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''A review on Clinical Research and Clinical Trails''

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Abstract:

It is a prospective ethically designed investigation in human subjects to objectively discovered /verify/compare the result of two or more therapeutic measures (Drugs).clinical trials are designed to answer one or more precisely framed questions about the value of treating equivalent group of patient by two or more modalities (drug , dosages, regiment and other investigation).depending on other objectives of studies , clinical trial may be conducted in healthy volunteers or in volunteer patient.Healthy volunteers may be used to determine pharmacokinetics characteristics,tolerability,safety for the certain type of drug even efficacy. The research carried out to find a better treatment, improve healthcare, and benefit the current medical practice is termed clinical research. In phase I pharmacokinetics, safety, gross effects are studied on human volunteers, by clinical pharmacologists. If the drug passes the test, it enters phase II testings, where pharmacokinetics, safety, therapeutic efficiency are studied on selected patients by clinical pharmacologist, if passes hundreds of selected patients are now studied, primarily for safety and therapeutic effectiveness by clinical investigators in phase III. If this is passed the drug is now approved and marketed. Even after marketing, physicians from various hospitals and clinics send their opinion about the drug, regarding ADR, efficacy in phase IV.In this paper we discuss about clinical trials and clinical trials in India.

Keywords:

Clinical Research, Clinical Trial, Human Health, Safety and Efficacy, Volunteers study, ICH Guideline, Preclinical Study, In-Vitro study, Adverse effect, Randomization.

INTRODUCTION:

The preceding paper in this series (Herbert 2000) considered how reports of clinical trials can be used to obtain unbiased estimates of the size of a treatment's effects. That paper discussed how readers of clinical trials can extract simple estimates of treatment effect size when trial outcomes are measured on a continuous scale. The approach incorporates clinical intuition and patient preferences into clinical decision-making. It was suggested that, when making decisions about therapy for individual patients,

optimal decision-making involves modifying effect size estimates on the basis of patient characteristics and comparing such estimates with the "smallest clinically worthwhile effect". In this paper, the same process is applied to clinical trials in which outcomes are measured on a dichotomous scale.

Dichotomous outcomes:

The examples in the preceding paper were of clinical trials in which outcomes were measured as continuous variables. Continuous variables are those that can take on any of an infinite number of values between their upper and lower extremes. Oedema, self-reported pain on a VAS scale and lung function tests are all examples of continuous variables. Other outcomes are measured as "dichotomous" variables.

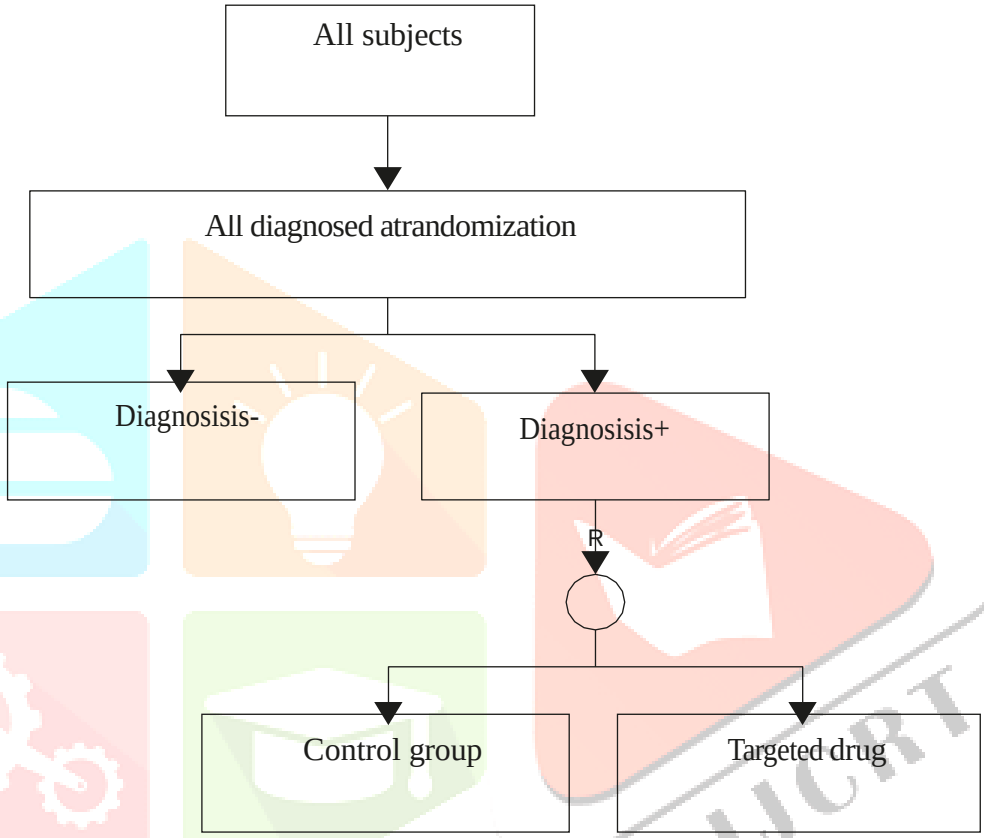

Fig 1. Diagram for enrichment design. R=randomization[2]

