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Understanding Clinical Research and Career Considerations

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***Abstract*: Clinical research is a branch of science for testing of new drugs that are made to improve the quality of life. It is an important element for development of the drug and ensure the drug is safe for human use. Clinical research begins from the initial start of the phase i.e., pre-clinical trial to ensure about the safety and efficacy for human by testing on animal models. The review article also describes about the methodology used for comparative study and gives a brief idea about the different studies involved in clinical trial. The article also details about the career process flow in clinical research.**

***Keywords*: Clinical research, phase, clinical studies, randomization; clinical trial (CT), career opportunities.**

1. Introduction

All research on human beings is referred to in clinical research. It aims to improve disease knowledge, develop diagnostic methods and new treatments or medical devices to provide better patient care. The methodology for the collection of evidence for treatment in clinical research. Clinical Research Objectives is (a) to understand key concepts for responsible research conduct, capable of conducting research and meet the highest protection standards for subjects of human research (b) to evaluate the medical scientific literature, including the published and proposed methodology (c) makeup research question independently concerning the protocol and study design (d) to address the issue to design and conduct concerning the study, present and publish the results of research (e) identifying a focus for future research and scientific work (f) to developing specialist expertise in the relevant clinical field and/or research methods [1]. The most elemental goal of clinical research is to improve the quality of life. Clinical research is necessary for the development of an innovative treatment that will help people prolong their life with fewer impairments. Computer modelling and animal testing are useful, but their capacity to predict how a novel method would operate in the human body is narrow. Clinical Trials can aid in the evaluation of a novel procedure's effectiveness and safety in humans. The intervention works better than the previous group of people and is acceptable to more patients than the current procedure [2]. Clinical studies do not restrict to new interventions but also surgical methods, a new approach to radiation therapies, or any combination of standard treatment.

2. Clinical Research from the Scratch

Clinical research begins after the drug discovery and on the initiation of a clinical trial. A clinical trial is defined as a prospective scientific experiment that is usually conducted in groups of subjects to assess the safety and effectiveness of an intervention [3]. Drugs, biologics, medical devices, and screening methods are examples of interventions that can be diagnostic, preventative, or therapeutic. Trials are conducted to improve the quality of life of study participants or to better understand how the intervention works in them [4]. Trials are conducted in different phases as from pre-clinical to phase IV. (As depicted in Figure1).

1) Preclinical: Laboratory Studies

Preclinical studies provide data to decide whether a drug is ready for a clinical trial (human use). Preclinical studies reveal preliminary safety, toxicity, and efficacy data of the new drug or treatment [5]. These studies involve testing of drugs using in vitro (test tube or cell culture), in vivo (animal), and some cases in silico (computer) models. Preclinical studies are performed in compliance with GLP (Good Laboratory Practices) guidelines.

2) Phase 0: Human Micro-dosing Studies

Clinical studies at phase 0 are used to see if and how a new drug works. Even though phase 0 investigations are conducted in humans, they are not the same as the rest of the CT stages. The purpose of this phase is to speed up and simplify the drug approval process. Researchers may use phase 0 trials to see if the medications do what they're supposed to do. In phase 0 investigations, the normal doses given are 100 times less than the intended therapeutic dose therefore there is less risk for those taking part in the trial because the medicine dosage is minimal [6]. Phase 0 studies aren't extensively used, and they aren't always useful for particular drugs. Phase 0 trials do not give any information on the new drug's safety and effectiveness. The subject number range from 10-15.

3) Phase I: Human Pharmacological Trials

Phase I trials are conducted to access the tolerance of new drugs to humans. These trials also look at Pharmacodynamics (what effect drug has on the human body) and Pharmacokinetics (what effect does the human body has on the drug). These studies explore drug metabolism and drug interactions with other medications. Phase I trials also aid in

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determining the new drug's MTD (Maximum Tolerated Dose) that may be safely provided without causing any side effects [7]. Although the medication has been studied in laboratory and animal research, it is impossible to predict the negative effects in humans. Phase I studies also aid in determining the optimum method of administering the new therapy. The duration of these trials is from 3-6 months and the subject number ranges from 20-80.

4) Phase II: Exploratory Clinical Trials

The major purpose of the phase II trial is to determine the drug's short-term risks (safety) and to examine the preliminary effectiveness of the drug in subjects. Phase II studies also explore the effective dose and the dosing regimen of the new drug. It provides the basis for confirmatory study designs, endpoints, and methodologies. Phase II trials consist of two phases i.e., Phase II-a and Phase II-b. Phase II-a assesses dosing requirements while Phase II-b assesses study efficacy. Phase II studies have a duration of one year and the subject number ranges from 100-300.

