IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

# A Comprehensive Study Of: Clinical Research & Research Methodology

[1]Mr. Kaushik .S. Koli, [2]Mr. Sampat Bangar, [3]Mr. Sarvesh .S. Talekar, [4]Ms. Jyoti .H. Jankar, [5]Ms. Rucha .V. Pandit

[1]Student, [2]assistant prof., [3]student ,[4]student, [5]student

DEPARTMENT OF PHARMACOLOGY

PHARMACOLOGY
SHREE SARASWATI INSTITUTE OF PHARMACY, TONDIVALI, INDIA

Abstract

Clinical research requires a systematic approach with diligent planning, execution and sampling in order to obtain reliable and validated results, as well as an understanding of each research methodology is essential for researchers. Indeed, selecting an inappropriate study type, an error that cannot be corrected after the beginning of a study, results in flawed methodology. The results of clinical research studies enhance the repertoire of knowledge regarding a disease pathogenicity, an existing or newly discovered medication, surgical or diagnostic procedure or medical device.

Medical research can be divided into primary and secondary research, where primary research involves conducting studies and collecting raw data, which is then analysed and evaluated in secondary research. The successful deployment of clinical research

## INTRODUCTION

Medical research is the cornerstone of medical progress.

**1.** It is the systematic study of participants for the diagnosis of health and disease, with the goal of developing effective treatments, preventive measures, and diagnostic tools.

**2.** By rigorous methods and ethical considerations, clinical research translates lab findings into real-world applications, ultimately improving patient outcomes and public health.

- What is Clinical Research? Clinical research is a branch of medical science dealing with any research or study in living humans. 'Clinical trials' is the term interchangeably used with the terms 'clinical research' or 'clinical study'. Although there are many definitions of clinical trials, they are generally considered to be biomedical or health related research studies in human beings that follow a pre-defined and designed protocol. Clinical trial is defined as

—a systematic study of new drug(s) in human subject(s) to generate data for discovering and/ or verifying the

clinical pharmacological (including pharmacodynamic and pharmacokinetic) and/ or adverse effects with the objective of determining safety and/ or efficacy of the new drug‖.1 Clinical trial is companysponsored, meant for a new drug or device and carried out for a specific new use of an intervention; while clinical research is meant for academic and pharmacovigilance. Large number of literatures describes on clinical trial and its phases. However, it has been now started to include a detailed description on clinical research or study.

- What are Clinical Trials?

Clinical trials are performed to evaluate the safety and efficacy of new drugs and medical devices. Clinical trials are studies research regarding human/animals' members to assess the protection and effectiveness of latest scientific interventions. These interventions can include

I. Drugs: New medicinal drugs or combinations of present tablets.

II. Medical gadgets: Implants, prosthetics, or diagnostic gadget.

III. Surgical techniques: Innovative surgical approaches.

IV. Behavioural interventions: Lifestyle adjustments, treatment plans, or counselling.

V. Prevention strategies: Vaccines or lifestyle changes to prevent ailment. By cautiously designed and monitored studies, scientific trials offer crucial statistics to decide if a new remedy is secure, powerful, and probably higher than existing alternatives.

Why are Clinical Research/Trials important?

Clinical research and clinical trials are the underpinning elements for betterment in health care and assurance of human health

respectively. They act as the basis for the following: Development of new treatments: Experimental drugs, medical devices, and therapies are tested, thus helping identify prospective and effective treatments for illnesses that were either incurable or poorly managing earlier.

Developing existing treatments: Clinical trials can also be a means by which already existing treatments are improved to make them more competent and safer. Prevention of disease: The findings in research can lead to the development of vaccines and lifestyle changes that help in the early identification of diseases.

Make patient life better: This is through the understanding of the progression of the disease and responses by the patients in the development of a customized treatment regime that will result in better patient outcomes.

Advancing medical knowledge: Clinical research provides the knowledge base needed to understand human biology and disease,

which acts to promote innovation and discovery.

