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A REVIEW: NEW CAREER AVENUES IN CLINICAL RESEARCH AND ASSOCIATED DOMAIN.

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ABSTRACT
Research is essential for the growth and development of any medical science. The status of research in developing nations is very primitive mainly because of lack of funds and lack of motivation. India is doing good academic progress and the situation of clinical research in India is nowadays improving rapidly. Several organization have Sponsered the development of short duration modules of mobile research workshop in india. that include Clinical trials, clinical research are important step in developing new medicine safely use and distributed. Clinical trials are used through out the world to determine the safety and efficacy of a chemical or biological compound with respect to its action on symptoms or a known disease process. Trials are closely monitored by an investigator and the pharmaceutical company involved in the research and development of a medicinal product. Pharmacovigilance, also referred to as drug safety, is the science of understanding the adverse effects caused by a drug and assessing whether the benefit will outweigh the risk. This includes detection of adverse effects during the clinical trial and post marketed phases Research publication are a desirable qualification nowadays for promotion amongst faculty members. This has led to a great enthusiasm amongst faculty members to get their research studies published this article describes the current status of clinical research in developing nations and discusses the measures undertaken to improve research activities in world.

KEYWORDS: Research, Scenario of CR, Associated Domain, CR including Major Challenges and Opportunities.

- **Why the clinical trials conducted**

The clinical trials are conducted to know the safety and effectiveness of the new drug and to know the clinical use the drug with the involving of the human subjects

- **What we will study in clinical trials**

Pharmacodynamic activity of the drug. Absorption, distribution, metabolism, excretion of the new drug and adverse effects of the new drug

- **Sponsor**

Throughout the clinical trial, the sponsor is responsible for accurately informing the local site investigators of the true historical safety record of the drug, device or other medical treatments to be tested, and of any potential interactions of the study treatment(s) with already approved medical treatments.

INTRODUCTION
British chemist William Harvey once said "What is research, but a blind date with knowledge?" Global competitiveness among nations in the emerging knowledge economy of the world is often assessed from the research outputs originating from the country .Research should be undertaken because it promotes basic knowledge, develops new tools like drugs and instruments, informs the public regarding health promotion and provides effective planning to guide health policies and action. Research is essential for the growth and development of the any medical science. clinical research can make all the difference when it comes to saving peoples' lives, or improving their quality of life. Not only do clinical trials trial new drugs and medicines for general use by the population, they also tackle diseases that were previously thought incurable, such as heart disease, rheumatoid arthritis and nervous system disorders like Alzheimer's,Viral disease.

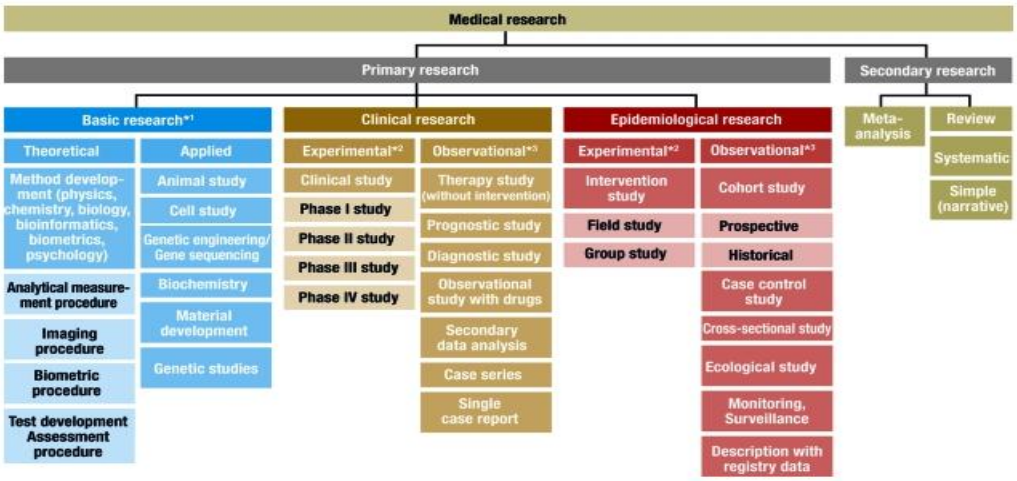
India is one of those Asian countries doing excellent academic progress. Thomson Reuters predicts that

India's research productivity will be on par with most G8 nations within 7 to 8 years and could overtake them none the less, the situation of clinical research in India is said to be fast improving and more and more medical, paramedical and science graduates are enrolling for clinical research training. India is fast becoming a hub of clinical trials. Foreign companies are opening clinical research organizations in all parts of our country and research work is being carried out in medical teaching institutes as well. The major attraction to conduct clinical trials in Asia is attributed to the increasing prevalence of western diseases like diabetes mellitus, hypertension, dyslipidemia etc. with the changing dietary pattern and sedentary lifestyle. India has the added benefits of a vast genetically diverse population, well equipped hospitals and highly qualified English speaking investigators making it one of the preferred destinations for conducting global clinical trials.

Clinical Research

Clinical research is the study of health and illness in people. It is the way we learn how to prevent, diagnose and treat illness. Clinical research describes many different elements of scientific investigation. Simply put, it involves human participants and helps translate basic research (done in labs) into new treatments and information to benefit patients. Clinical trials as well as research in epidemiology, physiology and pathophysiology, health services, education, outcomes and mental health can all fall under the clinical research umbrella.

Classification of research according to medical-



➢ **Basic research**

Medical research (otherwise known as experimental research) includes animal experiments, cell studies, biochemical, genetic and physiological investigations, and studies on the properties of drugs and materials. In almost all experiments, at least one independent variable is varied and the effects on the dependent variable are investigated. The procedure and the experimental design can be precisely specified and implemented. For example, the population, number of groups, case numbers, treatments and dosages can be exactly specified. It is also important that confounding factors should be specifically controlled or reduced. In experiments, specific hypotheses are investigated and causal statements are made. High internal validity (= unambiguity) is achieved by setting up standardized experimental conditions, with lowvariability in the units of observation (for example, cells, animals or materials). External validity is a more difficult issue. Laboratory conditions cannot always be directly transferred to normal clinical practice and processes in isolated cells or in animals are not equivalent to those in man (= generalizability).

➢ **Clinical studies**

Clinical studies include both interventional (or experimental) studies and noninterventional (or observational) studies. A clinical drug study is an interventional clinical study, defined "any study performed on man with the purpose of studying or demonstrating the clinical or pharmacological effects of drugs, to establish side effects, or to investigate absorption, distribution, metabolism or elimination, with the aim of providing clear evidence of the efficacy or safety of the drug. Interventional studies also include studies on medical devices and studies in which surgical, physical or psychotherapeutic procedures are examined. "A noninterventional study is a study in the context of which knowledge from the treatment of persons with drugs in accordance with the instructions for use specified in their registration is analyzed using epidemiological methods. The diagnosis, treatment and monitoring are not performed according to a previously specified study protocol, but exclusively according to medical practice."

A well designed clinical study must also include case number planning. This ensures that the assumed therapeutic effect can be recognized as such, with a

previously specified statistical probability (statistical power) .It is important for the performance of a clinical trial that it should be carefully planned and that the exact clinical details and methods should be specified in the study protocol It is, however, also important that the implementation of the study according to the protocol, as well as data collection, must be monitored.

contrast, noninterventional clinical studies (NIS) are patient-related observational studies, in which patients are given an individually specified therapy. The responsible physician specifies the therapy on the basis of the medical diagnosis and the patient's wishes. NIS include noninterventional therapeutic studies, prognostic studies, observational drug studies, secondary data analyses, case series and single case analyses Similarly to clinical studies, noninterventional therapy studies include comparison between therapies; however, the treatment is exclusively according to the physician's discretion. The evaluation is often retrospective. Prognostic studies examine the influence of prognostic factors (such as tumor stage, functional state, or body mass index) on the further course of a disease. Diagnostic studies are another class of observational studies, in which either the quality of a diagnostic method is compared to an established method (ideally a gold standard), or an investigator is compared with one or several other investigators (inter-rater comparison) or with himself at different time points (intra-rater comparison) . If an event is very rare (such as a rare disease or an individual course of treatment), a single-case study, or a case series, are possibilities. A case series is a study on a larger patient group with a specific disease. For example, after the discovery of the AIDS virus, the Center for Disease Control (CDC) in the USA collected a case series of 1000 patients, in order to study frequent complications of this infection. The lack of a control group is a disadvantage of case series. For this reason, case series are primarily used for descriptive purposes.

Table 2
Advantages and disadvantages of observational studies (taken from [16])*

	Ecological study	Cross-sectional study	Case control study	Cohort study
Selection bias	N/A	2	3	1
Recall bias	N/A	3	3	1
Loss to follow-up	N/A	N/A	1	3
Confounding	3	2	2	1
Time required	1	2	2	3
Costs	1	2	2	3

1 = slight; 2 = moderate; 3 = high; N/A, not applicable.

*Individual cases may deviate from this pattern.

- **Epidemiological studies**

The main point of interest in epidemiological studies is to investigate the distribution and historical changes in the frequency of diseases and the causes for these. Analogously to clinical studies, a distinction is made between experimental and observational epidemiological studies Interventional studies are experimental in character and are further subdivided into field studies (sample from an area, such as a large region or a country) and group studies (sample from a specific group, such as a specific social or ethnic group). One example was the investigation of the iodine supplementation of cooking salt to prevent cretinism in a region with iodine deficiency. On the other hand, many interventions are unsuitable for randomized intervention studies, for ethical, social or political reasons, as the exposure may be harmful to the subjects.

Observational epidemiological studies can be further subdivided into cohort studies (follow-up studies), case control studies, cross-sectional studies (prevalence studies), and ecological studies (correlation studies or studies with aggregated data).

Classification of clinical research are used depending on what the researchers are studying.

1. **Treatment Research**- generally involves an intervention such as medication, psychotherapy, new dev-ices, or new approaches to surgery or radiation therapy.

2. **Prevention Research**- looks for better ways to prevent disorders from developing or returning. Different kinds of prevention research may study medicinens, vitamins, vaccines, minerals, or lifestyle changes.

3. **Diagnostic Research** - the practice of looking for better ways to identify a particular disorder or condition.

4. **Screening Research**- find the best ways to detect certain disorders or health conditions.

5. **Quality of Life Research**- explores ways to improve comfort and the quality of life for individuals with a chronic illness.

6. **Genetic studies** - aim to improve the prediction of disorders by identifying and understanding how genes and illnesses may be related. Research in this area may explore ways in which a person's genes make him or her more or less likely to develop a disorder. This may lead to development of tailor-made treatments based on a patient's genetic make-up.

7. **Observational Studies** - These clinical research studies do not examine any drugs or their effects on human illness. Examiners are involved in observing participants of the trials by monitoring their health over a period of time and collect relevant data. Examiners enhance their medical knowledge by continuous follow-up of the patients in the reference centers.

8. **Interventional Studies** - These studies furnish scientific verification of the efficacy and welfare of an innovative drug, a new caution device or a new organization in the context of a disease or illness. These clinical trials or interventional studies are obligatory steps for the conversion of a new molecule into an innovative drug or any newly discovered device to be noticed.

Clinical trials

Clinical trials are a key research tool for advancing medical knowledge and patient care. Clinical research is Clinical trials are a key research tool. done only if doctors do not know whether a new approach works well in people and is safe, and which treatments or strategies work best for certain illnesses or groups of people.

Clinical trials are important for discovering new treatments for diseases, as well as new ways to detect, diagnose, and reduce the chance of developing the disease. Clinical trials can show researchers what does and doesn't work in humans that cannot be learned in the laboratory or in animals. Clinical trials also help doctors decide if the side effects of a new treatment are acceptable when weighed against the potential benefits. Researchers don't know what the results of clinical trials will be. (If they did, they wouldn't have to do the trials!) This uncertainty can make it hard for a patient to decide to participate in a clinical trial. While in rare cases, patient volunteers have been hurt by the treatment or procedure on a clinical trial, millions of people have been helped because other people before them chose to participate in a trial that resulted in a new, more effective treatment.

Clinical trials type

clinical development procedure of a drug is called a clinical trial –

1. **Open clinical trial:** An open clinical trial is a clinical trial without a control group, as opposed to a controlled clinical trial. It can also be a non-blinded clinical trial, as opposed to a single-blind or double-blind clinical trial.

2. **Single-blind clinical trial:** Trial in which the subject, but not the observer, does not know which of the possible treatments he is receiving.

3. **Double-blind clinical trial:** Trial in which neither the subject nor the observer know which treatment is being administered.

4. **Triple-blind clinical trial:** Clinical trial in which the participating subject, the observer-researcher and the researcher who analyzes the data do not know which treatment is being received. This is done when the clinical variables examined are soft, that is, they can be interpreted in different ways.

