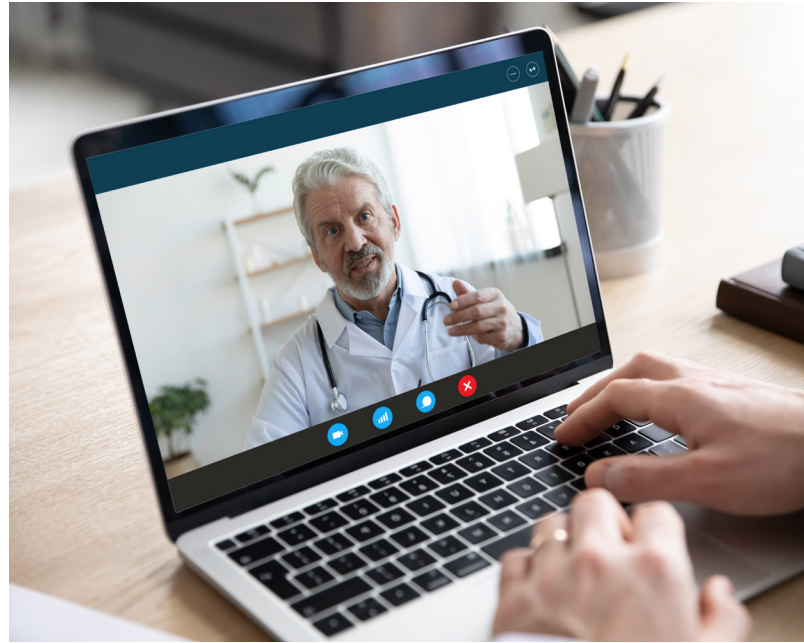




Mastering the basics of clinical trials

Exploring the key aspects
of clinical trials



Introduction

New treatments can't reach patients without clinical trial volunteers. Recent events, particularly the COVID-19 pandemic, have put the importance of these trials at the forefront, and we've seen increased interest in taking part.

At Antidote, we receive a lot of questions about participating in a clinical trial. Here, we're going back to basics. Read on to explore key aspects of clinical trials, such as:

- What is a clinical trial?
- How do clinical trials work?
- Why consider participating in research?
- How do you find, match, and screen for a trial?
- What should you expect once you've joined a trial?
- What happens after the trial is over?

What is a clinical trial?

Clinical trials are a kind of clinical research designed to evaluate and test new medical interventions, such as drugs, devices, or behavioral changes. In the United States, medications and medical devices can't reach patients without being approved by the Food and Drug Administration (FDA). Each potential new treatment must make its way through several clinical trial phases that test for safety and effectiveness. Clinical trials may also help researchers discover what medical approaches work best for certain groups of people.



There are two main types of clinical trials: interventional studies and observational studies.

Interventional studies are clinical trials testing whether a specific intervention (such as a drug, device, or behavioral change) affects health-related outcomes.¹ Different groups of people are assigned at random to receive and not receive the intervention in a process called randomization. Typically the group that does not receive the intervention – also known as the control arm – receives either the current standard of care or a placebo (a fake version of the intervention), depending on the condition. Interventional trials are also typically blinded, meaning that participants are not aware if they are in the control group or receiving the intervention, or double-blinded, meaning that both the researcher and the participants are not aware.

Observational studies, on the other hand, are trials in which researchers ask patients with the same disease or treatment plan to be observed over a period of time.¹ During this time, researchers watch how patients are responding to their treatments and take into account different variables that patients might be exposed to.



Clinical research is often categorized based on what is being studied:²

- **Treatment research** generally involves an intervention.
- **Prevention research** looks for better ways to keep disorders from developing or returning.
- **Diagnostic research** refers to the practice of looking for better ways to identify a particular disorder or condition.
- **Screening research** aims to find the best ways to detect certain disorders or health conditions.
- **Quality of life research** explores ways to improve comfort and quality of life for individuals with a chronic illness.
- **Genetic studies** aim to improve the prediction of disorders by identifying and understanding how genes and illnesses may be related.
- **Epidemiological studies** seek to identify the patterns, causes, and control of health conditions in groups of people.

