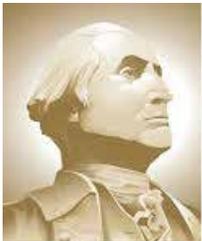




The Impact of Clinical Research *on Health Care*



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Clinical research professionals provide vitally important contributions to modern medicine and health care. Whether it's the continued pursuit to cure for ovarian cancer or testing new investigational drugs to curing HIV/AIDS, the discovery of new medicines and technologies address unmet medical needs that are a cornerstone to innovations in modern medicine. This free guide introduces you to the history of clinical research, standard processes, the different types of clinical research, examples of important breakthroughs, and the current technologies and tools used by research professionals.

Historical Events in Clinical Research

- Dr. James Lind, a Scottish physician, is typically credited with performing the [first modern clinical trial](#) for his work on sailors suffering from scurvy in the mid-18th century. Twelve men were given six different treatments for the malady, which included a mixture of garlic, mustard and horseradish; doses of vinegar; and even seawater. Two men who were given oranges and lemons every day recovered in less than a week. Dr. Lind published his findings [in 1757](#), but Lind questioned the validity of his work since conclusions were drawn based solely on observation.
- It was not until after World War II that modern clinical studies began to take shape in the United States. The most widely known is that of the polio vaccine (developed by Dr. Jonas Salk and his team), which proved to be effective in preventing the devastating disease.
- The increase of clinical research trials across Europe and the United States has led to more legislation and standards for best practices. A vast majority of clinical

trials are performed in North America and Western Europe, but only 10% of the world's population live in those areas. Cultural views, along with lack of resources in heavily-populated cities around the world, make for difficult conditions to perform clinical trials where populations are readily-available and willing to participate.

- Studies that used non-consenting human subjects were outlawed by the [National Research Act of 1974](#), which also established a set of ethical standards for human trials. The International Conference on Harmonization Good Clinical Practice (ICH GCP) of 1996 created universal scientific, design, reporting and [ethical standards for clinical trials](#) performed in the European Union, Japan and the United States.
- Currently in the US, the [Food and Drug Administration develops guidance and regulatory direction](#) for all medical devices and products to maximize safety and efficiency, while the [Office of Human Research Protections oversees the safety and well-being of human subjects](#) participating in federally-funded clinical trials.



Overview of Drug Development Stages

The process of taking an investigational drug from concept to market is complex and time consuming. The process can take up to 14 years to complete and, according to the Tufts Center for the Study of Drug Development, [costs about \\$2.6 billion](#). In fact, only 10% of drugs make it all the way from the investigational stage of development to FDA approval and the provider's prescription pad.

Preclinical research involves [thoroughly testing compounds](#) that have been determined to have potential medical uses in human subjects. The compounds' safety for human use is assessed either in [vitro \(on microorganism\)](#) or in [vivo \(on lab animals\)](#). Researchers observe several variables including safe and effective dosage as well as the potential chromosomal or genetic changes that may occur at specific doses. Those [data derived from preclinical research](#) are used to support or block the next phase of the clinical research. In successful preclinical research trials, an Investigational New Drug (IND) application filed with the FDA to utilize the compound for either commercial or

research purposes. The FDA only approves the application when the compound has tangible therapeutic value and meets all safety criteria.

- **Phase I:** The first phase of clinical research commences with a small group of volunteer subjects (typically 20 to 30 people). These subjects are either healthy volunteers or, individuals suffering from the disease or condition that the investigational drug is being evaluated to treat. Phase I determines how the body absorbs the compound and how it's metabolized. Phase I spans anywhere from a few months to a year. The FDA estimates that [70% of drugs pass this stage](#) and move forward to Phase II clinical trials.
- **Phase II:** The second phase explores an experimental compound's effectiveness at treating specific ailments. Side effects and other risk factors are assessed, along with finalizing dosages amounts. During this phase, researchers determine the best method of administration (injections, tablets, etc.). Controlled testing begins when some patients are given the compound and others a placebo or no treatment. Phase



The Impact of Clinical Research on Health Care

II trials span several years and include hundreds of patients. The drug moves to Phase III if efficacy and safety have been demonstrated.