5. **Crossover clinical trial:** Clinical trial in which each individual consecutively receives each of the treatments under study.

6. **N-of-1 clinical trial:** Trial in which the total population is a single patient and in which the order of administration of the treatments compared is determined in a random way.

7. **Explanatory clinical trial:** Said of the trial whose aim is fundamentally to acquire scientific knowledge and biological explanations about efficacy. It is usually done in the earliest phases of the development of a drug, with restricted inclusion criteria, in order to obtain a homogenous sample of participants, representative only of specific sub-groups of population, of a limited size. The main parameters measured are mainly biological ones (for example, deobstruction of coronary arteries in patients who have suffered a myocardial infarction). It is usually done in conditions which are different from those of habitual practice and includes the analysis of patients who complete the trial, as opposed to an intention-to-treat analysis.

   In explanatory clinical trials it is usually easier to avoid Type-I and Type-II errors, but their power of inference is lower than in pragmatic trials.

8. **Unicenter clinical trial:** A trial carried out by a single researcher or research team in one hospital or another type of centre.

9. **Multicenter clinical trial:** According to Royal Decree 561/1993, "A trial carried out in two or more centres with the same protocol and a coordinator who is responsible for processing all the data and for analysing the results".

10. **Parallel clinical trial:** Clinical trial in which each group of patients receives a single treatment simultaneously.

11. **Sequential clinical trial:** Clinical trial in which the observations are assessed as they are produced and the total number of participants is not predetermined, but depends on the accumulated results. The subjects of the experimental group and the control group are arranged in pairs (one who receives the experimental treatment and the other who receives the reference treatment), are examined and added to the results obtained up to that time.

12. **Community trial:** Clinical trial in which the elements allocated randomly are communities or populations, instead of individuals This is usually carried out when an assessment of the impact of a community intervention is required, for example, fluorination of water (in which populations are randomized) or when it is important to prevent

contamination, from one group to another (for example, the periodic administration of Vitamin A supplements to malnourished children, in developing countries).

Classification of the types of design

a) Cross-sectional descriptive studies

- Prevalence studies.
- Series of cross-sectional cases.
- Evaluation of diagnostic tests
- Concordance studies.
- Case-crossover studies.

b) Longitudinal descriptive studies

- Incidence studies
- Description of the effects of a non-deliberate intervention Natural history description.

c) Observational analytical studies:

- Cause-effect sequence: cohort studies.
- Effect-cause sequence: case-control studies.

d) Experimental analytical studies:

- Controlled trials.
- Uncontrolled trials: (Not recommended in manual therapy).

Note

Experimental clinical trial: study of an osteopathic technique.

Descriptive or observational analytical trial: study of a diagnostic test.

13. **Pilot study:** Initial application, on a small scale, of a study protocol, with the aim of checking whether the design is appropriate, establishing its viability or obtaining information to determine the sample size for the definitive study.

14. **Descriptive study:** Part of statistics which summaries the information about the sample. The information collected and summarized in statistics is used to estimate population parameters. Study designed solely for describing the distribution of certain variables, but which is not concerned about the associations between them. It generally has a cross-sectional design.

15. **Observational study:** Analytical epidemiological study in which the researcher does not determine the allocation of the subjects to each group, but simply records (observes) what actually happens. It can be a cohort, case-control or cross-sectional study.

a) **Observational descriptive study:** This is carried out when little is known about the occurrence, natural history or determinants of a disease. Its objectives include estimating the frequency of a disease or attribute, the temporal trend in a particular population and elaborating or generating more specific etiological hypotheses.

b) **Observational analytical study:** An analytical (etiological) study is carried out when enough information is known about the disease before the research, which means that a priori hypotheses already exist and these can be tested in the study.

The objectives usually involve identifying risk factors for the disease, estimating the effect of exposure on the disease and therefore deducing possible strategic interventions.

It can be cohort, and cross sectional, case-controls studies.

16. **Experimental study:** In epidemiology, controlled clinical trial or community trial with random distribution. The researcher manipulates the research conditions and randomly distributes the groups. The objective of experimental studies is to estimate the efficacy of a preventive, curative or rehabilitative intervention. The groups which are compared are similar in those characteristics which may have an effect on the response, except for the intervention which is being assessed. The study groups are formed randomly. The use of another active treatment or intervention as a comparative group is to examine the benefit/risk relation of the new treatment in a specific clinical situation.

17. **Cross-sectional studies:** These are studies in which the data of each subject represents essentially a moment of time. This data may correspond to the presence, absence or different degrees of a characteristic or disease. It consists of examining the relationship between different variables in a defined population at a specific moment in time. These designs do not permit the study of an alleged cause-effect relationship.

Cross sectional studies are descriptive by definition.

Epidemiological strategy in which observations of numerous factors at the same time are recorded and then a comparison is made between them presence or absence of a disease or other variables (or, if they are quantitative, their level) are determined in each subject.

The analysis of the results can be made in two senses: by comparing all the variables in the individuals who suffer from the disease being studied, comparing them with those who do not suffer from it, or by comparing the prevalence of the disease in different subgroups of the population.

18. **Longitudinal studies:** These are studies in which there is a time lapse between the different variables, so that a time sequence can be established between them.

They can be both descriptive and analytical.

In analytical studies, it should be taken into account whether the time sequence is from the cause to the outcome (experimental studies and cohort studies), or from the outcome to the cause (case-control studies). Any study not focused on an alleged cause-effect relationship, but whose data is used for purely descriptive purposes is considered descriptive.

This type of study is useful for generating etiological hypotheses which should subsequently be contrasted with analytical studies. Any study which evaluates an alleged cause-effect relationship is considered analytical. The alleged causal agent may be a factor which is suspected of being able to lead etiologically to a disease or a treatment to prevent or improve a clinical situation.

19. **Feasibility study:** Preliminary study with the objective of determining whether a programme, procedure or study protocol is practicable, as well as finding out data to help in determining the sample size for a definitive study.
20. **Crossover study:** In clinical trials and in cohort studies, the moving of subjects from the group they were in at the beginning of the observation to another group. In both types of design, the crossover is the cause of an infraestimation of the possible differences between the groups compared.

21. **Analytical study:** Study designed to examine associations, with the final object usually of identifying or measuring the effects of risk factors or specific interventions on health. Analytical studies can be controlled clinical trials, cohort studies, case-control studies or cross-sectional studies.

22. **Prospective study:** Study in which the patients are included from the time the start of the study is decided.

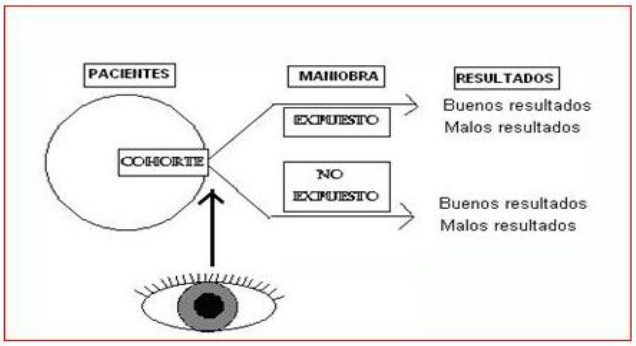
23. **Retrospective study:** Study in which the data collected refers to events which have occurred.

24. **Case-control study:** This type of study identifies people with a disease (or another variable of interest) and compares them with an appropriate control group which does not have the disease. An examination is made, comparing the frequency of exposure to this or other factors between the cases and the controls .It is an analytical observational study which enables the cause-effect relationship to be followed. If the frequency of exposure or the cause is greater in the group of cases with the disease than in the control group, we can say that there is an association between the cause and effect. The measurement of the association which quantifies this association is called the "odds ratio"(OR).In medicine, a case-control study is a cross-sectional type of study which is used to research the etiology of a disease or a given resul

Study in which people with a certain disease or symptom (cases) are compared with others who do not present the disease or symptom under study (controls), with regard to prior exposure to risk factors.This has been incorrectly called Retrospective Study.

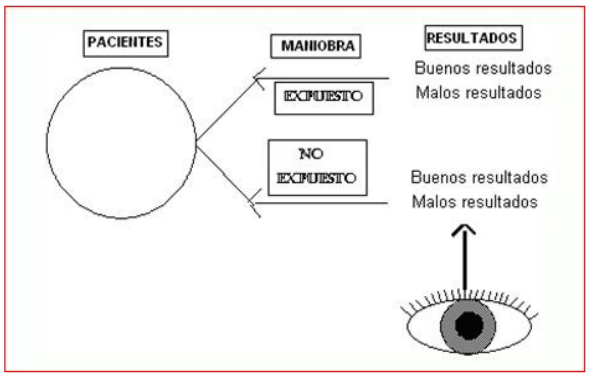
In a case-control study, a single disease but various risk factors or exposures are examined.

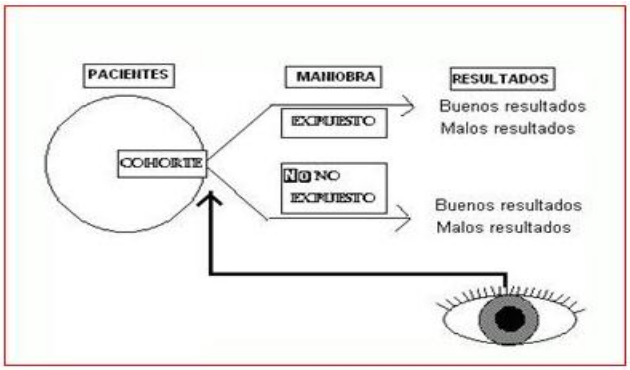
27. **Cohort study:** In the Roman militia, a centuria was made up of 60 soldiers. Two centurias formed a manipulo. The manipulos could be made up of hastate (young, less experienced soldiers, spear throwers or those with swords or light weapons), principes (soldiers with several years of service and several campaigns) or triarii (veterans).At camps and during marches, they formed cohorts, made up of one manipulo of hastatis, one manipulo of principes and one centuria of triarii, that is, a total of 300 soldiers Epidemiology adopted this term to refer to the idea of a simultaneous advancement, in time, of a group of individuals defined for possessing a common characteristic or group of characteristics. The common characteristic is usually exposure to a factor (environmental, pharmacological, occupational, etc).



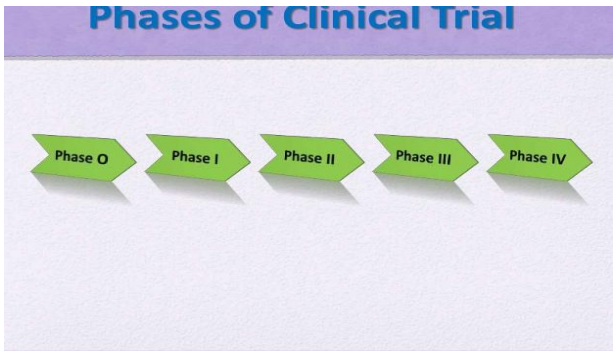
The term "cohort" is used to designate a group of subjects with a common characteristic or group of characteristics who are monitored over a period of time.

A large number of cases (300 or more) is necessary





Phase of clinical trial



Clinical trials advance through four phases to test a treatment, find the appropriate dosage, and look for side effects. If, after the first three phases, researchers find a drug or other intervention to be safe and effective, the FDA approves it for clinical use and continues to monitor its effects. Clinical trials of drugs are usually described based on their phase. The FDA typically requires Phase 0,I, II, and III trials to be conducted to determine if the drug can be approved for use.

➢ **Microdosing / phase 0 study**

Study of new drug is microdose to derive PK information in human before undertaking phase l studies is called as PHASE 0.

- **Microdose:** Less than 1/100 of dose of a test substance calculated to produce pharmacological effect with a max dose < 100 micrograms.

- **Objective**-To obtain preliminary pharmacokinetic data.

- **Preclinical Data**- Sabacute toxicit study in one species by two routes of administration.

