

Review article

An overview of challenges and dire need of clinical trials

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Abstract

Clinical trial is an inextricable link between advances in medical research technology and improved health care. It is a component of medical health research intended to produce knowledge valuable for understanding human disease, preventing and treating illness and promoting health. The pharmaceutical industry is now a more significant investor in clinical trials, but in addition to these opportunities, it is being challenged by the financial impact of managed care and medicaid regulations on academic medical-center revenues. Besides that, there is growing public concern about our systems for protection of human subjects, along with some conflicts. There are public expectations that clinical research will yield substantial advances in the health of the public. Clinical trials are currently challenged in several ways, such as imperfect public understanding, data inadequacy, insufficient funding, work force issues, poor coordination between Health management organizations (HMOs) and the academic medical centers and financial risk for academic medical centers. The final point is that there is no clear and dynamic agenda for clinical trials. The recommendation is that clinical research needs to be conveyed in an exciting way to students and residents to stimulate interest in clinical research careers. This paper enlightened the facts about clinical trials to clear the extensive need of it for better health services.

Key words: Clinical trials, health, challenges, health management organizations (HMOs)

Introduction

The most commonly performed clinical trials evaluate new drugs, medical devices, biologics, or other interventions on patients in strictly scientifically controlled settings, and are required for regulatory authority approval of new therapies. Trials may be designed to assess the safety and efficacy of an experimental therapy, to evaluate whether the new intervention is better than standard therapy and to compare the efficacy of two standard or marketed interventions. Recently clinical trials are facing lot of challenges. Firstly there is no common acceptance from experts upon the definition of clinical research. Secondly, an imperfect public understanding of clinical

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research¹, it means that a relatively small percentage of people who volunteer to participate in clinical research trials for example, for adult patients with cancer, the volunteer rate is only five percent. The third problem is that the data are inadequate to tell whether investment in clinical

research is being well spent or not. Fourth problem is about the insufficient funding in certain areas of clinical trials. The fifth and sixth problem is related to work force issues involved in clinical trial.

The seventh problem is poor coordination between HMOs and the academic medical centers, between schools of nursing and schools of medicine on the other. Eighth problem is concern with the financial risk for academic medical centers and their ability to sustain their systems for clinical research. The output of all challenges is that there is no clear and dynamic agenda for clinical research. There is a need to set up a clinical research task force to examine what the academic medical centers need to do to strengthen their clinical research programs. The task force should divide its role into four specific tasks: examining the current status of clinical research education in medical schools and teaching hospitals, describing the optimal infrastructure for the different categories of clinical research, addressing the organization & administration of clinical trials and exploring the interface of clinical research with evolving clinical delivery systems that are academically affiliated. So there is need of sophisticated work force for more clinical investigation, to carry better job of educating all practitioners about clinical research, to persuade students and residents to stimulate their interest in clinical research careers. In other words health system needs to bring more research into practice. Keeping the above facts this paper tries to attract the concern of general public, pharmacist and practitioner by including the general details about clinical trials.

1. Clinical Trial

A clinical trial is a research study in which a treatment or therapy is tested in people to observe whether it is safe and effective. The information obtained from clinical trials helps to improve health care and to keep people healthier. It is also conducted by researchers to find out which treatments are more effective than others. The results of clinical studies give better knowledge about diseases and its conditions. Clinical trials are also called medical research, research studies, or clinical studies². Each trial follows a protocol, a written detailed plan that explains why there is a need for the study, what it is intended to do and how it will be conducted. The protocol is written by the trial's principal investigator

2. Types of clinical trials

Clinical trials are used to study many aspects of medical care³:

- 2.1 *Treatment trials*: It involves test treatments for a specific disease, new combination of drugs or new approaches to surgery or radiation therapy.
- 2.2 *Supportive care trials (Quality-of-life trials)*: It explores ways to improve comfort and the quality of life for individuals with a chronic illness.
- 2.3 *Prevention trials*: It looks for better way to prevent disease in people who have never had the disease or to prevent a disease from returning

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- 2.4 *Screening trials*: It includes study new ways of finding diseases or conditions in people who are at risk, before they have any signs or symptoms.
- 2.5 *Diagnostic trials*: These are conducted to find better tests or procedures for diagnosing a particular disease or conditions.

3. Phases of a clinical trial

Clinical trials take place in phases⁴. The trials at each phase have a different purpose as the therapy will be tested in people. Before a clinical trial can start, there is need to do preclinical studies, which include cell studies and animal studies. Phases of a clinical trial are given below:

3.1 *Phase I*: It is the first stage of testing in human subjects. In this 20-80 groups of healthy volunteers will be selected. This phase includes trials designed to assess the pharmacovigilance, tolerability, pharmacokinetic and pharmacodynamics of a therapy. There are two specific kinds of Phase I trials-

SAD (Single Ascending Dose) studies in which group of 3-6 patient receives a small dose of the drug and observed for a specific period of time. If no adverse effect was observed, a new group of patient is then given higher dose. This is continued until MTD (Maximum Tolerated Dose) is shown.

MAD (Multiple Ascending Dose) studies in this a group of patient receives a low dose of drug than dose is subsequently escalated and sample is collected at various times. It is conducted for better understanding of the pharmacokinetic and pharmacodynamics of the drug.