- **Phase III:** The third phase treats several thousand patients, a large number of patients that is statistically significant enough to demonstrate real benefits to patients. The larger population and longer duration of Phase III (up to four years) also allows researchers to detect more side effects that may have been missed in the first two phases.
- **Registration and Approval:** If a drug has successfully gone through each of the phases, the next step to bringing a new drug to the market. This process may vary from country to country. The European Medicines Agency, an agency of the European Union, has an application process that requires both an eligibility request and notification of intent to apply for marketing authorization. The FDA requires a New Drug Application (NDA), the same procedure that has been around for all new drugs since 1938. If the new drug meets the criteria set forth by the respective regulatory agency, a license to market and sell the product for a specific purpose is issued.



- **Phase IV:** Post-marketing studies to determine potential long-term side effects and rare adverse reactions are required after regulatory approval. These studies are performed on different and more diverse populations numbering in the thousands, to observe impacts unseen in previous trials. For instance, the new drug may be tested on pregnant women or patients currently taking other drugs (i.e. beta blockers) to ascertain any adverse reactions.

Types of Clinical Research Trials

There are a number of types of clinical research trials that the professional may engage in during their career. These include:

1. Cohort studies are observational trials that examine patients over time to determine the cause of particular ailments. These studies can be both prospective (longitudinal) or retrospective (draw on existing data). Cohort studies are the most effective and ethical method for determining risk factors for development of disease. Prospective studies are more effective than their retrospective counterparts since researchers cannot fill in missing data (i.e. lifestyle changes in cohorts) in the latter.
2. Randomized controlled trials (RCT) are most frequently used to determine the efficacy of a drug or a device. One group is chosen at random to receive a particular treatment, while a control group receives a placebo or no intervention at all. The outcomes of RCTs provide concrete data for answering medical questions while comparing the interventions between subjects. There are many ethical issues with RCTs that eliminate them from consideration to answer certain medical questions. For example, it would be unethical for one group to eat high-fat, processed foods for an extended period of time to measure diabetes risks because it could do harm to them over time.

3. Cross-sectional studies aim to describe characteristics of a population or subgroup of a population in a given time period. They are used to correlate risk factors and hypothesized results (i.e. smoking causes cancer) in given populations. A survey is a form of cross-sectional study because it asks subjects specific questions about behaviors, attitudes, lifestyle, etc. in certain occupational or residential settings. For instance, office workers whose jobs include a lot of typing may be asked if they are being treated for arthritis. A high [number of affirmative results cannot determine etiology](#) (causation) but could begin the process thereof. Cross-sectional studies are particularly useful in public health planning, but due to prevalence-incidence (Neyman) bias and the short time frames, they are conducted to limit their causal inference ability.
4. Systematic reviews draw conclusion by compiling data from pre-existing studies. A high-quality systematic review utilizes the same rigorous standards in compiling said data as it took to originally produce it. Therefore, the researcher must discover all relevant existing studies pertaining to their specific question and determine the quality of each for use. Systematic reviews are essential to clinical research due to millions of articles being published every year. The significant amount of information disseminated in the area of clinical research makes it nearly impossible for researchers to know what has already been discovered with specific scientific inquiries. For example, a 2010 systematic review on prostate cancer screening published in The British Medical Journal (BMJ) cited 48 different randomized controlled trials. It concluded that [routine screening helps with early detection](#), but ultimately does not affect mortality rates.

5. Meta-analyses are [systematic reviews that combine the statistical results](#) of the compiled studies; thus creating a new, larger study. There are also case-control studies which compare subjects with a particular ailment (cases) versus those without them (controls). These types of studies are considered the highest level of evidence.

Recent Breakthroughs in Clinical Research
The discoveries of new drugs and vaccines have led to the eradication of several potentially deadly diseases, including tetanus, yellow fever and measles, in the last 60 years. Recent breakthroughs, led by the clinical research professionals, will cure diseases we now consider fatal and increase quality of life for individuals who suffer from chronic conditions.