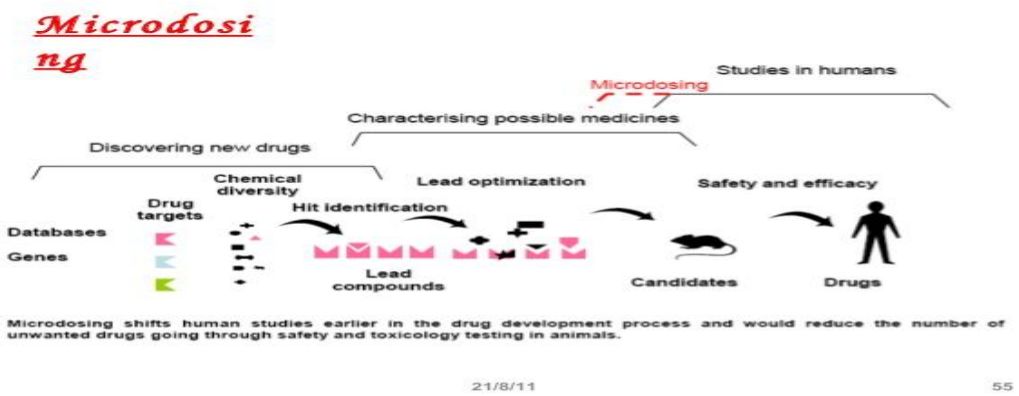
Early studies of the **pharmacodynamic and pharmacokinetic** properties of a potential drug in human Microdosing approaches could 'accelerate' drug development without compromising clinical safety. Microdosing helps researchers select better drug candidate for clinical trials by providing **early human PK and bioavailability data.**

Advantage

- Less chances of adverse
- Short duration
- Less no.of volunteers.
- Reduced costs of development
- Reduced drug development time

Limitations

1) study mainly based on PK parameters- not efficacy and safety based .
2) Agents having different kinetic characteristics between microdose and full dose are not evaluated by phase 0 trials.
3) Of Limited use for agents having non linear PKs.
4) The laboratory parameters are very limited and expensive, researchers have to depend on BA/ BE labs.



Phase I

Clinical trial tests an experimental treatment on a small group of often healthy people (20 to 80) to judge its safety and side effects and to find the correct drug dosage.

Determine

- Safety
- Pharmacokinetics
- Pharmacodynamic
- Determine maximum tolerated dose and adverse effects of this dose

Phase II

trial uses more people (100 to 300). While the emphasis in Phase I is on safety, the emphasis in Phase II is on effectiveness. This phase aims to obtain preliminary data on whether the drug works in people who have a certain disease or condition. These trials also continue to study safety, including short-term side effects. This phase can last several years.

Phase	Name	Conducted on	Blinding and control	Purpose
I	Human Pharmacology and safety	**Healthy** volunteers (20 – 100)	**OPEN LABEL** (No blinding)	– **To know maximum tolerable dose (MTD)** – Safety and tolerability
II	Therapeutic exploratory	100 – 150 **Patients (homogenous** population)	**Single blind** Controlled	– **To establish therapeutic efficacy** – Dose ranging and ceiling effect
III	Therapeutic confirmatory	Upto 5000 patients from several centres (**heterogenous** population)	**Double blind** Randomized Controlled	– **To confirm therapeutic efficacy** – To establish the value of drug in relation to existing therapy
IV	Post marketing surveillance	Large number of patients being treated by practicing physicians	—	– To know **rare and long-term adverse effects** – Special groups like children, pregnancy etc can be tested
O (Zero)	**Microdosing** studies	**Healthy** volunteers (small number)	—	– Very low dose 1/100th of human dose; max 100 µg) of drug is administered **to know pharmacokinetics**. This could avoid costly phase I studies for candidate drugs with unsuitable pharmacokinetics.

Determine

- Therapeutic efficacy
- Effective dose range
- Safety re-evaluation
- Further pharmokinetic data

Phase III-

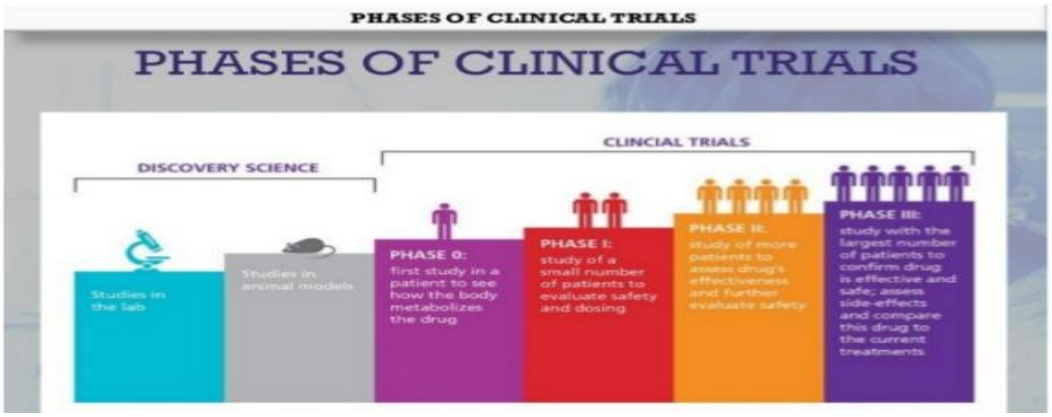
Clinical trial gathers more information about safety and effectiveness, studying different populations and different dosages, using the drug in combination with other drugs. The number of subjects usually ranges from several hundred to about 3,000 people. If the FDA agrees that the trial results are positive, it will approve the experimental drug or device.

Determine

- How the new treatment compare with the current standard or or how It compares with placebo
- Long term effectiveness and safety.
- Then drug will be submitted to the relevant regulatory authorities for listening .
- It takes 5 to 7 years normally to complete phase 1, 2, 3 trials.

- On completion of the three phases 'NEW DURG APPLICATION' is submitted to drug controlling authority.
- It includes complete detailed monographs of products,result of the trials,the proposed name of this product, and package insert.
- Then data are reviewed by drug controlling authorities .(DCGI,FDA)
- If acceptable then it can allow the drug to enter the market with 'NEW DURG STATUS'.

Phase IV -
Clinical trial for drugs or devices takes place after the FDA approves their use. A device or drug's yeffectiveness and safety are monitored in large, diverse populations. Sometimes, the side effects of a drug may not become clear until more people have taken it over a longer period of time.



New drug development
Introduction
Development of new drug is very arduous ,time consuming & very expensive process.

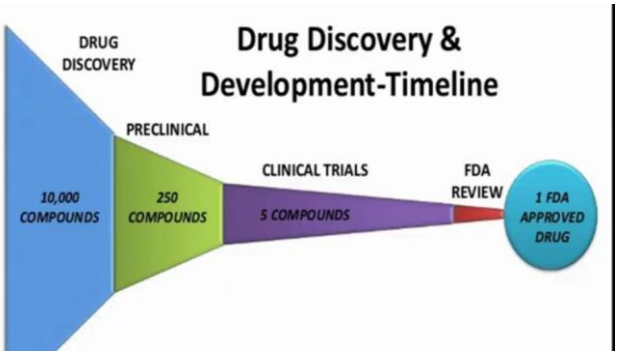
During last 50 years, hundreds of new drugs have been introduced,& many older drugs have been deleted (withdrawn).
< 1% of compounds that go into test eventually become licensed medicines.

To bring a new drug to market requires a good understanding of drug development process and integral role preclinical testing plays in that process.

5000-10000 Compounds yield 1 new drug to market.

overall time required for successful results is 10 to 12 years.

A Pyramid of uncertainty
- Time – It takes 12 years on average for an Experimental drug to travel from lab to medicine chest
- Success- Only five in 5000 compounds that enter preclinical testing make it to human testing
  One this five tested in humans is approved.



Step in new drug development
A. Idea or Basic Research
B. New drug discovery
C. Screening
D. Preclinical studies
E. Formulation development
F. IND application
G. FDA Review

A. Basic research
Typically, researchers discover new drugs through:

New insights into a disease process that allow researchers to design a product to stop or reverse the effects of the disease.

Many tests of molecular compounds to find possible beneficial effects against any of a large number of diseases.
Existing treatments that have unanticipated effects.

New technologies, such as those that provide new ways to target medical products to specific sites within the body or to manipulate genetic material.

At this stage in the process, thousands of compounds may be potential candidates for development as a medical treatment. After early testing, however, only a small number of compounds look promising and call for further study.

Development

Once researchers identify a promising compound for development, they conduct experiments to gather information on:

- How it is absorbed, distributed, metabolized, and excreted.
- Its potential benefits and mechanisms of action.
- The best dosage.
- The best way to give the drug (such as by mouth or injection).
- Side effects or adverse events that can often be referred to as toxicity.
- How it affects different groups of people (such as by gender, race, or ethnicity) differently.
- How it interacts with other drugs and treatments.
- Its effectiveness as compared with similar drugs.

Investigation disease

- Investigate each component of a disease:
- What is /are the symptoms?
- What is the cause?
- Which is the target organ?
- What is /are Biochemical pathways?

B. New drug discovery

- **Targate identification**
- **Targate evalidation**
- **Lead identification**
- **Lead Optimization**

Target identification and validation

Often Begins with **target identification-** choosing a biochemical mechanism involved in a disease condition.

Drugs usually act on either cellular or genetic chemicals within our body, known as targets believed to be associated with the disease .

Drug candidates are tested for their interaction with drug target.

up to 5000-10000 molecules for each potential drug candidate are subject two rigorous screening process.

Once scientists confirm interaction with drug target they, typically Validate that target by checking activity against the disease condition for which the drug is being developed.

Lead identification

Lead compounds or substance is one that is believed to have potential to treat disease. laboratory scientists compare known substances with new compounds to determine their likelihood up success.

Leads are sometime developed as collection, or libraries ,of individual molecules that process properties needed in new drug .Testing in then done on each of these molecule to confirm its effect on drug target.

Lead optimization

Compares property of various lead compounds and provide information to help Pharmaceuticals and biotechnology Components select compounds Mystic attacked with greatest potential to be developed into safe and effective medicine.

Often During this same stage of development Lead prioritization studies are conducted in living Organisms (in vivo) and in cells in a test tube (in vitro) to compare various lead compounds ,their metabolism ,etc.

Characteristics of ideal drug candidate

- High potency
- High selectivity
- Good oral Bioavailability
- Low or no interaction with CYP450
- Less or minimal adverse effects
- Good therapeutic index

C. Screening

NCEs are subject to battery of screening test designed to determine different types of biological activity.
Such test include studies of animal behaviour isolated tissue intact animal a 1 in every 4000-5000 NCEs screened is marketed.

Pharmacological screening of candidates molecules

Pharmacological observations are made, depending on expected pharmacological properties e.g.
falling BP, falling blood glucose, etc.

Pharmacological screening of candidate molecules-

Add the cellular level , it is possible to understand the mechanism of action of action of a drug whether is act as:
- receptor agonist antagonist if so its affinity and selectivity
-inhibitor of key enzyme, etc.

Through this process one can rapidly identify active compounds, antibodies or genes which modulate a particular biomolecule pathway.

The results of these experiments provide starting point for drug design and for understanding the interaction or role of a particular biochemical process in biology.

D. pre-clinical studies

Before testing a drug in people, researchers must find out whether it has the potential to cause serious harm, also called toxicity. The two types of preclinical research are:

In Vitro

In Vivo

FDA requires researchers to use good laboratory practices (GLP), defined in medical product development regulations, for preclinical laboratory studies. The GLP regulations are found in 21 CFR Part 58.1: Good Laboratory Practice for Nonclinical Laboratory Studies. These regulations set the minimum basic requirements for:

- **study conduct**
- **personnel**
- **facilities**
- **equipment**
- **written protocols**
- **operating procedures**
- **study reports**

and a system of quality assurance oversight for each study to help assure the safety of FDA-regulated product

Usually, preclinical studies are not very large. However, these studies must provide detailed information on dosing and toxicity levels. After preclinical testing, researchers review their findings and decide whether the drug should be tested in people.

E. Formulation development

DRUG +

Additives: filler, lubricant, coating, stabilizer, colour, binder, disintegrator

Dosage form: capsule, tablet, injection other?

Manipulate duration/ profile:e.g.sustained release

Bioequivalence

Bioavailability

Ease of use

F. IND application

IND application is a result of successful preclinical development program.