CLINICAL RESEARCH

Clinical Research are performed to evaluate the safety and efficacy of new drugs and medical devices. Medical trials occupy a greater part of clinical trials and exceed in number over other types of clinical trials. Explanatory clinical studies are the most widely accepted and executed type of clinical researches/ trials. They explain not only the therapeutic aspects of a drug but also provide with a detailed description on adverse events and pharmacovigilance. Any new drug to be marketed first requires proving its safety, efficacy and the need over existing product range by passing through various phases of clinical trial that follows animal studies. For this reason, randomized controlled trials (RCTs) with placebo control and blinding fashion is the only accepted form clinical trials with few exceptions. Besides explanatory,

descriptive clinical research is also useful for certain types of studies such as epidemiological research. While conducting RCTs on humans (either healthy volunteers or patients), various components of the trials viz. study design, patient population, control group, randomization, blinding or nonblinding, treatment considerations and outcome measures are important to strengthen the outcomes of the trial. Similarly, proper utilization of statistics, for sample-size calculation, data collection, compilation and analysis by applying proper statistical tests, signifies the outcomes of the clinical research. The presented article includes a brief, however, an informative review of literature on methods in clinical research including clinical trial.

 Types of Clinical Research

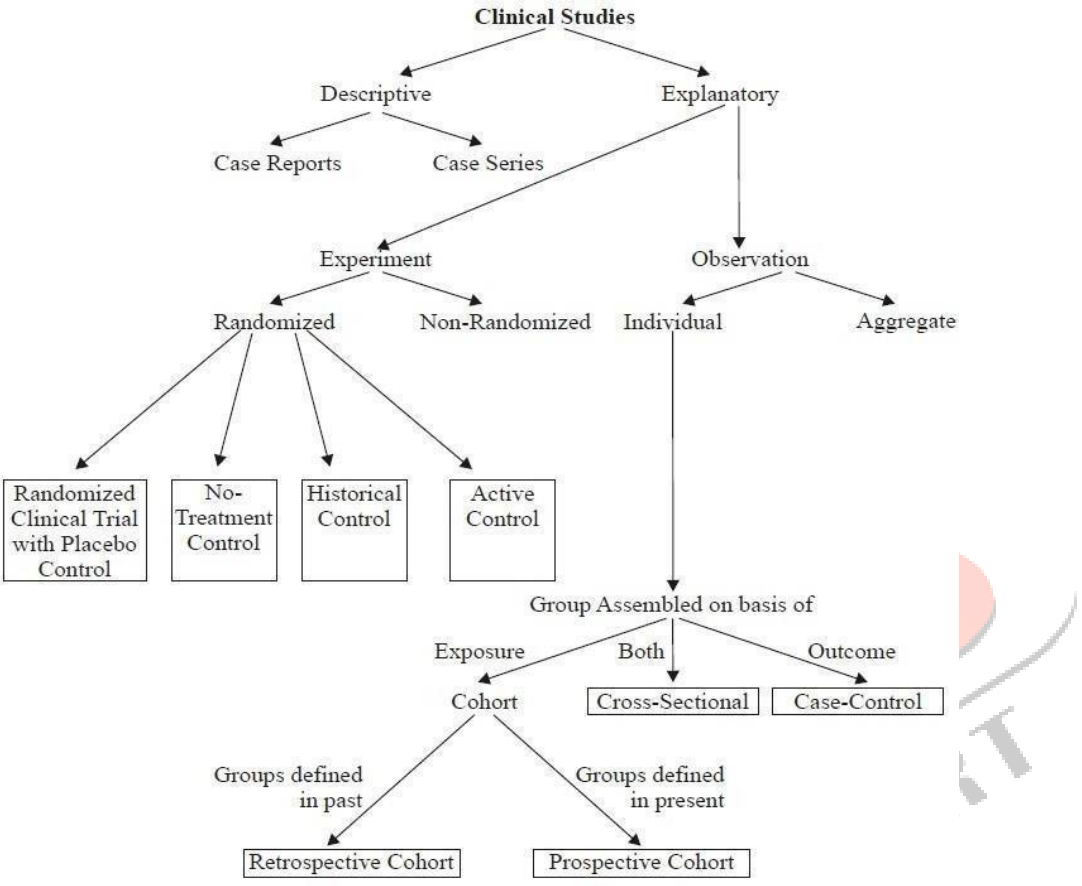


fig. no.: 1: types of clinical studies

1.Descriptive studies

Descriptive studies report unusual or new events such as the occurrence of sudden infant death syndrome (SIDS) in several siblings within a single family, prevalence of albinismin a single family etc. The researcher events observed with possible reason. These are neither randomized nor pre-designed

