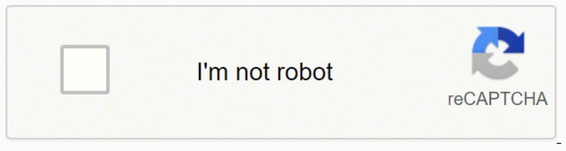

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How does human trials work

A protocol is a plan that explains how the trial will work, what will be done during the trial, and why. The trial sponsor, often the pharmaceutical company that develops the therapy or medication, designs the protocol for the clinical trial. While designing a protocol, sponsors often work with the Foundation to get feedback from research experts and people with CF. Key information in a protocol includes: How many people will participate Who is eligible to participate What tests participants will get and how often What type of data will be collected How long the study will last What medication and dosages participants will receive, if appropriate The protocol must go through many layers of review before a study can begin. Once a protocol is approved, the sponsor chooses principal investigators to run the trial. Each investigator follows the same protocol to ensure that the study is conducted in the same way at each participating center. Ensuring Trials are Unbiased Bias refers to human choices or other factors (unrelated to the protocol) that might affect a trial's results. For example, if doctors could choose which people to assign to comparison groups in a study, some might assign sicker people to the treatment group and healthier people to the placebo group. The doctors might not even realize they are doing this, and it could affect trial results. Researchers can avoid bias by designing a study in a certain way: Randomization helps ensure that researchers don't introduce bias into the trial. In many clinical trials that test the effectiveness of a medication, half of the participants receive the medication in question. The other half receive a placebo, which contains no medication. Randomization involves assigning participants to these comparison groups by chance, rather than choice. Blinding can also help avoid bias. In a blinded trial, researchers will not know which participants are receiving treatment and which ones are receiving a placebo. Who Can Participate? All clinical trials have guidelines about who can join, known as inclusion and exclusion criteria. These criteria exist to ensure that the trial results are accurate and useful, and also to protect participant's safety. Criteria are based on factors such as: Age CFTR mutation Current state of health Previous treatment history Other medical conditions The criteria depend on the type of trial. For example, if researchers are testing how well a particular antibiotic works in fighting Pseudomonas aeruginosa, then the trial would have inclusion criteria specifying that only people with CF who are infected with that bacterium can join the trial. Those who do not have that bacterial infection would be excluded from the trial. Another example is the age requirement for a trial. Drugs work differently in kids than they do in adults. To reduce the risk for younger kids with CF who participate in a trial, drugs must first be shown to be safe and effective in adults with CF. Clinical trials for a new drug will usually start in adults 18 years and older before moving down to younger age groups. The Four Phases of Clinical Research For any new drug to receive approval by the U.S. Food and Drug Administration (FDA) and become available to the public, it must pass through three phases of interventional clinical trials to show that it is safe and effective in treating the disease. If the FDA approves the drug, researchers will continue to monitor for safety and effectiveness in what is known as a Phase 4 study. The infographic below shows a breakdown of the questions that researchers try to answer, the number of participants needed, and the length of participation for each phase of research. Please note that the length of time refers to the time it takes to participate in a trial, not the entire length of the phase. It takes additional time to enroll participants and to process and analyze the results of each phase. All told, it typically takes 10 to 14 years from the time a drug is discovered in a laboratory to its possible approval by the FDA for people with CF. About Study Sponsors Clinical research can be sponsored (i.e., paid for) in part or entirely by any number of organizations or individuals. For example, medical institutions, universities, foundations, voluntary groups, drug companies, and federal agencies, such as the National Institutes of Health (NIH), all sponsor research. The CF Foundation is the primary supporter of CF research in the United States. Nearly all approved CF therapies available today were made possible because of research funded by the Foundation. We facilitate and financially support clinical trials through our Therapeutics Development Network (TDN), which is made up of CF care centers with an expertise in clinical research. Medically reviewed by Seunggu Han, M.D. — Written by Hannah Nichols on May 18, 2018Clinical trials are research studies that aim to determine whether a medical strategy, treatment, or device is safe for use or consumption by humans.These studies may also assess how effective a medical approach is for specific conditions or groups of people.Overall, they add to medical knowledge and provide reliable data to assist in health care decision-making and guidelines.To ensure participant safety, trials start with small groups and examine whether a new method causes any harm or unsatisfactory side effects. This is because a technique that is successful in a laboratory or in animals may not be safe or effective for humans.The main purpose of clinical trials is research. Trials are designed to add to medical knowledge related to the treatment, diagnosis, and prevention of diseases or conditions.Share on PinterestClinical