IND is a vehicle through which the sponsor advance to the next stage of drug development - clinical trial

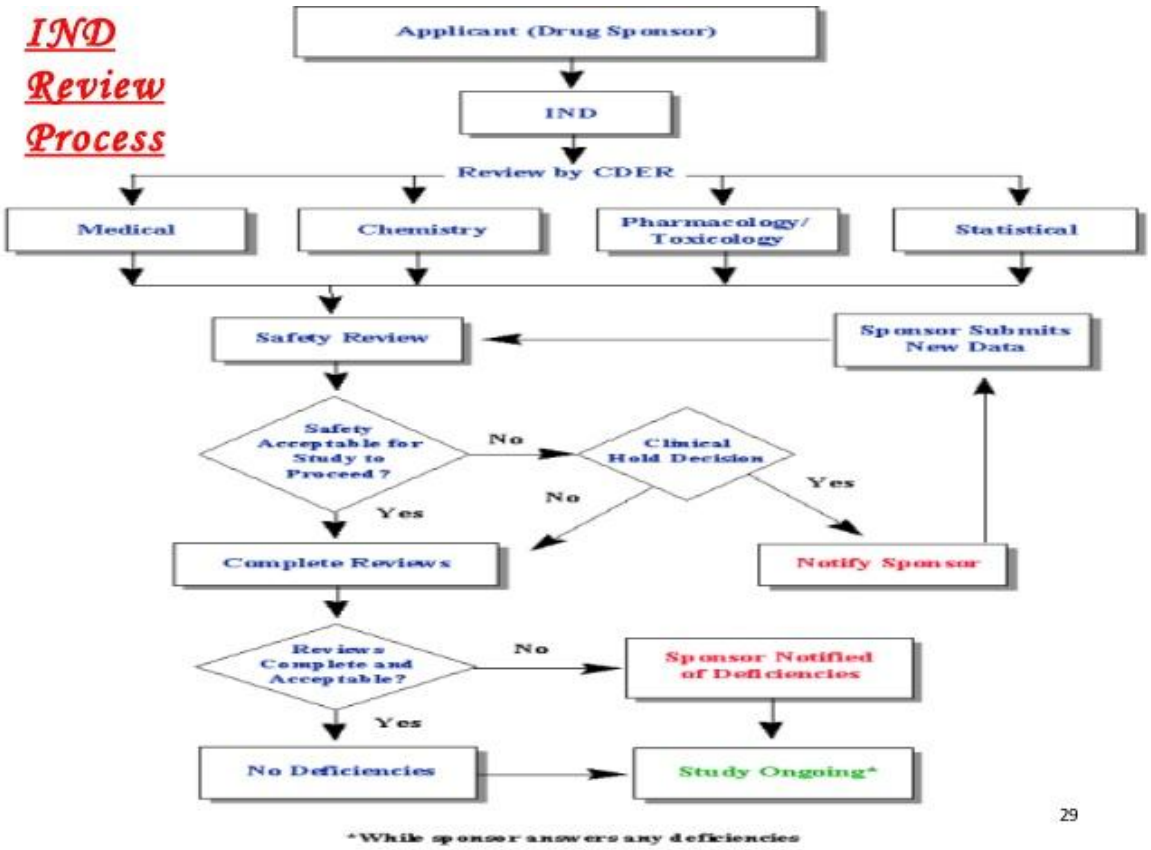
IND not an application for marketing approval.

Contents:

Animal pharmacological & toxicology studies.

Manufacturing information.

Clinical protocols and investigator information.



Sponsor/FDA meetings (Pre-IND)

Prior to clinical studies, the sponsor needs evidence that the compound is biologically active , and both sponsor and FDA need data showing that the drug is reasonably safe for initial administration to humans.

Meeting at such an early stage in the process are useful opportunities for open discussion about testing phases , data, requirements, and any scientific issue that may need to be resolved prior IND submission.

FDA drug review

If a drug developer has evidence from its early tests and preclinical and clinical research that a drug is safe and effective for its intended use, the company can file an application to market the drug. The FDA review team thoroughly examines all submitted data on the drug and makes a decision to approve or not to approve it.

New drug application

A New Drug Application (NDA) tells the full story of a drug. Its purpose is to demonstrate that a drug is safe and effective for its intended use in the population studied. A drug developer must include everything about a drug—from preclinical data to Phase 3 trial data—in an NDA. Developers must include reports on all studies, data, and analyses. Along with clinical results, developers must include:

- **Proposed labeling**
- **Safety updates**
- **Drug abuse information**
- **Patent information**
- **Any data from studies that may have been conducted outside the United States**
- **Institutional review board compliance information**
- **Directions for use**

- **FDA review**

Once FDA receives an NDA, the review team decides if it is complete. If it is not complete, the review team can refuse to file the NDA. If it is complete, the review team has 6 to 10 months to make a decision on whether to approve the drug. The process includes the following.

Each member of the review team conducts a full review of his or her section of the application. For example, the medical officer and the statistician review clinical data, while a pharmacologist reviews the data from animal studies. Within each technical discipline represented on the team, there is also a supervisory review.

FDA inspectors travel to clinical study sites to conduct a routine inspection. The Agency looks for evidence of fabrication, manipulation, or withholding of data.

The project manager assembles all individual reviews and other documents, such as the inspection report, into an "action package." This document becomes the record for FDA review. The review team issues a recommendation, and a senior FDA official makes a decision.

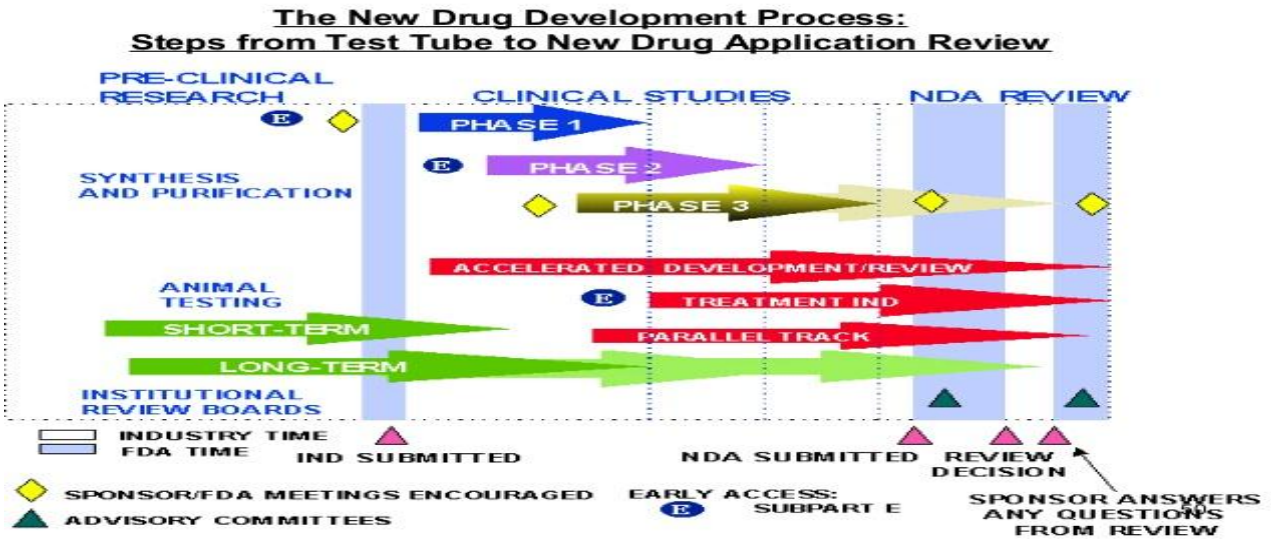
- **FDA approval**

In cases where FDA determines that a drug has been shown to be safe and effective for its intended use, it is then necessary to work with the applicant to develop and refine prescribing information. This is referred to as "labeling." Labeling accurately and objectively describes the basis for approval and how best to use the drug.

Often, though, remaining issues need to be resolved before the drug can be approved for marketing. Sometimes FDA requires the developer to address questions based on existing data. In other cases, FDA requires additional studies. At this point, the developer can decide whether or not to continue further development. If a developer disagrees with an FDA decision, there are mechanisms for formal appeal.

G. FDA advisory committees

Often, the NDA contains sufficient data for FDA to determine the safety and effectiveness of a drug. Sometimes, tho, questions arise that require additional consideration. In these cases, FDA may organize a meeting of one of its Advisory Committees to get independent, expert advice and to permit the public to make comments. These Advisory Committees include a Patient Representative that provides input from the patient perspective. Learn more about FDA Advisory **Committees.**



History of clinical trial

- **Clinical trials timeline (605 BC -1986 AD)**

605-562 BC:

The first clinical trial was carried out by king Nebuchadnezzar ll.

1537:

It was by chance surgeon ambroise pare

The history of clinical research

1900 – 1930:

In the early 1900's, vaccines were the only form of treatment against a world full of endemic and epidemic diseases such as influenza, smallpox, malaria, diphtheria, tetanus, typhus, and plague. The life span in the U.S. at this time was approximately 30 years old.

Walter reed (U.S. army physician)

Walter Reed tested and proved Carlos Finlay's theory that yellow fever (an acute viral disease) is transmitted by disease carrying mosquitoes, and not by direct contact between individuals. Reed was the first person to get formal consent from test subjects.

1902 Biologics control act

13 children died in MO after being administered a diphtheria antitoxin that was contaminated with tetanus spores in 1901 and nine children in NJ died from receiving a contaminated smallpox vaccine. These events prompted the creation of the Biologics Control Act in 1902, which established standards and required that pharmaceutical companies be licensed to make vaccines, antitoxins, and a variety of other serums.

Early regulations & governing bodies

The Pure Food and Drug Act created a regulatory authority called the U.S. Bureau of Chemistry to prevent the use of and transportation of filthy, decomposed, or putrid food substances and adulterated drugs. It also required that certain drugs, such as alcohol, cocaine, heroin, morphine, and cannabis, have accurate labels that specify the dosage and contents.

In the 1890's, Coke was directly marketed as a medicinal drink. The U.S. Bureau of Chemistry was reorganized into the Food, Drug, and Insecticide Organization in 1927. It became known as the Food and Drug Administration (FDA)in 1930.

Marie curie (physicist and chemist)

Marie Curie pioneered research on radioactivity. In 1903, she became the first female to win the Nobel Prize, and in 1911 she became the first person and only female to win it twice. She had many accomplishments, some of which include developing the theory of radioactivity, developing ways to isolate radioactive isotopes, and discovering the elements polonium and radium. She also directed the first studies on treating neoplasms with radioactive isotopes. Curie lived through many historic events, including millions perishing in the Spanish flu pandemic (1918 - 1919), World War I (1914 - 1918), and women gaining the right to vote (1920). Like many before her, Marie Curie's death was caused by her studies of what made her famous: she died in 1934 due to aplastic anemia brought on by exposure to radiation.

1903 Nobel prize portrait of marie curie.

Alexander Fleming (Scottish biologist, pharmacologist, and botanist)

Alexander Fleming discovered the antiseptic lysozyme in the early 1920's. Lysozyme is a natural antiseptic that can be found in many of the body's fluids, including tears, saliva, and mucus. Fleming presented his findings on penicillin in 1929 in the British Journal of Experimental Pathology, but no one paid much notice. He continued to work with penicillin for several years, but found it difficult to cultivate and test in clinical trials.

1930 - 1950

Many clinical trials began at the dawn of the Great Depression (1929) and continued through the end of World War II (1945). After that, a review of the studies brought several years of whirlwind changes to clinical research regulations.

- **1932: The "Tuskegee study of untreated syphilis in the negro male" begins**

The "Tuskegee Study of Untreated Syphilis in the Negro Male" was a joint venture between the U.S. Public Health Service and the Tuskegee Institute to follow the effects of untreated syphilis in black men in Alabama. At that time, 35% of the black, reproductive aged population suffered from syphilis and there was no effective cure. The study followed 600 men. 399 of them had syphilis before the study began, and 201 of them did not.

- **1937: Sulfa craze**

Sulfonamide drugs were the first systemic antibiotics. It treated a wide range of bacterial infections and was very effective against infections caused by streptococci and other cocci. The active molecule was called sulfanilamide (sulfa, for short) and was frequently used in the dye-making industry.

- **1938: Federal food, drug, & cosmetic act**

The Federal Food, Drug, and Cosmetic Act was created in response to the sulfa craze. It replaced the Pure Food and Drug Act of 1906. The Federal Food, Drug, and Cosmetic Act required new drugs to be proven safe before they were marketed to the public. It also authorized factory inspections, extended FDA control to cosmetics and devices, and authorized standards of quality for food.

- **1946: Nuremburg trials**

From 1939 to 1945, the Nazi's performed experiments on concentration camp prisoners. These studies were meant to prove the racial ideology of the Third Reich, help the German militia in combat situations, create new weapons, and aid in the recovery of injured military members.

Josef Mengele was one of the leaders in the concentration camp experiments. These experiments were unscientific and conducted without consent. One of Mengele's experiments involved injecting blue dye into brown eyes in an attempt to change eye color. Other Nazi experimentation crimes involved:
Sterilization experiments
Sea water experiments
Mustard gas experiments
Poison experiments
Removing sections of bones, muscles, and nerves without anesthesia
A variety of studies on twins (One study involved sewing a pair of twins together back to back to create conjoined twins. The children died of gangrene several days later)

- **1947: Nuremburg code**

In May of 1947, Dr. Leo Alexander submitted six point that defined legitimate medical research to the Counsel for War Crimes. The "Doctor's Trial" verdict adopted the six points and added another four points to them. These ten points comprised the Nuremberg Code.