researches. They may be presented as case reports whereby certain individual patients with distinguished clinical characteristics are included in the study. All the baseline characteristics are recorded and the individual patient is treated as unique case with control over all the variables. The patient is observed and evaluated for the possible outcome. The results are compared with baseline values or are expressed as success or failure of the treatment given. If the treatment succeeded, a hypothesis is generated for an expanded and more rigorous study to find the relationship between the treatment and the outcome observed. In caseseries, observations are documented at regular intervals from patients exposed to a particular drug or a group of drugs. They may also cover prior histories of patients with the same outcome, to find a possible cause-effect relationship if exists.

These are useful in predicting the incidence of an adverse event of newly-marketed drug when reports on such events are limited.

## 1. Explanatory studies

### A. Observation studies

In an observational study, the subject to be observed chooses whether or not to take the drug or to have the surgery being studied.

Errors that are likely to occur include the differences in profile of the subjects since variables such as age, family history of disease, cause and severity of disease etc. may not be defined. For example, two patients have left ventricular (LV) dysfunction, in one it is because of ischemic heart disease (IHD) and in another it is because of severe mitral valve stenosis. Thus, the therapy of both the diseases differs due to different oetioes and hence both the patients cannot be compared in one study. Another example is of two patients suffering from headache, one because of migraine and the other because of common cold. These two patients cannot be compared for the analgesic activity of one drug since the cause and the severity of headache and hence the analgesic activity of the drug would vary greatly.

Observational studies can never be blinded. Hence, biases from patients, observer and experimenter may result into systematic and random errors.

### a. Aggregate observation studies

Pandemic and epidemic studies on communicable diseases and their treatments are generally carried out as aggregate observation studies e.g. occurrence and effective treatment of malaria and its relapse in particular geographical area.

### b. Individual observation studies

In individual observational study, the patients/ subjects are individually observed and they are assembled in groups on the basis of outcome or exposure or both. Depending upon the basis of the grouping, the individual observational study is sub-classified as i) Case-control; ii) Cohort and iii) Cross-sectional.

**i)** Case-control study

Case-control study involves assembling of subjects in groups on the basis of the outcome found in those subjects. It compares the subjects with outcome in question (the group behaves as a case group) with the subjects without the outcome (the group acts as a control) e.g. occurrence or non-occurrence of myocardial infarction (MI) in patients with hypertension (HT). It generally follows the retrospective design and evaluates how the exposure is related to the well- defined outcome using control group.19 However, grouping on the basis of outcome incorporates subjects with variety of distinguished characteristics. It is quick and inexpensive.
Further, patients with rare outcome can be assembled in a group to study oetioes, pathophysiology and prognosis of a disease. Results are generally expressed in terms of odds ratio (OR) and risk ratio/ relative risk (RR). Although multiple exposure variables can be correlated with outcome, it does not allow the correlation of temporal sequence of cause and effect with the final outcome.

**ii)** Cohort

It includes groups assembled on the basis of exposure. Here the exposure is well-defined but the outcome is variable. Thus, it allows study of one exposure with many more outcomes Cohort study can be retrospective wherein the groups are defined in past or it can be prospective wherein the groups are defined in present. The retrospective cohort correlates the exposure occurred in past with the outcome resulted just in recent past. Here the patients have been followed forward and hence it associates the exposure with some temporal outcomes though not all. If the patients have been treated with different treatments to control outcome related variables, it limits the correlation between exposure and one outcome only. Like casecontrol study, it is also quick and inexpensive.