Some clinical research is “outpatient,” meaning that participants do not stay overnight at the hospital, while some is “inpatient,” meaning that participants will need to stay for at least one night in the hospital or research center.

How do clinical trials work?

During a trial, volunteers receive an intervention based on a clinical trial protocol put together by the researchers running the study. This means they'll either receive the new treatment or device being tested, or they will receive a placebo or the current standard of care, depending on the condition. For life-threatening illnesses with available treatment, such as cancer, placebos are rarely used.

As the treatments are administered to volunteers, researchers measure outcomes – things like how the patient feels, changes in symptoms, decrease in spread of disease, etc. These measurements help them determine the efficacy of the trial – that is, whether the treatment or device being evaluated works to improve outcomes as anticipated. Researchers also keep careful track of how volunteers react to the interventions being tested in order to determine its safety.



Clinical trials move through phases, testing interventions in larger groups until they are determined safe and effective. The typical timeline looks like this:

- **Phase 0** is a relatively new step in the clinical trial process. This early stage is intended to quickly weed out ineffective drugs, or establish that a drug will work as expected in the body. This stage only enrolls a few volunteers, who are given just 1% of the dose of the drug being researched.³ These short trials give researchers a sense of how the drug will behave in the body. This phase is not required by the FDA, but is suggested particularly for drugs that aim to treat serious diseases.

- **Phase 1:** These trials typically enroll 20 to 100 healthy volunteers or people with the condition being studied, and last several months.⁴ This phase measures safety by testing for any adverse side effects of the treatment, but not necessarily how effective the drug or device is.

● **Phase 2:** Around 70% of potential new drugs pass Phase 1 and enter Phase 2, which continues to measure safety, while also looking at how effective the treatment is and carefully investigating side effects. Phase 2 trials recruit up to several hundred patients with the condition to take part. This phase typically lasts several months to two years.⁴

● **Phase 3:** Just 33% of drugs make it past Phase 2 and into Phase 3, which tests the potential treatment in the largest number of people. This phase measures both safety and effectiveness with many volunteers, sometimes thousands. Phase 3 trials last from one to four years.⁴

● **FDA Approval:** After Phase 3, a pharmaceutical company may submit a New Drug Application (NDA) or a biologics license application (BLA) for the treatment to the Food and Drug Administration (FDA). The FDA then reviews results from all stages of the trial to determine whether it will approve the drug and allow the pharmaceutical company to begin marketing it to the public.⁵

● **Phase 4:** This phase is often called “Post-Approval Research and Monitoring.” After a new treatment is approved by the FDA, the pharmaceutical or device company may want to continue monitoring patients to learn more about the treatment’s longer-term effects, while comparing it against other already-approved options. It may take time for long-term side effects to appear, making this an important phase.⁵

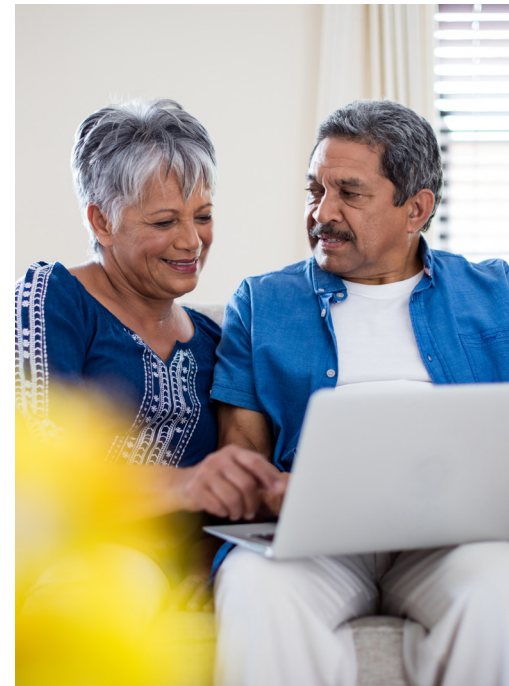
Looking at the big picture, it takes approximately ten years for a new treatment to complete the journey from initial discovery to the marketplace. Clinical trials alone take six to seven years on average to complete.⁵



Why consider participating in research studies?