Dichotomous outcomes are discrete events - things that either happen or do not - such as death, injury, or "satisfied with treatment". We quantify. these outcomes of therapy in terms of the proportion of subjects who experienced the event of interest, usually within some specified period of time. This tells us about the risk of the event for individuals from that population. A good example is provided by a recent trial of the effects of prophylactic chest physiotherapy on respiratory complications following major abdominal surgery (Olsen et al 1997). In this study, the event of interest was the development of a respiratory complication. Fifty-two of 192 subjects in the control group experienced respiratory complications within six days of surgery, so the risk of respiratory complications for these subjects was 0.27 (or 27%). [1] For targeted clinical trials, in addition to the usual inclusion criteria based on clinical signs, symptoms, and clinical laboratory results, the presence of the molecular targets is one of the most important inclusion criteria. The enrichment design 9 is one of the designs suggested in the FDA draft concept paper for targeted clinical trials. Figure 1 provides a diagram for enrichment design. Under the enrichment design, patients are screened using the diagnostic device for identification of the molecular targets and only those with a positive diagnosis for the molecular target are randomized to receive either the targeted treatment or the untargeted concurrent control.

Types of clinical trial:

Clinical trials can be classified in to various ways One way is to classify clinical trials on basis of mode of study

1) Interventional Study:

In this study researchers measure how the subjects' health changes. They give the research subjects a particular medicine and then compare the treated subjects with those receiving no treatment or the standard treatment. This is a type of a comparative study.

2) Clinical observational study:

In this study the researchers observe the subjects given with new medicine and measure their outcomes. Another way is to classify trials is by their purpose • Prevention trials to prevent disease in people who have never had the disease or to prevent a disease from returning. These approaches may include medicines, vitamins, vaccines, minerals, or lifestyle changes.

• Screening trials test the best way to detect certain diseases or health conditions.

• Diagnostic trials are conducted to find better tests or procedures for diagnosing a particular disease or condition.

• Treatment trials test experimental treatments, new combinations of drugs, or new approaches to surgery or radiation therapy.

• Quality of life trials (supportive care trials) explore ways to improve comfort and the quality of life for individuals with a chronic illness.

• Compassionate use trials or expanded access trials provide partially tested, unapproved therapeutics to a small number of patients who have no other realistic options. This involves a disease for which no effective therapy has been approved, or a patient who has already failed all standard treatments and whose health is too compromised to qualify for participation in randomized clinical trials. [3]

Consider a randomized phase III clinical trial in which patients are randomized to one of two treatment arms. The main goal of performing such a study is usually the estimation of some overall measure of treatment effect based on all eligible patients enrolled in the study. Given the resources and effort required to conduct a clinical trial, it is current practice in most reported clinical trial analyses to also estimate treatment effects and test hypotheses within different subsets of patients. The use of such subset analyses, however, is controversial. The statistical concerns include the issue of inflation of alpha levels due to repeated testing, i.e. the possibility that significant results will emerge by chance alone when one examines multiple subgroups of patients. The other major concern is the real possibility of lack of power to detect treatment effects within smaller subgroups of patients. This is likely to produce false negative results, and it is particularly relevant since most clinical trials are designed to have enough power for a primary test of treatment effect only for the whole study population. Results from subset analyses therefore should always be treated and presented with caution. [4]

Advantages and Limitations of Clinical Trials for Safety Evaluation:

Clinical trials are often considered the pinnacle of evidence based medical research, and the data from safety outcomes are of high quality, ensured by prospective and uniform data collection, fastidious review and follow-up, and diligent querying and cleaning. Further, centralized labs and event adjudication are often adopted in clinical trials, which further improve the consistency of data collection and quality. Standardized medical dictionaries, such as MedDRA and WHO-DD, allow for the consistency of reporting of numerous safety outcomes.2,14,29 Safety data collected in clinical trials are also rich and multifaceted. For example, it is possible to write detailed narratives of severe AEs that summarize the details surrounding these events to enable understanding of the circumstances that may have led to the occurrence and its subsequent management and outcome. Often these narratives include details on medical history, concomitant medications taken at the time of the event or prescribed as a result of the event, measurements of important chemical analytes or other laboratory parameters, details on

hospitalizations, and whether or not the patient ultimately recovered. Direct interactions with investigators allow for the collection of data necessary to accurately describe a patient's safety profile. On the other hand, data quality, lack of important detail, and consistency of collection are several hurdles to overcome in the analysis of pharmacovigilance (PV) databases.[5]