If carried out on the basis of well-defined, - controlled exposure and followed with control over variables, retrospective cohort study suffices the requirements of prospective study with additional advantage of less time and money consumption. In prospective cohort study, the groups are observed for outcomes at particular, pre-decided time intervals. Thus, it finds firmly whether a particular exposure or sign or symptom is related with the outcomes. If the outcome is rare, the study requires inclusion of large number of patients and longer follow-up. Thus, it is expensive in terms of time and money. If the patients are not randomized and blinded, the outcomes may be influenced by bias and confounding.

**iii)** Cross-sectional

Cross-sectional study assesses both the exposure and outcome concurrently.
Generally, it is survey- or review based. Crosssectional study is, therefore, good for prevalence research. However, it is not suitable for causal outcome assessment.

**B.** Experimental studies a.Non- randomized studies

Patients are selected on the basis of selection criteria. They are not randomized to the particular treatment(s) and are given a treatment depending upon course of disease. Generally, phase IV of clinical trial follows this way. Further, in many experimental studies in humans, randomization is not possible. Many of the surgical experiments have evolved with specific indication and application. They have a focused patient group and therefore, randomization is not possible or is unethical. For example, patients with both the kidneys failed require undergoing kidney transplantation. Although dialysis is an available option it is not comparable with renal transplantation and hence patients cannot be randomized to such options.

**b.** Randomized controlled trials

In the studies which are randomized, controlled clinical trials (RCTs), human subjects (either healthy volunteers or patients) do not choose the therapy being studied or compared. Experimental clinical studies are generally RCTs. Randomized controlled trials are, as the name indicates, based on randomization. When a new drug successfully passes the pre-clinical studies, it is challenged to clinical experiments that follow random assignment of subjects to two or more groups one of which behaves as control group and therefore, such clinical experiments are called RCTs. The several components to be considered include i) Study design; ii) Patient population; iii) Control group; iv) Randomization; v) Blinding or non-blinding/ open-labelling; vi) Treatment considerations and vii) Outcome measures.

**i)** Study design

The common study designs employed in RCTs include

parallel group design, matched pairs and cross- over designs. In parallel group design, the patients are enrolled, followed and observed for outcomes on parallel basis. Parallel group design requires large number of patients. In matched pairs, patients are matched for different variables and those matching the required variables are then randomized to various treatment groups. This type of study design overcomes the influence of variables on outcomes, although it is difficult to follow.

Cross-over design is particularly used when

the effect of a drug is reversible and transient. In crossover design, the patients are given more than one treatment but in sequence i.e. one after another when the effect of previous treatment is washed out. Cross-over design, thus, requires a smaller number of patients.

**ii)** Patient population

As a common and required method, the RCTs are carried out on specific subject population selected on the basis of ―selection criteria‖ which are derived in line with various fixed, independent and dependent variables. This is to overcome the misleading by variables. For example, if effects of angiotensin-converting enzyme inhibitor (ACEI) on cardiac function are to be studied in patients with LV systolic dysfunction, variables like family history of cardiac disease, presence of other cardiac diseases such as heart block or valve failure etc. should be avoided as patients with these variables are different from those not having the variables. Further, they may reveal different outcomes viz. the cardiac function and even survival. Depending upon the defined criteria, patients or healthy subjects are included in the study to randomize to various treatments for the comparison of outcomes and thus, to conclude. The criteria are namely (a) inclusion criteria; (b) exclusion

criteria and (c) withdrawal criteria. (a) Inclusion criteria: Specifications of subjects (patients or healthy volunteers) with regard to age, gender, ethnic groups, body mass index, prognostic factor, diagnostic admission criteria, should be clearly mentioned wherever relevant. (b) Exclusion criteria: These specify the characteristics of the subjects on the basis of which they are excluded from the trial. For example, severity of the disease, concurrent medication etc. Withdrawal criteria: These specify the subjects on who the trial shall be terminated and mention when and how to withdraw the subjects from the study and to stop further follow-up in those.10 To have comparison possible between or among various treatment groups, selection of patients must be done on the basis of inclusion and exclusion criteria. This allows enrolment of subjects with corresponding clinical characteristics.