- **1948: First randomized controlled clinical trial**

The first trial using properly randomized treatment and control groups was executed in 1948 by the Medical Research Council. It involved using streptomycin as a treatment for pulmonary tuberculosis.

1950 - 1980

- **1951: Durham-humphrey amendment**

The Durham-Humphrey Amendment was co-sponsored by Carl Durham and Hubert H. Humphrey (who later became Vice President of the United States). This bill defines two types of medications: prescriptions (also called legend) and over-the-counter (OTC).

- **1953: DNA is discovered**

James Watson and Francis Crick discovered the double helix structure of deoxyribose nucleic acid (DNA). They published their discovery in the scientific journal *Nature* in an article titled "Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid" on April 25th, 1953. This discovery had a major impact on the fields of genetics and biology, and later led to an understanding of the genetic code.

- **1960: Oral contraceptive pill approved by FDA**

Margaret Sanger opened the first birth-control clinic in America in 1916. Biochemist Gregory Pincus and and gynecologist John Rock developed a birth-control pill. Clinical trials for the pill began in 1954 and involved using synthetic progesterone and estrogen to suppress ovulation females. The pill was approved by the FDA on May 9th, 1960.

- **1961: Thalidomide tragedy**

Thalidomide was developed by a German pharmaceutical company and was known as a wonder drug that could treat insomnia, anxiety, gastritis, coughs, colds, headaches, and morning sickness. Clinical trials on thalidomide began in November of 1956.

- **1962: Kefauver-Harris Amendment**

The Kefauver-Harris Amendment to the Federal Food, Drug, and Cosmetic Act was also called the Drug Efficacy Amendment and was a direct reaction to the thalidomide tragedy. It requires drug manufacturers to prove the safety and effectiveness of their drug prior to approval.

- **1964: Declaration of helsinki adopted by the world medical association**

The Declaration of Helsinki combined the ten principals of the Nuremberg Code with the Declaration of Geneva and specifically addressed clinical research practices and new, relaxed, guidelines for conditions of consent.

- **1972: The "tuskegee study of untreated syphilis in the negro male" ends**

The previous post in this series addressed the start of the Tuskegee Study of Untreated Syphilis in the Negro Male in 1932. In the late 1940's, penicillin became the standard treatment for syphilis.

- **1974 - 1979: National research act & the belmont report**

As a response to the inadequate oversight of human research in the Tuskegee syphilis study, it was recommended that public regulations be defined and put into place to protect future human research participants. This led to the National Research Act of 1974.

- **1981: Immunodeficiency first reported in gay men in los angeles, new york city, and san francisco**

On June 5th, 1981, the Morbidity and Mortality Weekly Report reported five cases of *Pneumocystis carinii*pneumonia (PCP) in Los Angeles. These cases occurred in young men who had previously been healthyIn 1983, the CDC announced guidance for the prevention of the disease.

- **1982: Chicago tylenol murders**

In October of 1982, seven people died after taking Extra-Strength Tylenol capsules that had been laced with potassium cyanide. Investigators were able to determine that the culprit acquired the bottles from drug and grocery stores, added the poison to the capsules, and then placed the bottles back on the shelves of the stores.

- **1983: Orphan drug act**

In 1983, the Orphan Drug Act was passed to encourage manufacturers to develop treatments for rare conditions and diseases. Drugs for rare disease and conditions are commonly called orphan drugs. Congress found that there are many rare diseases such as Lou Gehrig's disease (ALS), Huntington's disease, and muscular dystrophy that can be considered rare in the United States because they affect such a small population of its residents.

- **1990: Human genome project is launched**

Planning for the Human Genome Project (HGP) began in 1984. The project itself began in 1990 and was completed in 2003. The HGP was an international scientific research project. Its goal was to map the more than three billion nucleotides in a human haploid reference genome.

- **1992: Fda prescription drug user fee act**

The Prescription Drug User Fee Act(PDUFA) was passed by Congress in 1992. It requires drug manufacturers to pay application fees every time they file a Biologics License Application (BLA) or New Drug Application (NDA).

- **1994: Veristat is born & clinton administration declassifies human radiation studies**

Dr. Joseph G. Hamilton was the primary researcher for the human plutonium experiments done at U.C. San Francisco from 1944 to 1947.

- **1997: FDA food and drug administration modernization act**

The Food and Drug Administration Modernization Act (FDAMA) brought about the most widespread reform in FDA practice since the Federal Food, Drug, and Cosmetic Act of 1938.

- **1999: Jesse Gelsinger dies**

Jesse Gelsinger was the first gene therapy clinical trial participant to be publicly identified as having died as a result of the trial.

- **2001 - 2009: Stem cell research regulations**

In 1999, the Clinton Administration made it legal for the study of Human Embryonic Stem Cells (hESC) to be eligible for federal funding. The caveat was that the embryos could not be created for the sole purpose of experimentation, but instead had to come from embryos that were discarded after *in vitro* fertilization treatments. In 2001, the Bush Administration signed an order that prevented the National Institutes of Health from funding embryonic stem cell research beyond the 60 cell lines that already existed at that time.

Regulation & guideline-

Drug and cosmetic Act

- Schedule Y
- Indian GCP Guidelines
- Clinical Trials Permission
- Import License
- Export License
- BA BE Guidelines
- ICMR Guidelines for medical Ethics
- ICH GCP Guidelines
- USFDA
- EU Directives

Goals of clinical research:

- All clinical trials should meet certain goals to fulfill their design or use of conduct. It must :
- Enhance therapeutic understanding
- Be implemented by adroit persons,
- Take all important steps/actions to protect those who accommodate themselves to research,
- Acquire regulatory acceptance and take all the obligatory legal and ethical steps.
- Gather the assent of those involved in research.

What are the benefits of a clinical trial?

- You may get a new treatment for a disease before it is available to everyone.You play a more active role in your own health care
- Researchers may provide you with medical care and more frequent health check-ups as part of your treatment.
- You may have the chance to help others get a better treatment for their health problems in the future.
- You may be able to get information about support groups and resources.

What are the potential risks of a clinical trial?

- The new treatment may cause serious side effects or be uncomfortable.
- The new treatment may not work, or it may not be better than the standard treatment
- You may NOT be part of the treatment group (or experimental group) that gets the new treatment—for example, a new drug or device. Instead, you may be part of the control group, which means you get the standard treatment or a no-treatment placebo.
- The clinical trial could inconvenience you. For example, medical appointments could take a lot of time. You might need to travel to the study site several times or stay in the hospital.

Why people participate in a clinical trial?

There are many reasons why people choose to join a clinical trial. Some join a trial because the treatments they have tried for their health problem did not work. Others participate because there is no treatment for their health problem. By being part of a clinical trial, participants may find out about new treatments before they are widely available. Some studies are designed for, or include, people who are healthy but want to help find ways to prevent a disease, such as one that may be common in their family. Older couple posing with their grandson Many people say participating in a clinical trial is a way to play a more active role in their own health care. Other people say they want to help researchers learn more about certain health problems. Whatever the motivation, when you choose to participate in a clinical trial, you become a partner in scientific discovery. And, your contribution can help future generations lead healthier lives. Major medical breakthroughs could not happen without the generosity of clinical trial participants—young and old.

Why are older and diverse participants important in clinical trials?

Older Asian coupleIt is important for clinical trials to have participants of different ages, sexes, races, and ethnicities. When research involves a group of people who are similar, the findings may not apply to or benefit everyone. When clinical trials include diverse participants, the study results may have a much wider applicability.

Researchers need the participation of older people in their clinical trials so that scientists can learn more about how the new drugs, therapies, medical devices, surgical procedures, or tests will work for older people. Many older people have special health needs that are different from those of younger people. For example, as people age, their bodies may react differently to drugs. Older adults may need different dosages (or amounts) of a drug to have the right result. Also, some drugs may have different side effects in older people than younger people. Having seniors enrolled in drug trials helps researchers get the information they need to develop the right treatment for older people.

Challenges in clinical research

Cooperation among a diverse group of stakeholders—including research sponsors (industry, academia, government, nonprofit organizations, and patient advocates), clinical investigators, patients, payers, physicians, and regulators—is necessary in conducting a clinical trial today. Each stakeholder offers a different set of tools to support the essential components of a clinical trial. These resources form the infrastructure that currently supports clinical research in the United States. Time, money, personnel, materials (e.g., medical supplies), support systems (informatics as well as manpower), and a clear plan for completing the necessary steps in a trial are all part of the clinical research infrastructure. A number of workshop participants lamented that most clinical trials are conducted in a "one-off" manner. Significant time, energy, and money are spent on bringing the disparate resources for each trial together. Some workshop attendees suggested that efficiencies could be gained by streamlining the clinical trials infrastructure so that those investigating new research questions could quickly draw on resources already in place instead of reinventing the wheel for each trial. He first three challenges reflect broad, systemic issues in clinical research:

1) prioritizing of clinical research questions,
2) The divide between clinical research and clinical practice,
3) The globalization of clinical trials.

1. **prioritizing of clinical research question** - clinical trials prioritization of the gaps in medical evidence and an allocation of clinical research resources to efficiently and effectively fill these evidence gaps. The federal government, industry, academic institutions, patient advocacy organizations, voluntary health organizations, and payers each have incentives to develop research questions that suit their unique interests. The value of a particular research effort is judged by stakeholders according to their own cost–benefit calculation. Reflecting the diversity of stakeholder value judgments, and in the absence of a broad national agenda, clinical trials are conducted in a "one-off," narrowly focused fashion Because clinical trials are necessary to obtain regulatory approval in the United States, they are a high priority to companies. It was noted by a number of workshop participants that the prioritization of clinical research questions by companies seeking regulatory approval is distinctly different from the priorities of society in general, which may prioritize the comparison of two commonly used therapies. This divergence between the priorities of society and industry is notable as the nation discusses how to address the current gaps in clinical research and medical decision making.

2. **The divide between Clinical research and clinical practice** - Wood cock stressed that, to generate relevant research based in clinical practice, community practitioners must be actively involved in the clinical trial process. She suggested it is not surprising that the uptake of evidence-based practices is slow when practitioners are not engaged in the research that supports the changes. In many instances, the characteristics of the study population, their comorbidities and therapeutic regimens, and the setting and conditions under which the trial is conducted bear little resemblance to typical community practice. Indeed, the outcomes are often quite different as well. It is little wonder that community physicians may be hesitant to modify their treatment practices to reflect clinical findings developed in this manner. According to Woodcock, the divergence between physicians conducting research and those in community practice is one of the greatest barriers to successfully translating study results into clinical practice. She argued that, to develop a truly learning health care system capable of self-evaluation and improvement, the currently separate systems of clinical research and practice must converge.

3. **Globalization of clinical trials** -The increasing trend toward conducting clinical trials outside the United States is an important consideration in discussing ways to improve the efficiency of trials. The number of patients enrolled in clinical trials is decreasing in the United States and increasing abroad. According to Woodcock, when development programs are conducted entirely outside the United States, the FDA questions the extent to which the results can be translated to U.S. clinical practice. The applicability of foreign trials results depends on the disease being studied and the state of current clinical practice in that area.

Why are clinical trials important?

Clinical trials are a key research tool for advancing medical knowledge and patient care. Clinical research is Clinical trials are a key research tool. done only if doctors do not know whether a new approach works well in people and is safe, and which treatments or strategies work best for certain illnesses or groups of people. Clinical trials are important for discovering new treatments for diseases, as well as new ways to detect, diagnose, and reduce the chance of developing the disease. Clinical trials can show researchers what does and doesn't work in humans that cannot be learned in the laboratory or in animals. Clinical trials also help doctors decide if the side effects of a new treatment are acceptable when weighed against the potential benefits. Researchers don't know what the results of clinical trials will be. (If they did, they wouldn't have to do the trials!) This uncertainty can make it hard for a patient to decide to participate in a clinical trial. While in rare cases, patient volunteers have been hurt by the treatment or procedure on a clinical trial, millions of people have been helped because other people before them chose to participate in a trial that resulted in a new, more effective treatment.

While clinical trials are important, the choice to participate in one is very personal and depends on your unique situation. You and your doctor need to weigh the benefits against the risks and decide what's best for you, when presented with a clinical trial. According to the American Cancer Society, about 1,000 potential medicines are tested before one makes it to clinical trials. On average, new cancer treatments have been studied for at least six years (and sometimes many more) before a clinical trial is started. Usually by the time a treatment makes it to the stage of a clinical trial, it has been found to be safe and to have some chance of being effective. In some cases, a treatment is safe and already FDA-approved and standard practice in one disease, and the clinical trial is testing it in another type of disease.

