "My mother had cancer when I was very young and even though I didn't understand what she was going through, I saw how it impacted our family as a unit. Knowing that she was sick made me want to get involved with cancer research so that I could make a difference. And now as a doctor, it really impresses me how cancer patients can go through such major setbacks and then come out the other side. It's very inspirational."

Since becoming an oncologist, Dr. Gulati has started to focus more on cancer and blood clots (cancer-associated thrombosis). "There's a huge unmet need there. When patients with cancer get clots, we sometimes don't connect those dots. There's a lot of research that still needs to be done, especially now in the COVID era," she explains.

When the pandemic hit, Dr. Gulati started thinking about how COVID might affect cancer patients in particular. "The University of Cincinnati got involved with this national registry called CCC-19 – the COVID and Cancer Consortium. More than 100 institutions are now part of it. I'm part of the Consortium's thrombosis team and started collecting data for the registry. As part of that project, I became really interested in whether there's an overlap between patients with cancer-associated blood clots and patients with COVID-19 infection and that's why I applied for NATF's grant."

"Many patients with cancer may be taking medications or receiving treatments that heighten the risk of blood clots already. In the setting of COVID-19 infection, there might be a subset of those patients who need more aggressive doses of medication to prevent blood clots—what we call "thromboprophylaxis"—whether they're in the hospital or at home," says Dr. Gulati. "So that's what I want to study – if patients with cancer will have worse outcomes, especially clot-related outcomes, if they already have risk factors for blood clots and then get infected with COVID-19. I also hope to learn if there's anything specific that would help these patients, like counseling, additional drug support, or specific guidance related to COVID-19 in general."

The response to Dr. Gulati's work has been overwhelmingly positive. "My patients have been excited to hear about my research. I find that patients like to know when you're working on a project or thinking about ways to make their lives better, especially when they have multiple medical issues to manage. The reception from my colleagues and patients around this project is encouraging and I hope that this collaborative effort with CCC-19 will help us provide patients with some key information about cancer, COVID-19, and blood clots." ■

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North American Thrombosis Forum
368 Boylston Street
Brookline, MA 02445

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NATF Board and Staff

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STAFF

Kathryn Mikkelsen, MBA
Executive Director
KMikkelsen@natfonline.org

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Director of Operations
CJohnson@natfonline.org

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Director, Content Development
Managing Editor, *The Beat*
ASchwartz@natfonline.org