**iii)** Control group

Randomized controlled trial also includes control group (either placebo control or active control) to show the control nand effect over dependent variables and to obtain clear effects of drug under consideration. Control

group can be placebo control, no-treatment control, historical control or active control. The placebo means dummy to the drug under evaluation with regard to organoleptic properties but lacking any pharmacological actions. Thus, it is to overcome the psychological impact of drug administration manifested by an individual on disease progression. It allows the investigator to determine the true efficacy of the treatment being researched for a particular condition.

Some studies also include no-treatment control or historical control as types of controls. In notreatment control group, the patients do not receive the placebo even. Therefore, they know that they do not receive any treatment and hence, individual bias due to psychic

factors affects the study outcomes. In other words, it is least preferred type of control. Historical control is the control group of previous study that was a different with respect to treatment group. Here control group of one study is utilized for another study and both the studies differ with regard to treatment only. This is done for studies not allowing placebo control or no-treatment control and involving high mortality disease even after availability of effective treatment e.g. studies on treatment for cancer and human immunodeficiency virus (HIV) infection.

Inclusion of placebo in drug research and sham surgery has been debated. Moreover, when an effective established treatment is available, use of such placebo control group is unethical. For examples, a drug is to be assessed for its effects on cardiac function in patients with LV systolic dysfunction, as per American College of Cardiology/ American Heart Association (ACC or AHA) guidelines all the patients would be necessarily receiving ACEI, if not contraindicated. Therefore, in this type of study all the patients receive the recommended drug which has already proved its beneficial effect on cardiac function. Thus, one cannot have a placebo control group but will have an active control receiving the best current therapy. It provides information about relative efficacy of the investigational drug over existing one. In the present example, the patients would be randomly assigned to a group receiving ACEI or to a group receiving ACEI in addition to the drug being evaluated- the former behaving as an active control and the later as a treatment group.

**iv)** Randomization

Randomization is an optimal method of distributing the variables between the treatment and control groups. Therefore, the bias of selecting specific treatment does not occur. Random assignment of subjects to various groups provides equal distribution of all variables in all the groups and does not let them influence the final outcomes. Randomization techniques mainly used in RCTs are simple randomization, cluster randomization and stratified randomization. In simple randomization, patients matching the selection criteria are randomized to various treatment groups. In cluster randomization various groups of patients matching the criteria are randomized to treatment under investigation. This kind of trial is especially used to find the geographical, genetic variations. In stratified randomization technique, subjects are classified in groups i.e. strata and then within a group they are randomized to various treatment groups. In RCTs, three main methods of randomization include 1) Tables of random numbers; 2) Mathematical algorithms for pseudorandom number generators and 3) Physical randomization devices such as coins, cards or sophisticated devices such as Electronic Random Number Indicator Equipment (ERNIE).

**v)** Blinding

To avoid bias, trial is carried out in blind fashion. Blinding means ―concealing or masking of the patients- assignment to a study group (control or treatment) from those participating in the study i.e. patients, observer and experimenter‖. RCTs can be blinded or non-blinded. The non-blinded experiment is also called open-label study. In this type of study all three- the patient, the physician or the observer and the experimenter or the researcher, are aware of the treatment used. In many instances it is unethical to hide the treatment module from the patients especially those suffering from life-threatening disease such as cancer, AIDS, end-stage HF etc.

Additionally, open-label study permits the patients to buy brand of the drug of his choice independently. However, it has the biggest disadvantage of introducing bias from any of the three components of the RCTs. Blinding is carried out at the beginning of study. The blind RCT can be single-, double- or triple- blind. In a single-blind experiment, the participants either the patient or the healthy volunteer does not know whether he receives the test intervention or placebo. In double-blind trial, neither the patient/ subject nor the experimenter knows who belongs to the control group and who belongs to test group but the observer knows. In triple-blind RCT, none of the three components of study knows name or nature of the treatment given.

Therefore, the triple-blind RCT is totally devoid of any kind of biases and allows the outcomes to be free from any such influence. In double- and triple-blind experiment the keys identifying the patients/ human subjects and the group they belonged to are preserved by a separate another party and given to the researcher only at the end of the study.