5) Phase III: Therapeutic Confirmatory Trials

Before being licensed for general use, the drugs or treatments that pass the previous phases of clinical trials must complete phase III clinical studies. The primary goal of Phase III clinical trials is to determine the drug's effectiveness. This phase establishes the safety profile of the new drug and compares it against the current standard treatment. For comparison, subjects are picked at random (randomized) to administer new treatment or the standard treatment. Phase III studies are often multicenter studies. These studies also determine the long-term drug safety and monitor its side effects [7]. This provides a sufficient foundation for evaluating the benefit/risk relationship to warrant licensing. Phase III studies tend to last from 1-5 years and the subject number ranges from 300-3000.

6) Phase IV: Post Marketing Surveillance Studies

Phase IV studies gather information about the effectiveness of drug or treatment in the general population and define the relationship of benefit/risk in general and special populations like kids, expecting women, elderly patients, patients with kidney, liver, or other organ problems, as well as patients with comorbidities. These studies provide data for optimizing drug use and to detect rare or long-term adverse reactions [8]. Phase IV studies last for several years and include thousands of subjects, therefore it helps to take into account other components of the treatment, such as cost-effectiveness and patient's life expectancy.

Fig. 1. Summary of different phases in the clinical trial

3. Methodology of Clinical Studies

Clinical studies are subdivided into two types i.e., non-experimental (observational) and experimental (interventional). Observational studies are the ones in which researchers are observing, without attempting to change/the effect of a risk factor, diagnostic test, treatment, or any other procedure. Interventional studies are frequently proposed to design and evaluate the direct effects of therapy or prevention on disease. Based on the type and quality of data, each research design has its own set of outcome measurements. In addition, each design of the study has potentially more severe limitations that need to be addressed during the study design phase.

The design of the study can be classified retrospectively and prospective by the role played by time in the data collection. Retrospective studies are where data are collected either utilizing records that were then created or by inviting participants to remember their exposures or results [9]. Retrospective studies cannot as easily show temporality and are most susceptible to various partialities, in particular reminder bias. Prospective studies are progressing over time, gathering data during the process. Focused studies are less susceptible to certain types of bias and can more easily show that the disease preceded exposure, suggesting more causation.

A. Observation studies

These researches observe exposures and results, the study is classified as case studies, clinical series, ecological research, transversal research, cohort study, and retrospective studies.

1) Case Study/Clinical Series

A case study is a detailed written record of a patient's signs, symptoms, examination, therapy, and follow-up. A case study can incorporate a patient's demographic data, although they often describe a rare or novel event. Whereas, a case series is a form of medical research study that follows people that have had a documented exposure, such as patients who have had similar treatments, or investigates their medical history for exposure and outcome.

2) Ecological Research

More than one variable such as exposure or an outcome is examined at the group level of this study. The cancer occurrence rate in a certain community, the average blood pressure of patients treated at a clinic, the average exposure to the sun at a certain geographic location, or even a preventive service included in a health insurance package are all instances of group-level research. The incidence of infection is contrasted in the middle of groups with varying levels of exposure, allowing for at least one comparison group in this study design.

3) Transversal Research

It is a type of observational study and, is also known as cross-sectional study or prevalence study. An investigator uses a cross-sectional analysis to examine the outcome and exposures in study subjects at the same time. Prevalence designs are employed in community-based surveys and assessment of illness in clinic-based samples. This research can be used to assess the prevalence of disease in the population, but they're more often used to identify infection risk factors or serologic markers [10].

4) Cohort study

A well-designed cohort study can result in significant findings. In cohort research, the exposure or incidence of concern is used to utilize to select a disease-free study group, which is then tracked across time before the condition or event of interest arises. Cohort studies provide a temporal basis for assessing causality since exposure is detected before the result and therefore can provide the best empirical evidence.

5) A case-control study (Retrospective studies)

Individuals who develop the disease (cases) and those who do not develop the disease (controls) are identified, and the prior exposure for each case and control is determined. The case study group is made up of subjects who are considered to be affected by the condition or experience the result, while the control study group is made up of subjects who are not affected by the condition or outcome. The chances of being exposed are then compared amongst cases and controls. In a case-control analysis, the calculation of correlation is usually an odds ratio. In determining individual-level causality, a case-control analysis outperforms a cross-sectional study since we can be more confident that exposure followed the disease outcome [11].

4. Experimental Study

Epidemiologic trials with an experimental research design are intended to assess approaches to minimize the incidence of the seriousness of the disease. Clinical trials, community trials, and meta-analyses are the three types of experimental research designs.

1) Clinical Trial

The selection of the population best representative of the general population is important for the clinical trial. As a result, the study's findings can be applied to the entire population from which the sample was drawn. When planning a trial, it's often important to choose the right endpoints. Endpoints must be well-defined, repeatable, scientifically applicable, and attainable. Continuous endpoints, categorical, and event-time are examples of endpoint forms. Clinical studies are classified into randomized CT, non-randomized CT, and factorial CT.