3.2 *Phase II*: This phase shifts the focus of trials from safety to efficacy and performed on large groups of 100-300 individuals. Side effects from new drug product are also investigated, the development process for a new drug commonly fails during this phase due to poor efficacy or toxic effects. Studies are divided sometimes into Phase IIA (to assess dosing requirement) and Phase-IIB (to study efficacy).

3.3 *Phase III*: These are the longest most comprehensive, expensive and time consuming trial and design for chronic condition. Theses are controlled trial on large patient group (1000-2000 or more) and are used for assessment of the efficacy of new therapy, especially in comparison with current available alternatives. Compound that successfully complete this phase have a 95% chances of testing approved by the FDA.

3.4 *Phase IV*: It involves the post-launch safety surveillance and ongoing technical support of the drug. Studies may be mandated by regulatory authorities or may be undertaken by sponsoring company for competitive or other reasons. Post-launch safety surveillance is designed to detect any rare or long term adverse effect over a longer patient's population. Such adverse effects detected by this phase may result in the withdrawal or restriction of the drug (e.g Rofecoxib and Troglitazone).

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4. Elements of Clinical Trials

In this researchers might include randomization in the trial design, it is used in all phase III studies and in some phase II studies. It gives the best chance of knowing that the study results are caused by the treatment and not by some other factor, such as people's choices or beliefs. Each

participant in a randomized trial is assigned by chance (through a computer or a table of random numbers) to one of two groups⁴.

The investigational group- made up of people who will receive the therapy, also called the active treatment. The control group- made up of people who will receive either the standard treatment for their disease or condition, or a placebo. Each participant has an equal chance of being assigned to either group. In some complex trials, there are more than two groups. Trials can be double-blind, it means that neither the researchers nor the participants know who has been assigned to which group. Blinding is another way to help minimize the chance of bias influencing the trial results. The information is kept on file at a central office, so if there is an urgent need for the research team to find out who was assigned the active treatment, they can find it from file. Researchers design clinical trials to have one or more endpoints, an endpoint is a measure that determines whether the treatment under study has an effect or not. An example of an endpoint is that whether a person's tumor shrinks after receiving chemotherapy or not⁵.

5. Placebo

A placebo is designed to resemble as much as possible the treatment being studied in a clinical trial, except that the placebo is inactive. By giving one group of participants a placebo and to other group the active treatment, the researchers can compare how the two groups respond and get a perfect picture of the active treatment's effects. Another type of placebo is called a "sham" procedure. When the treatment under study is a procedure, a sham procedure may be designed that resembles the active treatment but does not have any active treatment qualities. For example, in a clinical trial of acupuncture, the sham procedure might consist of placing acupuncture needles in areas of the body that are not expected to have any therapeutic response.

In recent years, the definition of placebo has been expanded to include other things that could have an effect on the results of health care. Examples include how a patient and a health care provider interact, how a patient feels about receiving the care and what patients expects to happen from the care. Therefore, when a treatment is compared to a placebo in clinical trials, the patients should differ only in whether they receive treatment and not in other aspects. Not all clinical trials compare an active treatment to a placebo. No patient is denied treatment in a clinical trial if there is a standard therapy available that could improve the comfort and survival of the patient.

6. Benefits and risk of clinical trial

6.1 Benefits

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Volunteers of clinical trials are having following benefits:

- They receive expert medical care.
- Their health will be closely watched throughout the study.
- Clinical trials can be treatment or prevention option for a disease
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- They are first one to get benefit from a new treatment or new knowledge about a current treatment.
- They can help others by helping to advance medical and scientific knowledge.

6.2 Risks

Volunteers of clinical trials can face following risks:

- The treatment under study does not always turn out to be better than, or even as good as, standard treatment.
- The treatment may have side effects that are unknown to the researchers or different from what they expect.
- Like standard treatments, the treatment under study may not work for everyone.
- Participation may require more tests and more visits or treatments than regular care.
- There may be costs to participate, and these costs may not all be covered by health insurance plans.

7. Protections for people who participate in clinical trials

Many governments requires many protections for people who participate in federally funded clinical trials. Before a clinical trial can start, the written protocol⁶ must be approved and monitored by an Institutional Review Board (IRB). An IRB is an independent group of health care providers, which review protocols and the consent documents. Participants are also protected by a process called informed consent, means participant can ask any questions from authorities involved in clinical trial. The staff will also give a consent form to participant for his signature to decide to join the trial. Participating in a clinical trial is completely voluntary process. Participant can leave the trial at any time, for any reason-even after signing the consent form.

Conclusion

Clinical trials were not widely used until the middle of the 20th century. The results of the clinical trials proved to be more useful for efficacious treatment of disease. The biggest barrier to completing studies is the participation of people; one reason for not taking part in a clinical trial is that people are having lack of knowledge about the clinical studies. But there are many other reasons, some people may want to take part but aren't eligible for some reason, some people are uncomfortable with the idea of being a "subject" in a study. Others worry that they won't be treated fairly or could be harmed by an unproven treatment. To gain the participation from people

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there is need to deliver them all the facts about clinical trials and by doing this, researchers can overcome the hurdles and strengthen the practice of clinical trials.

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