Randomized controlled trial can also be conducted as PROBE. PROBE is an acronym us of Prospective, Randomized, Open-label, Blinded-End point as used earlier by Neutel and Smith (2003).23 This type of trial is easier to carry out than a double-blinded placebocontrolled design (DBPC) because it does not require the ―matched placebo group‖ and the ―open-label‖ allows the enrolled patients to receive a marketed preparation of the drug. However, the PROBE studies have only the end-point blinded i.e. observer is unaware of the treatment being studied while investigator and patients are aware of it.

Therefore, the investigator or the patient bias may be introduced and thus, the results obtained are less reliable than those with double- or tripleblind study.

**vi)** Treatment considerations

While conducting RCTs, the treatment (either being studied or behaving as active-control) must be considered with regard to its dosages, dosing frequency and other concurrent medication. A drug is generally available in various dosage forms viz. tablet, capsule or injectable etc. and it varies in strength.

Moreover, depending upon the dosage form, the route of administration differs and hence, the amount of administration and dosing frequency also. All these factors together affect the plasma concentration of drug and thereby the effects of the drug and hence the final outcome. Therefore, except dose and frequency of drug(s), all above-mentioned factors are kept unique and constant throughout the study. Whenever dose and frequency need to be changed, it is done gradually and stepwise. If two drugs are to be administered one of which is likely to interfere with the other either pharmacokinetically or pharmacodynamically, the dosage must be reconsidered to overcome the influence of such interference on study outcomes. Patient compliance is another important part of the treatment consideration. A treatment should not be non-compliant as the patient avoids or less prefers to take such medication resulting in erroneously less efficacious outcomes than those obtained with the other treatment group.

**vii)** Outcome measures

The objective of the study determines the outcomes of interest to be measured. These measures are nothing but the points of checking and recording to accomplish the comparison. In experiments the outcomes are measured in terms of efficacy end-points i.e. primary end-points and surrogate end-points which are also called secondary end-points.

For examples, in an experiment evaluating an antihypertensive agent, the clinical end-point of real interest is whether the treatment under investigation can reduce cardiovascular events; a surrogate is the ability of the treatment to reduce blood pressure. The primary end-points of the study are the main measures to support or refute the hypothesis of the study. They must be defined and specified by the investigator at the beginning of the study. Secondary measures, although prespecified before the commencement of the study, can be further elaborated during the study. For example, when diuretics are used for treating hypertension, serum glucose level measurement can also be added though serum electrolytes are usually measured as main secondary endpoint.

Although various measures are determined as primary and secondary end-points, quality of life is now- adays becoming main primary end-point.

MTD: maximum tolerated dose; SAD: single ascending dose; MAD: multiple ascending doses; NDA: new drug application; FDA: food and drug administration

table 1: the phases, types, and nature of clinical trial studies.

| Clinical trial phase | Type of the study | Nature of study |
|---|---|---|
| Phase 0 | Exploratory | Examines too low ($1/100^{th}$) concentrations (micro-dosing) of the drug for less time. Study the pharmacokinetics and determine the dose for phase I studies. Previously done in animals but now it is carried out in humans. |

| | | |
|---|---|---|
| Phase I, Phase Ia, Phase I-b | Non- therapeutic trial | Around <50 healthy subjects are recruited. Establishes a safe dose range, and the MTD. Examines the pharmacokinetic and pharmacodynamic effects. Usually singlecenter studies. Phase I-a: SAD, and MTD. Duration of one week to several months depending on the trial and includes 6-8 groups of 3-6 participants. Phase I-b: MAD and the dose is gradually narrowed down. Three groups of 8 individuals each. |
| Phase II, Phase II-a, Phase IIb | Exploratory therapeutic trial | Recruiting around 5-100 patients of either sex. Examines the effective dosage and the therapeutic effects on patients. It decides the therapeutic regimen and drug-drug interactions. Usually, multicentre studies. IIb includes 20-30 patients, and takes up to weeks/months. Phase IIb: Studies doseresponse relationship, drug-drug interactions, and comparison with a placebo. Phase II-a: Decides the drug dosage, |
| Phase III | Therapeutic confirmatory trial | More than 300 patients (up to 3000) of either sex are recruited in this study and are multicentric trials. Pre-marketing phase examines the efficacy and the safety of the drug. Comparison of the test drug with the placebo/standard drug. Adverse drug reactions/adverse events are noted. Initiate the process of NDA with appropriate regulatory agencies like the FDA. |