How clinical trials work

If you take part in a clinical trial, you may get tests or treatments in a hospital, clinic, or doctor's office .In some ways, taking part in a clinical trial is different from having regular care from your own doctor. For example, you may have more tests and medical exams than you would otherwise. The purpose of clinical trials is research, so the studies follow strict scientific standards. These standards protect patients and help produce reliable study results.

How to plan successful career in clinical research industry

A profession in clinical research is a wish for many individuals. Clinical research is a medical science function that consists of the screening of drugs, diagnostic equipment, and therapies and establishes their safety for human use. While there are several different paths an individual can take with this career, selecting the appropriate domain to suit ones abilities and aptitude is paramount. If an individual is seeking a career in clinical research, there is a lot that an individual has to get ready for it. In order to grab a job in clinical research industry, an individual must choose what career direction he/she wishes to take, get the suitable training, then get expertise in that specific domain.

The initial step in obtaining a job in clinical research is to choose what kind of job he/she wishes to pursue. Some examples of roles that an individual may perform in the field of clinical research are: clinical research associate (CRA), clinical research coordinator (CRC), clinical trial analyst (CTA), clinical trial manager (CTM), Medical Monitor, clinical trial pharmacist, Quality Associate, Clinical Logistics Professional, Pharmacovigilance professional, medical writer, and clinical data professional etc. An individual requires to take into consideration what his/her abilities, skills and passions are prior to deciding what type of career is right for him/her.

Skills required to become clinical research associate

- Good communication skills (written and oral) and the potential to develop efficient interactions with trial center employees and co-workers.
- Potential to inspire others.
- Numeracy and an eye for detail.
- Potential to multi-task and think on your feet.
- Great organisational, IT and management abilities – the job includes a lot of documentation and gathering of clinical trial information. Standard paper files are rapidly being substituted by electronic records, which need the use of different information systems

Skills required to become clinical research coordinator

- Understanding written phrases and paragraphs in work relevant documents.
- Giving full attention to what other individuals are saying, taking time to understand the things being made, requesting questions as acceptable, and not disturbing at inappropriate times.
- Communicating successfully in writing as suitable for the needs of the sponsors.
- Interacting with others to exchange ideas, opinions and facts successfully.
- Using logic and reasoning to recognize the benefits and drawbacks of alternative solutions.
- Assessing efficiency of your-self, other employees, or organizations to make changes or take corrective action.

Â Skills require to become a clinical research analyst

- Proven experience in protocol evaluation, IRB submission, and clinical trials budgeting.
- Solid working understanding of the full range of pre-award functions relevant to clinical trials.
- Good understanding of medical terms.

- Good understanding of research regulatory specifications (including FDA, HSA, CDSCO, EMA etc), GCP/ICH guidelines, and special specifications for drug and medical device studies.
- Proven excellence in negotiating abilities, such as the skills to solve issue among various groups and individuals with different backgrounds and objectives concerning sensitive and essential issues'€€ Proven skills to take part effectively in the planning and progression of multi-disciplinary, cross-departmental study programs.

Skills require to become pharmacovigilance professional

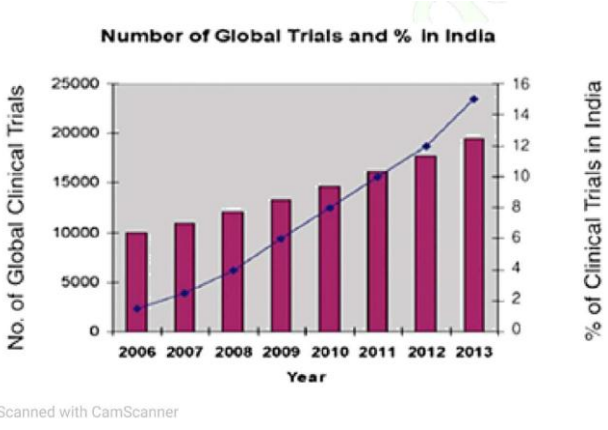
- Fundamental competence with medical and therapeutic terms.
- Capability to work individually but guided by recorded procedures, with proper support.
- Capable to work successfully as part of a team.
- Comprehension of patient safety regulatory requirements.
- Must be familiar pharmacovigilance and regulatory guidelines.
- Must be comfortable with pharmacovigilance terms.
- Great attention to detail.

Skills require to become a medical writer

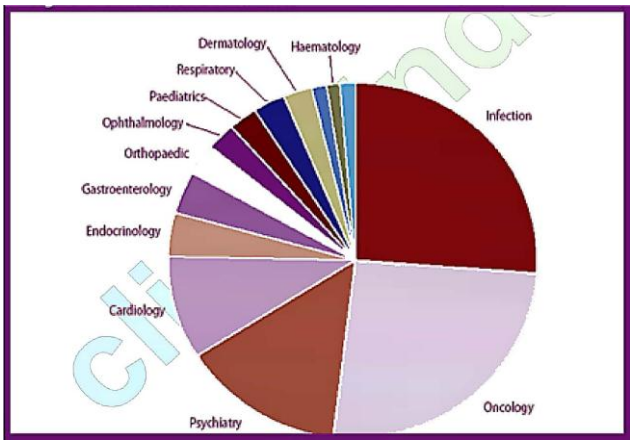
- Good standard of written English, and capability to communicate fluently and efficiently in English, both in writing and orally.
- Familiarity with the structural and material specifications of clinical protocols, study reports and related documents.
- Capability to incorporate, understand, and summarize information from a wide range of sources in a clear and concise way.
- Proficiency in finishing a good initial draft clinical study report in a routine therapeutic area inside an acceptable time-frame with limited assistance.
- Good comprehension of common statistical techniques used in clinical studies and interpretation of their outcomes.
- Capability to give a basic presentation to a project staff and/or client.

Skills require to become a clinical data analysis

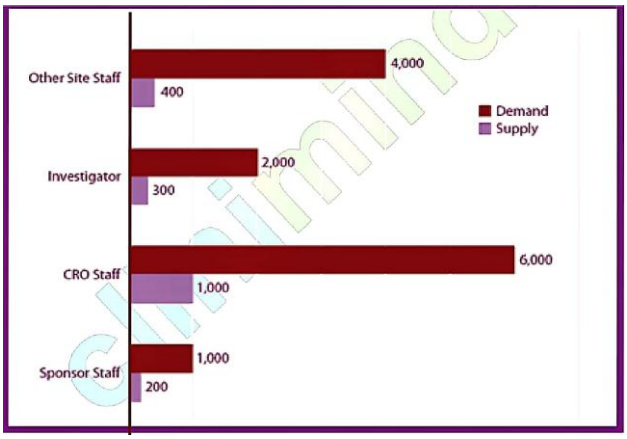
- Good understanding of electronic data capture and trial management.
- Strong interpersonal abilities, proven ability of working on several projects at a time.
- Solid written and oral communication skills.
- Proven project management abilities.
- Good understanding of clinical research stages, clinical data management systems and database development.
- Able to carry out well in a cross-functional team like as with clinical research associates, medical writing department, Pharmacovigilance and regulatory staff, project heads etc.
- Excellent time management abilities and potential to solve problems proactively is an advantage.



Percent of global trials in India-



Clinical trials done in India-



Demand Supply Gap in India-

CR Career pathway-

- Pharmaceutical Companies
- Clinical CROs (Contract Research Organizations)
- BA/BE Centers
- SMOs (Site Management Organizations)
- Data Management CROs
- IT Companies in Healthcare / Clinical Domain
- EDC Service Providers
- Central Laboratories

- Packaging & Labeling & Contract Manufacturers
- Investigator & Site Staff
- Training Centers.

Career in CROs / pharma / biotech companies

- Clinical Trial Assistant (CTA)
- Clinical Research Associate (CRA)
- Senior CRA
- Clinical Team Leader
- Project Manager
- Senior Project Manager
- Manager Medical & Regulatory
- Manager –Safety / Patents
- Manager Quality Assurance
- Medical Director
- Associate Director –Clinical
- Associate Director –Projects
- Director –Business Development
- Director / Head (Clinical Operations)
- General Manger / CEO / President

Phase I / II / III / IV trial

Project Management
Drug Development Planning
Monitoring
Source Data Verification
Safety Reporting
Regulatory Approval
QA Audits
Business Development

Career in SMO

- Clinical Research Coordinators (CRC) / Study Coordinators
- Principal Investigators / Co-Investigators
- Medical Monitors
- Project Manager / Senior Project Manager
- Manager Medical & Regulatory
- Manager Quality Assurance
- Manager –Business Development
- Medical Director
- Associate Director –Clinical
- Associate Director –Projects
- Director / Head (Clinical Operations)
- General Manager / CEO / President

Career opportunities in DM

- Data Entry Operator
- Data Validation Executive
- QA Executive
- Data Manager
- QA Manager
- Statistical Programmer
- Statistician
- Data Reviewer
- Data Base Designer
- Medical Writer
- Head –Data Management

Key Organizations into this area

- **Companies into clinical research Sponsor companies:** Johnson & Johnson,

Biocon, GlaxoSmithKline Beecham, Allergan, Astra Zeneca, Ranbaxy
Laboratories, Nicholas Piramal, Dr.Reddys Laboratories, Novo Nordisk,
Pfizer etc.

- **CROs:** Quintiles, Manipal Acunova, ICON International, Clintec, Clinigene

International, Accenture, Paraxel, Asian Clinical trials, Paragon, medpace, PPD ,Syneos Health.

- **Hospitals:** St. Johns Hospital, M S Ramiah Memorial Hospital, Kidwai

Memorial Hospital, Bangalore Institute of Oncology, Bangalore Diabetes Hospital, Wockhardt Hospital, Apollo Hospitals, sanchiti..

Key cities in india for clinical research

- Delhi & NCR Region
- Mumbai
- Pune
- Ahmedabad
- Vadodara
- Hyderabad
- Bangalore
- Chennai

There are some new cities like Chandigarh; Bhopal, Indore,
Coimbatore; Vizag are emerging as new centres for clinical trials

India is a hub of clinical research service

1. Diseases Diversity
2. Wide range CRO
3. Lot of manpower
4. Bulk drug formulation
5. Lower Cost
6. Many Hospital
7. IT structure

How clinical trials work

If you take part in a clinical trial, you may get tests or treatments in a hospital, clinic, or doctor's office .In some ways, taking part in a clinical trial is different from having regular care from your own doctor. For example, you may have more tests and medical exams than you would otherwise. The purpose of clinical trials is research, so the studies follow strict scientific standards. These standards protect patients and help produce reliable study results.

Comparison groups

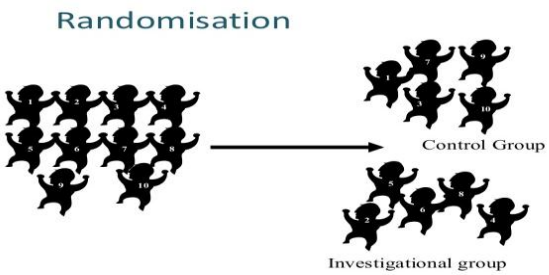
In most clinical trials, researchers use comparison groups. This means the patients taking part in a trial are assigned to one of two or more similar groups. Each group will receive different medical strategies. For example, one

group may get the current standard treatment for a condition, while another group gets a new treatment. Researchers can then compare the results to see whether one group has better outcomes than the other.

comparison groups also ensures that no one in a study is left without treatment for the sake of research. Sometimes, when no accepted standard treatment exists for a condition, people in one group may receive a placebo (inactive pill that looks like the test product). You'll be told if a placebo will be used in a study before you agree to take part.

Randomization

Some clinical trials that have comparison groups use randomization. This involves assigning patients to different comparison groups by chance, rather than choice. This method helps ensure that any differences observed during a trial are due to the different strategies being used, not to preexisting differences between the patients. Usually a computer program makes the group assignments.



Clinical trial protocol

Each clinical trial has a master plan called a protocol, which explains how the trial will work. The trial is led by a principal investigator (PI), who usually is a doctor. The PI prepares the protocol for the clinical trial. The protocol outlines what will be done during the clinical trial and why. Each medical center that does the study uses the same protocol, which is reviewed AND approved by various committees. The committees are in place to ensure patient protections and some potential of learning new information or benefitting patients with the disease. Clinical trials can show researchers what does and doesn't work in humans that cannot be learned in the laboratory or in animals .Key information in a protocol includes how many patients will take part in the clinical trial; who is eligible to take part in the clinical trial; what tests patients will get and how often they will get them; what type of data will be collected during the clinical trial; and detailed information about the treatment plan.

The researchers doing clinical trials take steps to avoid bias. "Bias" means that human choices or other factors not related to the protocol affect the trial's results.