2) Randomized CT

A design study that attributes participants randomly to any one of the arms out of the two i.e., experimental group or control group. The only expected difference in a randomized clinical trial (RCT) between the control and the experimental group is the result variable.

3) Non-randomized CT

A method of choosing controls without randomization is a non-randomized clinical trial. Typically, a pattern is followed by this kind of study design, for example, selection of subject matter and checks on some days of the week. The choice of subjects is predictable, and therefore the choice of patients and controls that raises concern about the validity of the acquired results is not a predictable strategy depending on the approach taken.

4) Factorial trial

A study design is used when two independent arms with independent effects on the same population are investigated. The population is categorized into four groups: medicinal drug A, drug B, drug A and B, neither drug A nor drug B. The results of drug A are compared to those of the second and fourth groups.

5) Community trial

Community trials include classes of people with and without diseases assigned to various intervention and experiment groups, which are also referred to as community intervention studies. Thus, the same intervention or experiment will be performed by groups of people from the same areas such as a city or a specific organization, such as a school or a college.

6) Meta-analysis

Meta-Analysis combines results that can be used to draw therapeutic efficiency findings or to devise new research projects. This process's core design and statistical challenges are examined. Protocol development, targets, search for literature, publishing distortions, measurements of research results, and data quality are some of the design difficulties. Statistically, the coherence (homogeneity) of results and methods for pooling results are included in several studies. Guidelines are provided to evaluate the quality of meta-analysis based on the conception and statistical problems [12].

5. Career Opportunities in Clinical Research

1) Under pharmaceutical company

The pharmaceutical industry is involved in the study, production, and discovery of new drugs, as well as the interaction with the concomitant, which ensures patient safety. [13 The various players involved in drug development and introduction, including the pharmaceutical industry, clinicians, advocacy groups, and regulatory bodies, need to work together to ensure patient access to quality care.

2) Under CRO or biotech companies

The CRO's primary responsibility is to prepare, organize, and conduct the processes involved in the implementation of a clinical trial, as well as to maintain relationships with the sponsor and other trials. CROs are important players in clinical research because they have the expertise and skills required for a clinical study's proper growth. Sponsors benefit from them because they reduce their workload while ensuring trial consistency and compliance with national and international standards [14]. At the same time, many CROs provide cutting-edge technical resources to improve study process performance, resulting in cost savings.

3) Under data management

Clinical data managers keep track of information such as medication side effects, daily experimental data, and ongoing study issues. Clinical data managers create and carry out data testing and analysis plans, ensuring high data quality and identifying process improvements. Create and implement SOPs, departmental guidelines, and data standards to ensure database quality control and data management compliance, and manage and track CRF flow [15]. In the last ten years or so, the clinical trials industry has exploded, with India emerging as one of the top global destinations for clinical trials. The movement was sparked by changes in intellectual property laws, and the key ideological underpinning of the growth of the clinical trial

industry in India is benefit maximization rather than altruistic motives. The paper delves into the ideological underpinnings of India's clinical trials industry's growth, as well as how the country's ruling classes have attempted to capitalize on this as a lucrative business opportunity. (as depicted in Figure 2).

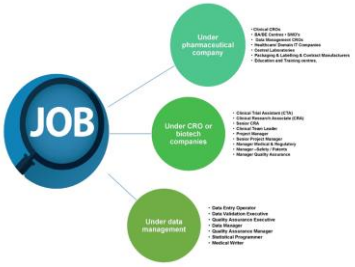

Fig. 2. Job opportunities in clinical research under different industry

6. Future with Clinical Research

India's pharmaceutical industry is Asia's second-biggest. In the coming years, it appears that job opportunities will increase by around 10% annually. Various multinational corporations are setting up research facilities in India, causing the clinical research industry to explode. According to a report, the number of career opportunities in the clinical industry would increase by more than 50,000. After graduation, one may seek employment in entry-level positions. A Master's degree is required for higher positions, and specialized qualification courses are required elsewhere. Ph.D. is the best option for those who choose to do extensive research. In this area, a good pair of hands is required in addition to the required education. Starting as a Clinical Research Associate, one may progress to Project Manager, then Director of the Clinical Department. Work ethic, practical experience, and strong communication skills can contribute to a competitive advantage in the Clinical Research Industry [16].

7. Conclusion

Clinical research is a thriving industry that offers aspirants rewarding career opportunities. It is critical in the introduction of new medicines and the improvement in health statistics. Clinical research in India is expanding to meet global standards, allowing new drugs to be introduced to treat a variety of illnesses. India will become a major center for clinical research in the coming years. Several well-established companies are taking steps to position students in this area professionally. Clinical trials are carried out at several partnered academic medical centers and research institutes.

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