Phase Post-approval After approval/post-licensure and postIV study marketing studies/surveillance studies. Following up on the patients for an exceptionally long time for potential adverse reactions and drug-drug interactions.

table 2: clinical trial designs, their advantages, and disadvantages.

| Trial design type | Type of the study | Nature of study | Advantages/disadvantages |
|---|---|---|---|
| Parallel | Randomized | This is the most frequent design wherein each arm of the study group is allocated a particular treatment (placebo (an inert substance)/therapeutic drug) | The placebo arm does not receive it |

| | | | |
|---|---|---|---|
| Crossover | Randomized | The patient in this trial gets each drug and the patients serve as a control themselves | Avoids participant bias in treatment and requires a small sample size. This design is not suitable for research on acute diseases. |
| Factorial | Nonrandomized | Two or more interventions on the complex participants and the study can provide information on the interactions between the drugs | The study design is |
| Randomized withdrawal approach | Randomized | This study evaluates the time/duration of the drug therapy | The study uses a placebo to understand the efficacy of a drug in treating the disease |
| Matched pairs | Postapproval study | Recruit patients with the same | Less variability characteristics |

CLINICAL RESEARCH IN INDIA

**1.** Introduction

In 2005, India became fully compliant to TRIPS. Since then, the policymakers have been trying to make changes in the policy framework and regulatory environment in order to promote clinical trials in India. These changes are known to have encouraged the international Clinical Research Organisations

(CROs) to expand their clinical research programmes in India. India hosts nearly a fifth of all global clinical trials with a huge potential for financial and scientific gains

(*The Lancet*, 2007; Bavdekar, 2008). CROs are taking advantage of getting large pool of patients, highly skilled medical investigators, lower drug development costs and timely completion of clinical trials in India (Kaur, 2006; Bhat, 2004; Singh, 2008). Recently, pharmaceutical companies that are involved in clinical trials are being trailed by a growing concern over the clinical research ethics followed in India. Global pharmaceutical companies are outsourcing their projects to India for several reasons: enhancing profit, cutting the cost of drug development and speeding regulatory approval, and, fostering a less hostile environment among the world′s impoverished ill. Clinical trials are more than 50 *per cent* cheaper in India compared to developed countries (Jayaraman, 2004; Singh. 2008; Bigoniya *et al*., 2010; Bajpai, 2013). The reasons for low cost of drug development are cheap human resource, low recruitment cost and lower rate of compensation for any injury sustained or death during the research process. In fact, CROs even recruit patients withoutany formal assurance of compensation because a large proportion of participants in India are illiterate and lured into trials by offers of free healthcare and financial inducements.

However, they are often unaware of the benefits and risks of taking part in a trial, and many may not even be able to distinguish between treatment and research. Also, the concept of informed consent before enrolling in a trial is not very clear. An important ethical question being raised in the debate is: Will the new drugs tested in India actually be of benefit to the local patients, and will these drugs be made available to them at reasonable prices? With 25 *per cent* of the Indian population living below poverty line, it is unlikely that these drugs will be ―affordable‖. Another important issue in this context is compensation for clinical trial related injury or death. Over the past five years, more than two thousand people have died because of clinical drug trials and amongst them, only a few have received compensation (*The Economic Times*, 2013).