Possible benefits and risks of clinical trials

Taking part in a clinical trial can have many benefits. For example, you may gain access to new treatments before they're widely available. If a new treatment is proven to work and you're in the group getting it, you might be among the first to benefit. If you're in a clinical trial and don't get the new strategy being tested, you may receive the current standard care for your condition. This treatment might be as good as, or better than, the new approach. You also will have the support of a team of health care providers, who will likely monitor your health closely.In late-phase clinical trials, possible benefits or risks of a treatment can be identified earlier than they would be in general medical practice. This is because late-phase trials have large groups of similar patients taking the same treatment the same way. These patients are closely watched by Data and Safety Monitoring Boards.

Even if you don't directly benefit from the results of the clinical trial you take part in, the information gathered can help others and add to scientific knowledge. People who take part in clinical trials are vital to the process of improving medical care. Many people volunteer because they want to help others.

- **List of clinical research courses with eligibility, scope, salary details**

Various courses are available nowadays for Clinical Research studies. You can get yourself enrolled in Diploma courses, Masters courses or even in Certification courses in Clinical research.

Diploma in clinical research: This course is usually annual having term examinations conducted every year by concerned universities. Enrolled candidates learn basic bioethics related to clinic or hospital. The course includes presentations, manuscripts preparations of various scientific meetings and journals of technical medicine. Students enrolled in this course will be modulated and trained to transform them into quality clinical research analysts having all the set of skills required to work in any hospital or clinic.

Candidates having Diploma in this field can have a wide array of career options. Be it a Medical department (hospital/ clinic) or working as a lecturer/teacher, candidates can choose any options according to their wishes.

Duration: 1-year full-time course.

Eligibility: 55 % score in graduation in any Medical science courses (MBBS, BDS, etc.) or Degree in Science, Life Sciences, Pharmacy, Pharmacology, Biotechnology, etc. from a recognized university.

Scope/ job positions: You can choose any job profile as you wish from plenty of career options available. You can be absorbed as a Clinical research Analyst, Clinical Research Associates, Clinical Research Coordinator, Clinical Research Physicians, Biostatistician, etc.

Salary: INR 2,50,000 – INR 5,00,000

Master of science (M.Sc. clinical research):
As of now, you all are aware of Clinical research and its benefits. It is known that this field utilizes a diverse array of experiments as well as research in clinics, especially with organisms. This master course includes various components like Drug studies & its medical management, Performing organic activities in the clinic, Study of various sub-related disciplines like Biostatistics, Epidemiology, Transplantation, etc. You can always choose your specialization after getting enrolled.

Duration: 2 years course

Eligibility: You should be a graduate in any discipline of Science with at least 50 % marks in aggregate. Fields / Disciplines included here are Life Sciences (Zoology, Microbiology, Botany, Toxicology, Biochemistry, Pharmacology or Biotechnology); B. Pharma, M. Pharma, Nursing, Physiotherapy. Candidates waiting for their final year/semester results are also eligible on a provisional basis.

Top Institutes: Galgotias University, Sharda University, Periyar Maniammai University, Amity University, Indian Institute of Public Health, School of Bio-Science, Apeejay Stya University, Indian Institute of Clinical Research India.

Scope/ Job positions: You can choose any career options from a wide range available after having this course of Clinical research according to your interest. To quote some – you can be a Project Manager – Clinical Research, Clinical Research Coordinator, Clinical Research Physician, Biostatistician, Clinical Research Analyst; Programmer – Clinical Research, Clinical Research Associate and such. You can also work as Medical Assistants – professionals in clinics, hospitals and Health Services Managers.

Average Salary: INR 3 – 12 Lacs per annum

Top Recruiting Areas: Pharmaceutical industry, educational institutes, CROs, SMOs, hospitals, DCGI office, and other govt. drug and food regulatory/ research organizations, etc.

Certification in Clinical Research:
This is a certification course of a very short duration which involves Hospital and Healthcare Management Programme. The aim of this course is to examine the safeguarding of general views on the moral values connected to bioethics and some highly complex issues of executing this basic knowledge to a different sets of situations.

Duration: Short course of 6 months

Eligibility: Graduates of Medical background (MDS, MBBS, BAMS, MS, MD, BUMS), UG & PG candidates of various allied streams of Science like – Pharmacology, Life Sciences, Medical laboratory, Pharmacy, Nursing, Biochemistry, Biotechnology, etc. All the professionals working with various Clinical Research organizations / Pharmaceutical companies are also eligible for this course.

Scope/ Job positions: Candidates after completing this certification course can assist in the presentations and manuscripts preparations of various scientific lectures/meetings including technical sessions of conferences or training programs. Candidates can also choose a teaching career (gov./private). Employment areas include Clinical research labs, Medical Universities / Colleges, Private clinics, Government hospitals, and Pharmacist shops.

Average Salary: INR 1,50,000 – INR 3,00,000

List of top companies hiring in the field of clinical research are:

- ACTREC
- TMC
- CDSA – THSTI
- ICMR
- Teva Pharmaceutical
- Pfizer
- Fortis Hospitals
- Panacea Biotec
- PPD
- St. John's Research Institute
- Medpace
- TCS
- PGIMER
- Cognizant
- Chiltern
- inVentiv Health
- Novartis
- ICON
- Novo Nordisk

All the above-mentioned courses will lend you to so many career options, you can choose according to your interests. Clinical Research is one of the fastest-growing industries at a surprising rate opening a wide array of career options for skilled and trained professionals. As of now, you can understand how important Clinical Trials are and its study as well as examination to market any drug or device. This research field provides vivid scientific analysis related to its impact, benefits, and risks associated with drugs. .

Scientific oversight

- **Institutional Review Board**

Institutional review boards (IRBs) help provide scientific oversight for clinical trials. An IRB is an independent committee created by the institution that sponsors a

clinical trial. IRB members are doctors, statisticians, and community members.

The IRB's purpose is to ensure that clinical trials are ethical and that the participants' rights are protected. The IRB reviews the trial's protocol before the study begins.

An IRB will only approve research that deals with medically important questions in a scientific and responsible way. The IRB also checks on results during the trial. All U.S. clinical trials are required to have an IRB.

- **Office for human research protections**

The U.S. Department of Health and Human Services' (HHS') Office for Human Research Protections (OHRP) oversees all research done or supported by HHS. The OHRP helps protect the rights, welfare, and well-being of research participants. It provides guidance and oversight to the IRBs, develops educational programs and materials, and offers advice on research-related issues.

- **Data safety monitoring board**

Every National Institutes of Health (NIH) phase III clinical trial is required to have a Data and Safety Monitoring Board (DSMB). This board consists of a group of research and study topic experts. The NIH also requires DSMBs for large trials comparing alternative strategies for diagnosis or treatment. In addition, the NIH requires DSMBs for some earlier phase trials that involve high-risk procedures (such as gene therapy) or vulnerable patients (such as children).

A DSMB's role is to review data from a clinical trial for safety problems or differences in results among different groups. The DSMB also reviews research results from other relevant studies. These results may reveal unknown patient risks, or they may even answer the NIH study's research question. Scientific oversight informs decisions about a trial while it's under way. For example, some trials are stopped early if benefits from a strategy or treatment are obvious. That way, wider access to the new strategy can occur sooner. Sponsors also may stop a trial, or part of a trial, early if the strategy or treatment is having harmful effects.

- **Food and drug administration**

In the United States, the Food and Drug Administration (FDA) provides oversight for clinical trials that are testing new medicines or medical devices. The FDA reviews applications for new medicines and devices before any testing on humans is done, and checks to make sure that the proposed studies have proper informed consent (see below) and protection for human subjects.

The FDA also provides oversight and guidance at various stages throughout the studies. For example, before large-scale phase III trials begin, the FDA provides input on how these studies should be done.

- **Patient rights: informed consent**

Informed consent includes details about the treatments and tests you may receive, and the benefits and risks they may have.Informed consent is the process of giving clinical trial participants all of the facts about a trial. This happens before they agree to take part and during the course of the trial. Informed consent includes details about the treatments and tests you may receive and the benefits and risks they may have.Before you decide whether to enroll in a clinical trial, a doctor or nurse will give you an informed consent form that presents the key facts of the study.

Treatments in the COVID-19 pandemic: an update on clinical trials

The coronavirus disease-19 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread rapidly and widely around the world, with more than 4,900,000 confirmed cases and more than 320,000 deaths reported as of 20 May 2020. The most common clinical symptoms are fever, cough, fatigue, and dyspnea, and a few patients have some other symptoms such as headache, hemoptysis, and diarrhea .Previous experience in the treatment of coronavirus, such as SARS-COV and MERS-COV, has provided clinicians with a reference point for dealing with the novel coronavirus. Although there is still no specific drug, the increasing number of COVID-19 related reports around the world provide relevant insights for clinical treatment. This paper will summarize and discuss the current therapeutic drugs treating COVID-19 based on these reports of clinical trials.

The antiviral agents of COVID-19

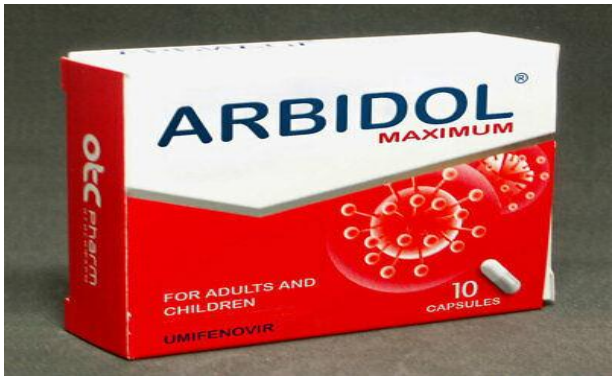
COVID-19 belongs to the same genus of CoV as SARS-COV and MERS-COV, both of which are beta-cov. Whole genome sequencing showed that COVID-19 shared 79.5% of sequence identity with SARS-CoV In combination with the treatment experience of SARS-COV and MERS-COV, several potential drugs have been proposed for treatment of SARS-CoV-2, including arbidol, chloroquine, and human immunodeficiency virus-1 (HIV-1) protease inhibitors (lopinavir/ritonavir), new nucleoside analogues (remdesivir, GS-5734) and convalescent plasma. As for clinical broad-spectrum antiviral drugs, neuraminidase inhibitors (oseltamivir, peramivir, zanamivir, etc.) are not recommended for clinical use, since the coronavirus does not produce neuraminidase. In addition, nucleoside analogues are not recommended neither due to their little efficacy in vitro experiments or existing clinical studies. However, nucleoside analogues can be used in combination with interferon for antiviral treatment .

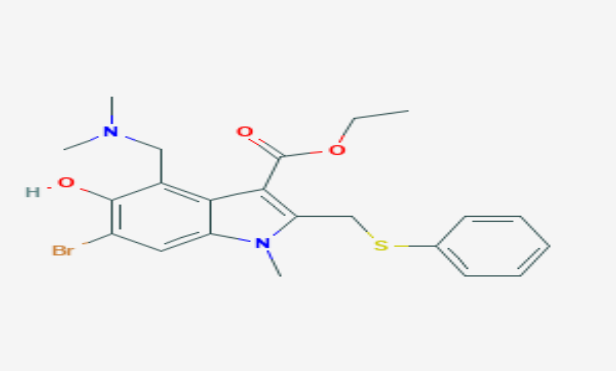
1. Arbidol

Arbidol (umifenovir) is a broad-spectrum antiviral compound approved in several countries for prophylaxis and treatment of influenza. It has been shown to inhibit SARS-CoV-2 in vitro In vivo, several retrospective

studies have discussed the antiviral effects and safety of arbidol in patients with COVID-19.

Clinical trials -A study comprising 69 patientsfound that arbidol could improve the rate of discharge and without deaths occurred. Another study showed that the participant group that was given arbidol had a shorter duration of positive RNA test compared to those in the lopinavir/ritonavir group, and no side effects were observed In addition, when compared tolopinavir/ritonavir only, combination group of arbidol and lopinavir/ritonavir was treatment significantly elevated negative conversion rate of coronavirus' test in 7-day and 14-day, and improved the chest CT scans in 7-day . However, a retrospective study found that for non-ICU COVID-19 patients, arbidol might not accelerate SARS-CoV-2 clearance nor improve prognosis, compared to the control group . These reports are all retrospective studies with a small sample size, and the conclusions are controversial. The efficacy and safety of arbidol needs to be further verified through randomized controlled clinical trials. Additionally, the current clinical dosage of arbidol (200 mg, 3 times/day) may not be the ideal dosage to inhibit SARS-CoV-2 infection whether a higher dosage of arbidol is required for COVID-19 patients needs to be studie.