trials are research studies that aim to determine whether a medical strategy, treatment, or device is safe for use or consumption by humans.Studies follow strict scientific standards and guidelines that aim to:protect participantsprovide reliable and accurate resultsClinical trials on humans occur in the final stages of a long, systematic, and thorough research process.The process often begins in a laboratory, where new concepts are developed and tested.Testing on animals enables scientists to see how the approach affects a living body.Finally, human testing is carried out in small and then larger groups.Trials may be carried out to:Evaluate one or more treatment interventions for a disease, syndrome or condition, such as drugs, medical devices, or approaches to surgery or therapiesAssess ways to prevent a disease or condition, for example, through medicines, vaccines, and lifestyle changesEvaluate one or more diagnosis interventions that might identify or diagnose a particular disease or conditionExamine identification methods for recognizing a condition or risk factors for that conditionExplore supportive care procedures to improve the comfort and quality of life of people with a chronic illnessThe outcome of a clinical trial may identify if a new medical strategy, treatment or device: has a positive effect on patient prognosiscauses unforeseen harmhas no positive benefits or has negative effectsClinical trials can provide valuable information regarding the cost-effectiveness of a treatment, the clinical value of a diagnostic test, and how a treatment improves quality of life.All clinical trials have a primary purpose. These can be broken down into the following categories:Treatment: Testing new treatments, new drug combinations, or new approaches to surgery or therapyPrevention: Examining ways to improve prevention or recurrence of disease through, for example, medicines, vitamins, vaccines, minerals, and lifestyle changesDiagnostic: Finding improved testing techniques and procedures for diagnosing diseases and conditionsScreening: Testing the best method of identifying certain diseases or health conditionsSupportive care: Investigating procedures to improve comfort and quality of life for patients with a chronic conditionHealth services research: Evaluating the delivery, process, management, organization, or financing of health careBasic science: Examining how an intervention worksClinical trials help improve and advance medical care. The studies provide factual evidence that can be used to improve patient care.Clinical research is only conducted if doctors are unaware of elements such as:whether a new approach works effectively in humans and is safewhat treatments or strategies work most successfully for certain illness and groups of individualsVarious elements are involved in setting up, running, and following up a clinical trial.Clinical trials protocolShare on PinterestA protocol is the written description of a clinical trial. It includes the study’s objectives, design, methods, scientific background, and statistical information.A trial follows a comprehensive plan, or protocol. A protocol is the written description of a clinical trial.It includes the study’s objectives, design and methods, relevant scientific background, and statistical information.Key information to include may be:the number of participantswho is eligible to take partwhat tests will be given and how oftentypes of data to be collectedthe length of the studydetailed information about the treatment planAvoiding biasResearchers must take measures to avoid bias.Bias refers to human choices or other factors that are not related to the protocol but which may affect the results of the trial.Steps that can help to avoid bias are comparison groups, randomization, and masking.Comparison groupsMost clinical trials use comparison groups to compare medical strategies and treatments. Results will show if one group has a better outcome than the other.This is usually conducted in one of two ways:One group receives an existing treatment for a condition, and the second group receives a new treatment. Researchers then compare which group has better results.One group receives a new treatment, and the second group receives a placebo, an inactive product that looks like the test product.Randomization Clinical trials with comparison groups often use randomization. Participants are allocated to comparison groups by chance rather than by choice. This means that any differences seen during a trial will be due to the strategy used and not because of pre-existing differences between participants.Masking or blindingMasking or blinding helps avoid bias by not informing either the participants or the researchers which treatment the participants will be receiving.Single blind: This is when either the participants or researchers are unaware, of which group is which.Double blind: This is when both participants and researchers are unaware.Confounding factorsA confounder can distort the true relationship between two or more characteristics.For example, one could conclude that people who carry a cigarette lighter are more likely to develop lung cancer because carrying a lighter causes lung cancer. Smoking is a confounder in this example.People who carry a cigarette lighter are more likely to be smokers, and smokers are more likely to develop lung cancer, but some people may carry a lighter for other purposes.Not taking this into consideration can lead to false conclusions.Who is in the research team?A principle investigator, who is usually a medical doctor, will lead each clinical study.The research team may include:doctorsnursessocial workershealth care professionalsscientistsdata managersclinical trial coordinatorsWhere are clinical trials conducted?The location will depend on