The Government of India continues to invite multinational companies for conducting clinical trials in order to attract foreign investments for financial and technological gains in this sector. The central ideology of clinical research is that it should be of wider benefit to society. There cannot be two societies—one that takes risks whilst the other reaps the benefits. Will India be able to bridge the gap between two societies, i.e., minimise risk and maximise benefit? Is the clinical trial practice of benefit to public health in general and to the pharmaceutical industry in particular? This study addresses the issues of benefit maximization and risk minimization by reviewing the progress of clinical trials industry in a systematic way. It has attempted to generate an evidence-based assessment to help policymakers shape future policies for development of the clinical trials industry. It also makes an attempt to direct the attention of the Indian policy-making apparatus to the legal and ethical questions being raised by researchers and civil society groups on the process of conducting trials involving human subjects.

## 2. Materials and Methods

In this study, we have used the following secondary level data sources: Clinical Trials.gov and CTRI (Clinical Trials Registry – India) dataset. ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted across the world; it is maintained by the National Institutes of Health (NIH), USA. This service currently lists all type of intervention (Drug and biological, behavioural, surgical as well as medical devices) and observational studies. Currently, 191,171 studies have been registered with locations in all 50 states in the US and in 190 countries. We have collected disease-wise clinical trial studies for 7 countries and analysed their data. The other source, CTRI dataset, is regularly published by the Indian Council of Medical Research (ICMR). The Drug Controller General of India (DCGI) has made trial registration with the CTRI mandatory before enrolment of first participant for any kind of intervention such as drugs, surgical procedures, preventive measures, lifestyle modifications, devices, educational or behavioural treatment, rehabilitation strategies as well as trials conducted in the purview of the Department of AYUSH. We also review the report and analyse the FDI factsheet data which

is regularly published by the Department of Industrial Policy and Promotion (DIPP) under Ministry of Commerce and Industry, Government of India. DIPP regularly publishes sector-wise as well as country-wise FDI equity inflows of all manufacturing and service sector industries

in India. We have separated the total FDI inflow for drug and pharmaceuticals, hospitals and diagnostic centres, and, medical and surgical appliances. We estimate the contribution of these drugs, pharmaceutical and healthcare industries to the total FDI inflows into the country over the past decade. This study also describes the relative position of the country in terms of cost effectiveness, availability of native patients, availability of medical professionals and technicians, and regulation. We have used the A.T. Kearney testimony data (A.T. Kearney: Wang, 2005) to reanalyse and represent it by using different statistical tools. Apart from the above-given data sources, we have collected evidence from various clinical study reports.

**3.** Government Regulation on CTs

Over the past few years, pharmaceutical industry has experienced a tremendous growth and government has allowed 100 *per cent* FDI with limited regulation. Indian pharmaceutical sector exports 32 per cent of drugs, of which 90 per cent is generic and marketing growth is about 20 per cent per annum (Sharma *et al*., 2008). India is able to produce low-cost generic drugs and the Indian drug makers' account for 40 per cent of generic drug imports to the US *(*based on volume) and 39 per cent of the total generic drug approvals by the Food and Drug Administration (FDA), an agency of the US federal government (Silverman, 2014). However, the process of drug development in India is rather controversial (Dieppe *et al*., 2004). The issue of unethical practices in clinical trials is placed at the top of the list. This controversy arises because of complicated regulatory policies and contradictory norms implemented by government agencies. As a result, many people have died or are severely injured due to clinical trials but have not been compensated properly. Only very few have received compensation and the amount of compensation is also very low. For example, in 2004, doctors at Bhopal Memorial Hospital and Research Centre recruited Bhopal gas tragedy survivors for clinical trials without taking informed consent (Bhatnagar, 2013) and it is reported that 14 participants died during the course of the trials. Similarly, between 2005 and 2010, 32 people died at an

Indore-based hospital because of clinical trials (Bhatnagar, 2013).

CONCLUSION:

Clinical research is a cornerstone of medical progress, enabling the development of effective treatments, preventive measures, and diagnostic tools. By meticulously designed and executed studies, researchers can uncover new insights into disease mechanisms, evaluate the safety and efficacy of interventions, and ultimately improve patient outcomes. The careful selection of appropriate research methodologies, such as descriptive and explanatory studies, including randomized controlled trials, is essential for generating reliable and valid scientific evidence. As clinical research continues to evolve, a deep understanding of its principles and methodologies will remain paramount in advancing healthcare and improving human health.

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