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Case example; The National Heart, Lung and Blood Institute (NHLBI) sponsored a study with 9,300 participants over the age of 50. The goal of this study, known as Systolic Blood Pressure Intervention Trial (SPRINT), was to give one group of individual's intensive treatment (three or more medications) to lower their systolic blood pressure to 120 or below. The other group was given a less intensive treatment (two or less medications) to achieve a systolic reading of 140 or below. The findings were published in The New England Journal of Medicine in November of 2015. Heart attacks and other cardiovascular events were reduced by 25% in participants in the intensive group versus their counterparts. Side effects of the intensive treatment included fainting and acute kidney damage, but researchers determined the benefits outweighed the slight risk.

The Systemization of Clinical Research; Tools for Success

Through the 1990s, tracking participant progress in clinical trials required mountains of paperwork and significant amounts of data entry. Advances in technology and software have made clinical trials more streamlined and standardized. Here are a few of the most widely used tools:

- [Research Match](#) is a not-for-profit website that brings together people who are trying to locate research studies and researchers who are looking for participants in their studies.
- [Research Electronic Data Capture \(REDCap\)](#) is another tool used by clinical researchers. This free, secure application manages databases and surveys captured via a web-based or mobile application. The mobile application is useful for offline data gathering in areas with weak or no Internet signal.
- [ClinRegs](#) is an online database offered through the National Institute of Allergy and Infectious Diseases (NIAID) that provides country-specific clinical research regulatory information and updates as laws and regulations are constantly changing across the globe.
- [PhenX Toolkit](#) is an online database of recommended, standard measures of phenotypes and environmental exposures to be used in biomedical research.

Newer Technologies

There are several recently developed tools that make clinical research even more efficient, many of which involve mobile applications for smartphones.

- Software development firm IVR Clinical Concepts introduced its app TeleDiary in late 2014. The interactive voice and response system (IVRS) streamlines the reporting requirements for patients in clinical trials. This is significant since patients who did their required reporting on paper were compliant only 11% of the time, [versus 85 to 95% when they were aware their responses were being monitored electronically](#). TeleDiary is compatible with both iOS and Android devices.
- Apple set out to help researchers find trial participants when it released a mobile medical platform called ResearchKit in early 2015. The app allows researchers to locate and enroll clinical research participants easily. Some of the early adopters of the platform include Oxford University and the Dana-Farber Cancer Institute. Apple has noted that the platform gives researchers access to hundreds of millions of iPhone and iPad users who would happily donate their time for scientific research. The company also released Parkinson's and asthma-specific apps that allow anyone to share stories of treatments and contribute to the greater good.
- The Institute of Medicine (IOM) released its report "[Envisioning a Transformed Clinical Trials Enterprise in the United States: Establishing an Agenda for 2020](#)" in April of 2012. The workshop brought together 150 leaders in various industries including pharmaceuticals, academia and regulatory agents. The two-day workshop explored the

The Impact of Clinical Research on Health Care

growing challenges that impede progress on clinical research and potential solutions. Among other ideas, the report suggests a utilizing a cloud-based infrastructure for clinical research to further streamline data collection, reporting and communication. The FDA released its guidance "[Guidance for Industry: Electronic Source Data in Clinical Investigations](#)" the following year, providing further guidance for these forthcoming changes to the industry.

Start Your Career in Clinical Research

Clinical trials play an essential role in the development of new drugs and therapies, enabling people to live longer and healthier lives. Today clinical research is the foundation of the entire medical industry and employment opportunities continue to grow. The Bureau of Labor Statistics projects that [jobs for clinical and laboratory technologists will grow 16%](#) from 2014 to 2024, much faster than the average of all

other occupations.

The online [Clinical Research Administration](#) program at the George Washington University is for those who have already completed a bachelor's degree and are working in a related field. GW's accelerated program options include a Graduate Certificate or Master of Science in Health Sciences in Clinical Research Administration.

For more information on the Clinical Research Administration program at the George Washington University, call 844-386-7323 or [request more information](#).



An advanced degree in clinical research can help you excel in the clinical research field; it can position you for advancement within your career.

Learn More Now!