the type of study and who is organizing it.Some common locations include:hospitalsuniversitiesmedical centersdoctors’ officescommunity clinicsfederally-funded and industry-funded research sitesHow long do trials last? This depends on what is being studied, among other factors. Some trials last days, while others continue for years.Before enrolling in a trial, participants will be told how long it is expected to last.There are different types of study, and different ways of organizing them. Here are some study types.Observational studiesCohort studies and case control studies are examples of observational studies.Cohort studyShare on PinterestA cohort study is an observational study in which participants are selected and followed forward in time, to see how likely disease is to develop within the group.A cohort study is an observational study in which the study population, or cohort, is selected.Information is gathered to establish which subjects have either:a particular characteristic, such as a blood group that is thought to be related to the development of the disease in questionexposure to a factor that may be linked to a disease, for example, cigarette smokingAn individual could be chosen because they smoke. They may then be followed forward in time to see how likely they are to develop a disease, compared with other people.This type of study is used to study the effect of suspected risk factors that cannot be controlled experimentally, such as the impact of smoking on lung cancer.The main advantages of cohort studies are:Exposure is measured in advance of disease onset and is therefore likely to be unbiased in terms of disease development.Rare exposures can be investigated by suitable selection of study cohorts.Multiple outcomes — or diseases — can be studied for any one exposure.Disease incidence can be calculated in both the exposed and unexposed groups.The main disadvantages of cohort studies are:They tend to be expensive and time-consuming, especially if they are conducted prospectively, which means moving forward.Changes in both exposure status and diagnostic criteria over time can affect the classification of individuals according to exposure and disease status.There could be information bias in the concluded outcome because the subject’s exposure status is known.Losses to follow-up may present selection bias.Case control studiesA case-control study can distinguish risk factors for a particular medical condition.Researchers compare people with a condition and those without it. Working backward through time, they identify how the two groups differ.Case-control studies are always retrospective — looking backward — because they begin with the outcome and then trace back to investigate exposures.The main advantages of case-control studies are:Findings can be obtained quickly.The study can take place with a minimum of funding or sponsorship.They are efficient for investigating rare diseases or diseases with a long induction period.A wide range of possible risk factors can be examined.Multiple exposures can be studied.They require few study subjects.The main disadvantages of case-controlled studies are:Incidence data cannot be generated.They are subject to bias.It can be difficult to obtain accurate, unbiased measures of past exposures if record keeping is inadequate or unreliable. This is called information bias.Selection of controls can be problematic. This may introduce selection bias.The chronological sequence between exposure and disease may be hard to identify.They are not appropriate for examining rare exposures, unless the exposure is responsible for a large percentage of cases.Nested case-control studyIn a nested case-control study, the groups — cases and controls — come from the same study population, or cohort.As the cohort is followed forward, the cases that arise become the “cases” in the case-control study. The unaffected participants of the cohort become the “controls.”Nested case-control studies are less costly and less time-consuming when compared with a cohort study.Incidence and prevalence rates of the disease can occasionally be projected from a nested case-control cohort study. This is not possible from a simple case-control study, as the total number of exposed individuals and the follow-up times are usually unknown.The main advantages of nested case-control studies are:Efficiency: Not all of the participants of the cohort require diagnostic testing.Flexibility: They allow the testing of hypotheses that were not anticipated when the cohort was planned.Reduction of selection bias: Cases and controls are sampled from the same population.Reduction of information bias: Risk factor exposure can be assessed with the investigator blind to case status.The main disadvantage is that the results have lower authority, due to the small sample size.Ecological studyAn ecological study looks at the relationship between exposure and outcome of the population or community.Common categories of ecological study include:geographical comparisonstime-trend analysisstudies of migrationThe main advantages of ecological studies are:They are inexpensive, as routinely collected health data can be utilized.They are less time-consuming than other studies.They are uncomplicated and straightforward to understand.The effect of exposures that are measured over groups or areas — such as diet, air pollution, and temperature — can be investigated.The main disadvantages of ecological studies are:Errors of deduction known as ecological fallacy can occur. It happens when researchers draw conclusions about individuals based solely on the analysis of group data.Exposure to outcome relationships is difficult to detect.There is a lack of information on confounding factors.There may be systematic differences between areas in how exposures are