There are several reasons to consider participating in research studies, from accessing the latest treatment options to helping move research forward. Participants weigh these benefits against potential risks and learn as much about a trial as they can before making their decision.

Thousands of clinical trials participants shared their attitudes about clinical research with us, and we learned that these are some of the most common motivators for participating in research:⁶



- **Access to potential new treatments:** Research studies investigate potential new treatments and interventions. That doesn't just mean medications; trials also explore lifestyle changes like diet and exercise, alternative therapies like massage and mindfulness, and new medical devices, too. For those whose symptoms aren't well managed on their current treatments, accessing a new option can make a real difference.

- **Help everyone living with your condition:** Knowing that you're making a difference for others living with your condition, as well as future generations, can be motivating. Some clinical trial participants feel motivated to get involved on behalf of future generations. It takes about a decade for an experimental drug to make it from the lab to pharmacy shelves. It's a long process that needs volunteers to ensure timelines don't become even longer.

- **Access better care:** Clinical trial participants report that they often receive extra attention during clinical trial visits versus normal doctor's appointments. You may be able to skip the waiting room, and have time for additional questions about the study and other medical questions you may have. Research is generally also conducted at top research universities and facilities, so you'll often receive care from physicians who are leaders in their field. If you join a clinical trial for your condition, you'll be working with researchers and physicians who are likely experts in your condition.

- **Compensation:** You may have heard that you can sometimes earn compensation for participating in clinical trials. Even for trials that don't offer compensation for your time, some researchers will reimburse your travel expenses or child care costs. Ask any questions you have about compensation at your trial intake session before making the decision to sign up.



Find and match with a trial

There are currently nearly 350,000 research studies in all 50 states and in over 200 countries that need volunteers to take part.⁷ Even with so many options, it can be difficult for interested patients to find opportunities near them.

These are some common ways that you can learn about clinical trials:

- Contact patient communities and advocacy groups
- Connect with other patients, either online or in person
- Ask a health care provider if there are any clinical trial opportunities that might be right for you
- Click on a digital advertisement to learn more about a specific trial
- Do your own research
- Fill out an online pre-screener to see if you qualify for a trial
- Sign up for a registry to be informed about upcoming matching trials
- Have conversations with family and friends

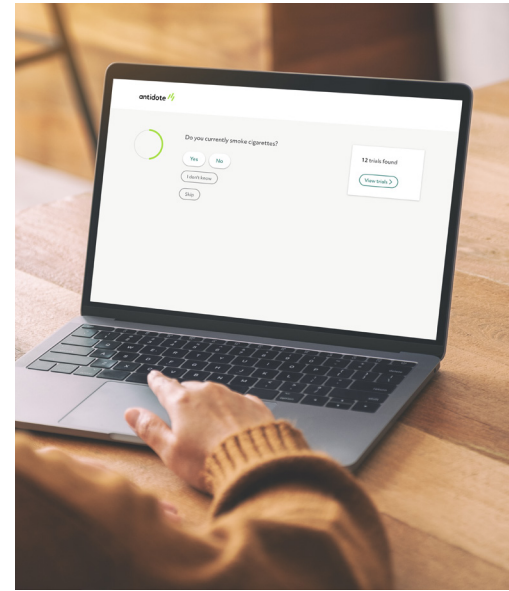
All clinical trials that are looking for patients are listed on ClinicalTrials.gov, but since the website was built for researchers rather than patients, it can be difficult to navigate. Antidote created a tool called Match that allows you to search for trials in your area based on questions about you and your health. Nonprofit organizations and other websites may have tools you can use specifically for your condition, too.