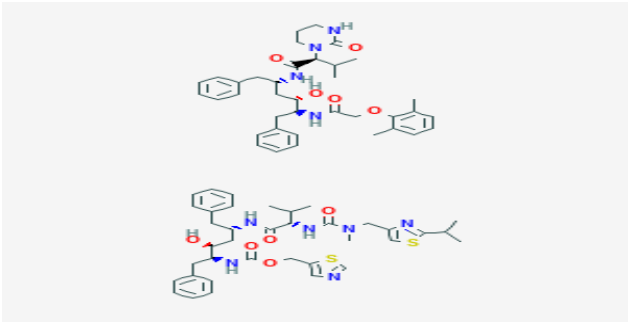




2. Lopinavir/ritonavir

Lopinavir/ritonavir (LPV/r) has been shown to inhibit virus replication in-vitro, in animal experiments, and to improve clinical outcomes in patients with SARS-COV or MERS-COV, making it a potential therapeutic option for SARS-CoV-2 . Efficacy of lopinavir/ritonavir in the clinical treatment of COVID-19 has been discussed in many cases . A newly reported retrospective single-center study of 94 patients found that the treatment regimen of interferon alfa (INF-α) + lopinavir/ritonavir and INF-α+ lopinavir/ritonavir + ribavirin may be beneficial for the treatment of COVID-19. In patients receiving this treatment, the clearance time of COVID-19 mRNA was positively correlated with the length of stay at the hospital. The clearance rate of COVID-19 mRNA was found to be significantly correlated with the decrease of serum creatine kinase (CK) and lactate dehydrogenase (LDH) levels. A decrease in serum LDH or CK may indicate a good response to COVID-19 therapy [28]. Another study comprising 10 patients also confirmed the positive effect of lopinavir on COVID-19, suggesting that eosinophil count was a predictor of disease progression. Changes in these biochemical factors provide new indicators for clinical observation during treatment.

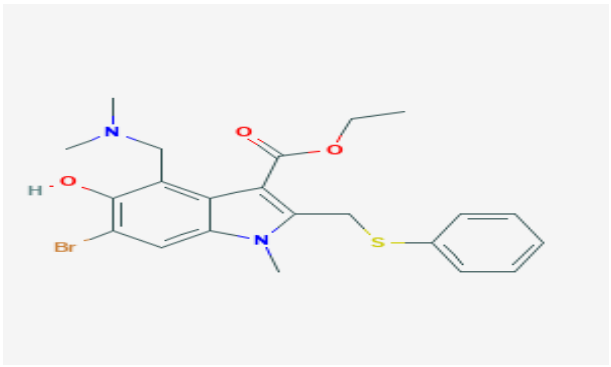
Clinical trials-, a study reported that the combination treatment of LPV-r and routine adjuvant medicine against pneumonia could produce much better efficacy on patients with COVID-19 infection compared to treatment with adjuvant medicine alone. The limitation of the above mentioned three reports is that the number of cases is limited and more clinical data is needed for verification. However, several studies did not find any clinical benefits of lopinavir/ritonavir, suggesting that lopinavir/ritonavir had no significant effect on mortality and virus clearance in patients [4,27,31–34]. A randomized, controlled, open-label trial involving 199 patients reported that treatment with lopinavir/ritonavir did not affect time to clinical improvement as compared to the standard-care group (hazard ratio for clinical improvement, 1.31; 95% confidence interval [CI], 0.95 to 1.80). Mortality at 28 days and the percentage of patients with detectable viral RNA at various time points were similar in the lopinavir/ritonavir group and the standard-care group. Adverse gastrointestinal effects were more common in the lopinavir/ritonavir group, but the standard-care group experienced more serious gastrointestinal problems . An observational cohort study from China found that arbidol and LPV/r did not promote the transformation of swab virus nucleic acid into negative nor did it improve symptoms in COVID-19 patients. Further, there was no significant increase in the incidence of adverse reactions after the combination of LPV-r or arbidol, such as gastrointestinal symptoms, which deter improvement of the disease. The efficacy of lopinavir/ritonavir in the treatment of COVID-19 remains to be verified by further studies. Meanwhile, note that if there are adverse effects to lopinavir/ritonavir, such as diarrhea, nausea, stomatitis, fever, anemia, leukopenia, and hyperbilirubinemia, the use of the drug should be suspended or discontinued, as may be appropriate. 2



3. Tocilizumab

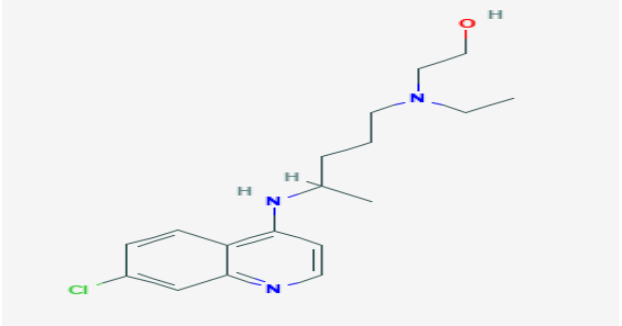
Tocilizumab is commonly used adjuvant therapies for COVID-19. The use of tocilizumab is based on the observation of excess pro-inflammatory cytokine production mediated cytokine storms in critically ill patients infected with COVID-19. Anti-interleukin-6 (IL-6) may play a key role in cytokine storms. In a retrospective multi-center study of 150 patients in Wuhan city, IL-6 levels in patients were found to be a clinical predictor of COVID-19 mortality. IL-6 is a potential therapeutic target for COVID-19 patients to prevent or relieve cytokine storms. As the first IL-6 blocking antibody to be marketed by targeting IL-6 receptors, tocilizumab appears to be an effective therapeutic option.

Clinical trials -Tocilizumab has been approved in China to treat patients with severe complications from COVID-19 that show elevated IL-6 plasmalevels, but no reliable evidence has been published regarding the safety or efficacy of tocilizumab in the treatment of COVID-19 patients. Retrospective studies have found that most patients with severe COVID-19 have improved clinical symptoms and good prognosis after treatment with tocilizumab. Compared with standard treatment alone, administering tocilizumab can reduce the rate of hospitalization and/or mortality in the intensive care unit ofCOVID-19 patients. However, the sample size of these studies is small, and there may be bias. A recent prospective study in a single center with 100 patients from Italy found that patients with severe COVID-19 pneumonia with hyper inflammatory syndrome and acute respiratory failure responded to tocilizumab rapidly and continually, and with significant clinical improvements. However, it is important to note that tocilizumab may cause serious adverse reactions, such as intestinal perforation, candida infection, and lipid metabolism disorder.



4. Hydroxychloroquine

Hydroxychloroquine and chloroquine are the most talked-about drugs being tested against COVID19, The drugs are essentially the same, but hydroxychloroquine is a safer, more commonly used version of chloroquine. Many drugmakers make their own versions of hydroxychloroquine, which was originally approved to treat malaria but is now commonly used to treat autoimmune diseases, including lupus and rheumatoid arthritis.

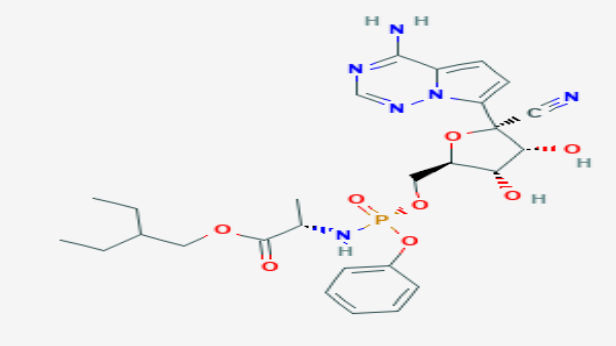


Clinical trials: There are 148 clinical trials involving hydroxychloroquine being conducted in the U.S. and abroad, according to Clinicaltrials.gov. The National Institutes of Health is assisting in a phase 3 trial for 510 adults hospitalized with COVID-19. The University of Minnesota is also in a phase 3 trial involving 3,000 participants. Hospitals in New Jersey, Utah, and Pennsylvania are also conducting hydroxychloroquine trials, Politico reported.

When to expect results: A spokesperson told Politico results from the NIH trial will come in "a couple of months." Results from the other trials depend on how quickly researchers can enroll participants.

5. Remdesivir

remdesivir is an intravenous drug that works by targeting the system coronaviruses use to replicate themselves. It hasn't been approved in the U.S., but it was tested to treat Ebola, so researchers already have some information about how humans respond to it. Researchers are hoping it can reduce the intensity and duration of COVID-19.

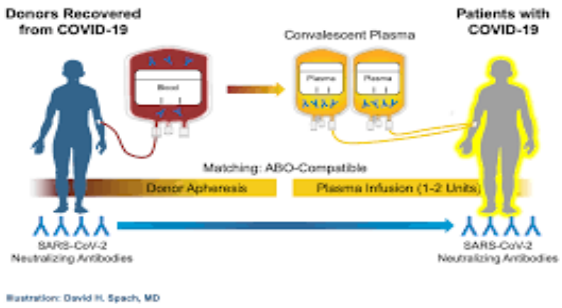


Clinical trials: Gilead is running two trials in the U.S., Asia and Europe, according to Politico. One is testing 6,000 severely ill COVID-19 patients, while the other is testing 600 moderately ill patients. The National Institute of Allergy and Infectious Diseases has also started the first randomized, controlled trial of the drug with 1,060 patients worldwide.

When to expect results: Gilead released the first results from its phase 3 clinical trial April 29, saying remdesivir proved effective against COVID-19. Data from Gilead's second clinical trial testing moderately ill patients is expected in late May. Data from the NIAID trial is also expected in late May, according to Politico.

6. Convalescent plasma

Convalescent plasma is antibody-rich blood products taken from blood donated by people who have recovered from COVID-19. The theory behind the treatment is that the antibodies from recovered COVID-19 patients can help sick COVID-19 patients recover.

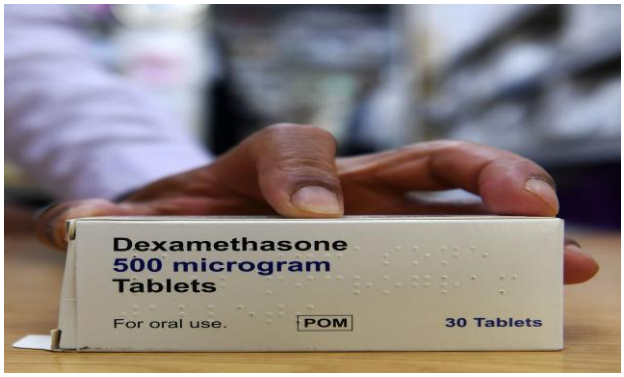


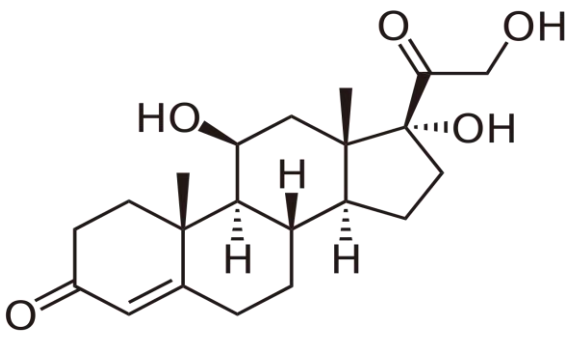
Clinical trials: Hackensack (N.J.) University Medical Center is conducting a phase 2 study with 55 participants to test convalescent plasma as a treatment for COVID-19, Politico reported. Several hospitals in the Netherlands and Spain are also conducting clinical trials. The FDA is also coordinating a study that will be conducted by NIAID.

When to expect results: There aren't any specific timelines on when clinical trial results will be released.

7. Steroids

Hospitals in China used corticosteroids to reduce inflammation in COVID-19 patients, but it's not clear if the strategy has been effective, according to the CDC. The CDC has warned against using steroids to treat COVID-19 because patients with MERS or the flu who were given steroids were more likely to die than those who didn't receive the drugs, according to Politico.





Clinical trials: A clinical trial in the U.K. began in March to test a low dose of the steroid dexamethasone, Politico reported. Scientists in South Korea are also recruiting people to test whether the steroid ciclesonide can help COVID-19 patients with mild symptoms.

When to expect results: There aren't any specific timelines on when clinical trial results will be released.

CONCLUSION

- Clinical trials is a human experiment design to study the efficacy and safety of a new drug / intervention.
- Involves phase 1-4 with specific objectives and end results.
- Applications to regulatory authority:
- IND – permission to conduct CT
- NDA- permission to market new drug
- Well designed and effectively executed clinical trials from the base of therapeutic decisions.
- CT must follow guidelines and protocol to ensure well being of participants.
- Clinical trials may occur in several different phases.Drug and developed in several different phases to meet the multiple objective in the safest most efficient manners.
- A career in clinical research is definitely challenging and satisfying**.**

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