measured.Experimental studiesApart from observational studies, there are also experimental studies, including treatment studies.Randomized controlled trialsShare on PinterestA randomized controlled trial randomly allocates individuals either to receive or not receive a particular intervention (consisting of two different treatments or treatment and placebo).A randomized controlled trial (RCT) randomly allocates individuals either to receive or not receive a particular intervention.One of two different treatments will be used, or a treatment and a placebo.This is the most effective study type for identifying which treatment works best. It reduces the influence of external variables.The main advantages of RCTs are:There is no conscious or subconscious bias on the part of the researcher. This essentially guarantees external validity.Confounding variables such as age, gender, weight, activity level, and so on, can be canceled out, as long as the sample group is large enough.The main disadvantages of RCTs are:They are time-consuming.They can be expensive.They require large sample groups.Rare events can be difficult to study.Both false-positive and false-negative statistical errors are possible.Adaptive clinical trialAn adaptive design method is based on collected data. It is both flexible and efficient. Modifications can be made to the trial and the statistical procedures of ongoing clinical trials.Quasi-experimentQuasi-experimental, or “nonrandomized” studies, include a broad range of intervention studies that are not randomized. This type of trial is frequently used when an RCT is not logistically feasible or ethical.A number of hierarchies of evidence have been founded to enable various research methods to be ranked according to the validity of their findings.Hierarchies of evidence make it possible to rank various research methods according to the validity of their findings.Not all research designs are equal in terms of the risk of error and bias in their results. Some methods of research provide better evidence than others.Below is an example of the hierarchy of evidence-based medicine in the form of a pyramid, ranging from a lower quality of evidence at the bottom to high-quality evidence at the top.Medical research studies are divided into different stages, called phases. For drug testing, these are defined by the FDA.Early phase trials investigate the safety of a drug and the side effects it may cause. Later trials test if a new treatment is better than an existing treatment.Phase 0 trials: Pharmacodynamics and pharmacokineticsPhase 0 is an exploratory phase that helps provide clinical information for a new drug at an earlier phase.This phase:is conducted early in phase 1involves very limited human exposurehas no therapeutic or diagnostic intent, being limited to screening and microdose studiesPhase 1 trials: Screening for safetyAfter phase 0, there are four more phases of trials in humans. These often overlap. Phases 1 through 3 take place before a license is granted.Phase 1 guidelines involve:between 20 and 80 healthy volunteersverification of the most frequent side effects of the drugfinding out how the drug is metabolized and excretedPhase 2 trials: Establishing effectivenessIf phase 1 studies do not reveal unacceptable toxicity levels, phase 2 studies can begin.This involves: between 36 and 300 participantscollecting preliminary data on whether the drug works in people with a certain disease or conditioncontrolled trials to compare those receiving the drug with people in a similar situation who are receiving a different drug or a placebocontinued safety evaluationstudies of short-term side effectsPhase 3 trials: Final confirmation of safety and effectivenessIf phase 2 has confirmed the effectiveness of a drug, the FDA and sponsors will discuss how to conduct large-scale studies in phase 3.This will involve:between 300 and 3,000 participantsgathering further information on safety and effectivenessstudies of different populationsexamining various dosages to determine the best prescription amountusing the drug in combination with other drugs to determine effectivenessAfter this phase, the complete information on the new drug is submitted to the health authorities.Review meetingIf the FDA approve the product for marketing, post-marketing requirement and commitment studies are conducted.The FDA use these studies to collect further safety, efficacy or optimal use information about the product.New Drug ApplicationShare on PinterestAfter the application is reviewed and before phase 4 trials, the FDA reviewers will either approve the new drug application or issue a response letter.A drug sponsor will complete a New Drug Application (NDA) to ask the FDA to consider approving a new drug for marketing in the U.S.An NDA includes:all animal and human dataanalysis of datainformation regarding drug behavior in the bodymanufacture detailsThe FDA has 60 days to decide whether to file it to be reviewed.If they decide to file the NDA, the FDA review team is assigned to evaluate the sponsor’s research on the drug’s safety and effectiveness.The following steps must then take place.Drug labeling: The FDA reviews the drug’s professional labeling and confirms appropriate information is shared with consumers and health professionals.Facility inspection: The FDA inspect the facilities where the drug will be manufactured.Drug approval: FDA reviewers either approve the application or issue a response letter.Phase 4 trials: Studies during salesPhase 4 trials take place after the drug has been approved for marketing. They are designed to include:over 1,000 patientscomprehensive experience in evaluating the safety and effectiveness of the new medicine in a larger group and subpopulations of patientscomparison and combination with other available