And remember it's always a good idea to talk to your doctor. Share trials you're interested in with your primary care physician or specialist. They can advise on whether they believe the trial is a good option for you considering your current treatment plan. If you have a few different trials you're choosing between, your doctor can help you make the final call.

Screen for a trial

Screening for a clinical trial these days often begins online, over the phone, or a combination of the two. This process is called pre-screening, and it helps save time for researchers and patients by testing initial eligibility for a particular trial. Pre-screening may also involve follow-up phone calls with those running the trial or a patient recruitment company to validate your symptoms, medication use and dosages, etc.

If you appear to be eligible to participate for a trial, the next step would be to visit a nearby research site for additional screening. At the screening visit, you'll meet with study staff (clinical study coordinators and the principal investigator). Before you sign on, you can ask the study team as many questions as you would like. Here are some ideas of questions to ask as you're evaluating the study and making your decision about participation:



- How long will the study last?
- What is the goal of the study?
- Will I be reimbursed for my expenses?
- Does the study include a placebo?
- How will I receive the treatment?
- Can I continue taking the study drug after the trial if it works for me?
- How will my privacy be protected?
- What can I expect at each study visit?
- What happens if I leave the study early?
- What happens if my condition gets worse or I am injured during the trial?
- Who will be conducting the study?
- What did previous studies find out about the treatment? Have the results been published?
- What are the potential risks and benefits of the study drug?
- Will I receive follow-up care after the study?
- Will the results of the trial be provided to me?
- What are the risks?
- What are my protections?

The trial team will answer all of your questions and go over the details of the trial. Once you are satisfied that you fully understand the trial and are comfortable with what will be expected of you, you'll be asked to sign an informed consent form to officially join the trial. Even after you sign the form, you can still leave the study at any time.

What to expect once you've joined a trial

Once you've joined a clinical trial, it's crucial that you adhere to the protocol (e.g., take the study drug as required), pay attention to your symptoms and potential side effects, attend study visits, and share your feedback.



Study visits: The study visits themselves will vary based on the kind of trial you've joined. Your visits may be similar to regular doctor's appointments, with additional attention and questions related to the clinical trial. For some trials, site visits are conducted virtually. In those trials, you'll talk with the study team over a webcam on your computer or a device provided by the researchers.

In between visits: Some trials may also ask you to keep a virtual or paper diary during the trial to track your symptoms or answer other questions related to your health, such as your exercise routine. It's important to record your diary entries as directed by the study team to ensure that the study is collecting accurate data.

It's also important that you get to know the study team. The below list will likely vary depending on your clinical trial site (a research university lab vs. a hospital vs. a doctor's office), but it's good to know the who's who of clinical research once you've joined a trial:

- **Principal investigators (PIs) and co-principal investigators (co-PIs):** A PI is the person in charge of a clinical trial or a scientific research grant. PIs and co-PIs prepare and carry out the clinical trial protocol or research paid for by the grant. The principal investigator also analyzes the data and reports the results of the trial or grant research.

- **Clinical research assistants (CRAs):** Duties will vary greatly based on the type of research setting in which they work, but typically, CRAs provide support to professionals who are conducting experiments or gathering and analyzing information and data. CRAs usually have a Bachelor of Science degree and some experience in the specific field being researched. Since clinical research assistants are often asked to handle a majority of the responsibility when it comes to finding and interviewing potential participants for a trial, their knowledge of the research protocol is extensive and unparalleled.

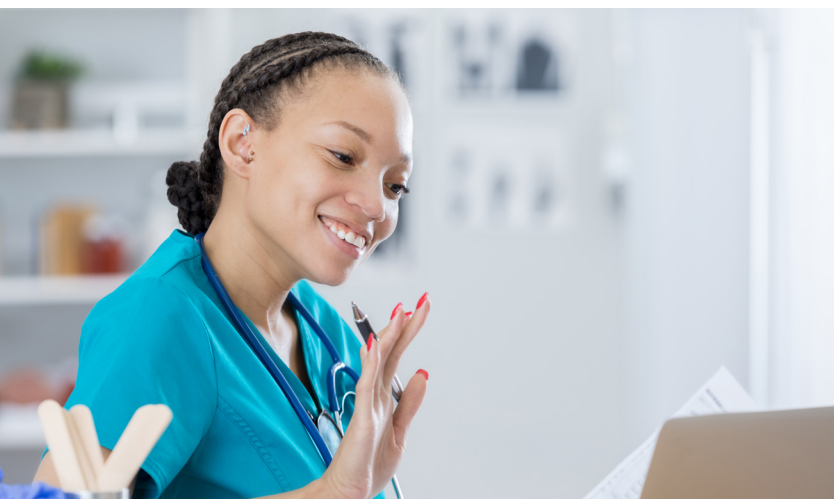
- **Clinical research coordinators (CRCs):** A CRC is a research professional who works with and under the direction of the PI. The CRC supports, facilitates, and coordinates the daily clinical trial activities and plays an essential role in the conduct of the study. CRCs are often involved in critical duties alongside the PI, such as conducting the informed consent process and ensuring compliance with the protocol. Often, the CRC and CRA roles intersect and overlap, but CRCs have more administrative responsibilities and assist with the study design, data analysis, and writing up results.

- **Clinical research fellows:** A clinical research fellow is normally a doctor (MD or PhD) who is employed in a research role. Clinical research fellows do original research as well as help guide, shape, and assist with other studies led by PIs. Their skills can be utilized at any part of clinical research, from clinical trials to addressing basic science questions in the laboratory.

- **Graduate and medical school students and interns:** Like clinical research fellows, graduate students and interns are helpful in many areas of clinical trials. One day, they might be helping design a study and analyzing the data with PIs, and another day they might be working with CRAs to meet with research volunteers.

- **Nurses:** If the clinical trial you're participating in requires minor medical procedures like a blood draw, a nurse might be on site. Nurses can perform an array of medical tests, including, but not limited to, vital signs, imaging studies, and electrocardiograms. They can also administer investigational medications and document your medical data and history.

- **Pharmacists:** A pharmacist is often needed to ensure that good clinical practice is in place. They're also, sometimes, the ones who have a hand in concocting the treatments or drugs that the research is studying.





After the trial

Once a trial is complete, you may be able to continue taking the study drug – the study team should let you know whether this is the case before you enroll, but if they don't, mention it.

You can also ask before the trial starts how you can see the results of the study after it's completed. Trial teams typically publish their results, so you should be able to find the study after it's complete, even if it's not directly shared.

Conclusion

Medical research can't move forward without clinical trial volunteers. But the decision to participate in a clinical trial is extremely personal. It's critical to understand the entire process to ensure that you are comfortable with all that helping accelerate the discovery of new treatment options entails.

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To learn more about Antidote and our work,
please get in touch.

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¹ <https://clinicaltrials.gov/ct2/about-studies/glossary>

² <https://www.fda.gov/patients/clinical-trials-what-patients-need-know/what-are-different-types-clinical-research>

³ https://journals.lww.com/oncology-times/Fulltext/2006/08100/FDA_Introduces_New_Phase_0_for_Clinical_Trials_.6.aspx

⁴ https://www.fda.gov/patients/drug-development-process/step-3-clinical-research#Clinical_Research_Phase_Studies

⁵ http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf

⁶ <https://www.antidote.me/partner-not-participant-understanding-the-clinical-trial-decision-making-process-whitepaper>

⁷ <https://www.clinicaltrials.gov/>