treatmentsevaluation of long-term side effects of the drugdetection of less common adverse eventscost-effectiveness of drug therapy compared with other traditional and new therapiesSafety reportAfter the FDA approves a drug, the post-marketing stage begins. The sponsor, usually the manufacturer, submits periodic safety updates to the FDA.Clinical trials and research can cost hundreds of millions of dollars. Groups that fund trials may include:pharmaceutical, biotechnology, and medical device companiesacademic medical centersvoluntary groups and foundationsNational Institutes of Healthgovernment departmentsphysicians and health providersindividualsThe protocol defines who is eligible to participate in a trial.Possible inclusion criteria may be:having a specific illness or conditionbeing “healthy,” with no health conditionExclusion criteria are the factors that exclude some people from joining a trial.Examples include age, gender, a specific type or stage of a disease, previous treatment history, and other medical conditions.Taking part in clinical trials can have both benefits and risks for participants.Possible benefits of clinical trials include the following:Participants have access to new treatments.If a treatment proves successful, participants will be among the first to benefit.Participants who are not in the group receiving a new treatment may receive the standard treatment for the particular condition, which may be as good or better than the new approach.Health is closely monitored and supported by a team of health providers.Information gathered from clinical trials adds to scientific knowledge, may help others, and ultimately improves health care.Possible risks include:Standard care for a particular condition can sometimes be better than the new strategy or treatments being studied.The new approach or treatment may work well for some participants but not necessarily for others.There may be unexpected or unforeseen side effects, especially in phase 1 and phase 2 trials and with approaches such as gene therapy or new biological treatments.Health insurance and health providers do not always cover patient care and costs for those participating in clinical trials.Share on PinterestParticipants are expected to read the consent document thoroughly, decide whether they want to enroll and sign before they can be included in the trial.The informed consent document explains the risks and potential benefits of taking part in a clinical trial.Elements that must appear in the document include, among others:purpose of researchforeseeable risks of discomfortspossible benefitsParticipants are expected to read the consent document thoroughly, decide whether they want to enroll and sign before they can be included in the trial.The FDA works to ensure that anyone who is considering joining a trial has access to all the reliable information they need to make an informed choice, including information about the risks.While risks to participants are controlled and monitored, some risks may be unavoidable, due to the nature of medical research studies.Share on PinterestGood clinical practice (GCP) is defined as a standard for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials or studies.Safety of participants is a high priority issue. In every trial, scientific oversight and patient rights contribute to their protection.Good clinical practice (GCP) aims to ensure that ethical and appropriate procedures are followed in trials.GCP compliance provides the public with confidence that the safety and rights of participants are protected.It aims to:to protect the rights, safety, and welfare of participantsto guarantee that data collected is reliable, has integrity, and is of an appropriate qualityto provide guidelines and standards for the conduct of clinical researchThe foundations of GCP were first laid out in 1947. The main points were that, during any trials, researchers must guarantee:voluntary participationinformed consentminimization of riskOver time, additions have ranged from establishing additional protection for vulnerable populations to providing guidance to bodies carrying out research.Patient rightsWays of protecting patient rights include the following:Informed consent is the process of supplying clinical trial participants with all of the facts about the trial. It happens before the participants agree to take part and during the course of the trial. Informed consent includes details about the treatments and tests that may be received and the possible benefits and risks.Other rights: The informed consent document is not a contract; participants may withdraw from the study at any time regardless of whether or not the trial is complete.Rights and protection for children: A parent or legal guardian must give legal consent if the child is aged 18 years or younger. If a trial may involve a risk that is greater than minimal, both parents must give permission. Children over the age of 7 years must agree to be involved in clinical trials.Information about current clinical trials can be found here. Last medically reviewed on May 18, 2018Clinical Trials / Drug TrialsRegulatory Affairs / Drug ApprovalsMedical News Today has strict sourcing guidelines and draws only from peer-reviewed studies, academic research institutions, and medical journals and associations. We avoid using tertiary references. We link primary sources — including studies, scientific references, and statistics — within each article and also list them in the resources section at the bottom of our articles. You can learn more about how we ensure our content is accurate and current by reading our editorial policy.About clinical trials. (n.d.) Abbas, & Hefny. (2012, December). Clinical “case series”: a concept analysis. 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