Statistical Applications and Risks Associated with Clinical Research:

The most important stage of clinical research is the step at which we reflect the results on the general population. Several statistical applications are used to assess the disease prevalence "and the incidence of a disease. They include likelihood ratio, odds ratio, hazard ratio, and median ratio. The risks associated with clinical research are not uncommon. Therefore, parameters like absolute, attributable, and relative risk are frequently applied to assess the risk in clinical research. In medicine, we require evidence i.e., the benefits of a drug, proof that the exposure causes the outcome, and the benefit to harm ratio. Since most clinical research trials/studies involve many subjects, it is important to find the efficacy of a research study using statistics. To be able to imply the clinical research results on a large population, just by performing the trials on a small representative group requires statistical analysis of the data obtained from clinical research/trial. To understand the results of clinical research and to be able to interpret their efficacy and usefulness in the patient care perspective, applying appropriate statistics is inevitable as evidenced from a previous research result. Although statistical inferences help in assessing the applicability of clinical research in real-world situations, they can also be used to misinterpret/ falsely project the usefulness of clinical research data for financial benefits. [6]

General Ethical Issues and Review Procedures in Clinical Research:

It is essential to understand the general ethical issues and the review process involved before conducting the clinical research. Since clinical research requires the participation of humans in the form of study subjects, individuals are recruited based on certain criteria and principles designated by the regulatory bodies in the form of informed consent. Among the basic principles which should be considered before enrolling the study participants, the respect for autonomy (participant must be allowed to decide by himself both participate and to stop participating if he/she wishes), beneficence (participant must get the benefit and should never be harmed), nonmaleficence (participants must be made completely aware of the study process), and justice (participants must be given the best deal irrespective of the study results). The study participants should be made aware of all the information regarding the duration, procedures followed, investigations to be conducted, potential risks including the foreseeable and those which may be unknown, benefits of the study both to the participants and to the society/community, compensation details, risk management procedures including the treatments available, confidentiality issues, loses (no loss of benefits if the participant withdraws) and benefits concerning commercialization.[7]

The process validation in clinical trials:

The major purpose of a clinical trial/drug developmentprocess is to generate quality and accurate data. The datamanagement of the clinical study should be in tune withthe study protocol and is required to satisfy the regulatoryagenciesthatincludethegoodclinicalpractice(GCP)guidelines, and the ICH. The data generated forms thebasis for the submission of a new drug application (NDA).The clinical data validation is conducted systematicallyand is done by the investigator (CRF accuracy, legibility,timeliness, patient diary), the trial monitor (source dataverification(SDV)verifiestheCRFentries),andtheclinicaldatamanagementteam/manager(statisticalanalysis, final reporting, edit check specifications (ECS)).Clinical trial data management (CDM) is a critical elementoftheclinicalstudywhichwilldecideitsqualityandaccuracy.The quality of theclinical trial output dependsontheCRFdesign,fieldmonitoringguidelines,sourcedata verification, missing data/CRF, electronic laboratorydata, anddata conventionsThe CRF must be designed as per the protocol, and it isbeneficialtopreparedifferentvariants/versionsoftheCRF.TheCRFsshouldcontain thepatient'streatmentregimens, dosage, and all other essential details. The fieldmonitoring guidelines invariably define the quality of datapresented to the sponsor. The coordination between themonitor and the CDM to check the correctness of the dataand its integrity delivers quality results. The integrity andthe quality of the data depend on the SDV. It ensures theaccuracy andthevalidityofthedatapresentedby theinvestigatortothesponsor.TheGCPguidelinesemphasize the need to verify and track down the missingdata/CRF. The date conventions are the aspect of differentdates of the receipt of the CRFs in the

case of the multi-centricstudies.Also,theelectroniclabdatageneratedmustbeidentifiedasbelongingtoasubjectbyusinguniqueid entifiers and minimizing the potential errors. The labvalues, their units of measurements must be decided at theprotocol design time. Finally, the written SOPs concerningevery phase/aspect of the clinical trial, and regular auditswill assure the quality of the study. The data validationplan (DVP), along with the other measures used by theCDM ensure the required edit checks of the collected dataregarding thestudy protocol andidentify any potentialdiscrepancies (missing data, incorrect data, deviation fromtheprotocol)asshowninfigure.[8]

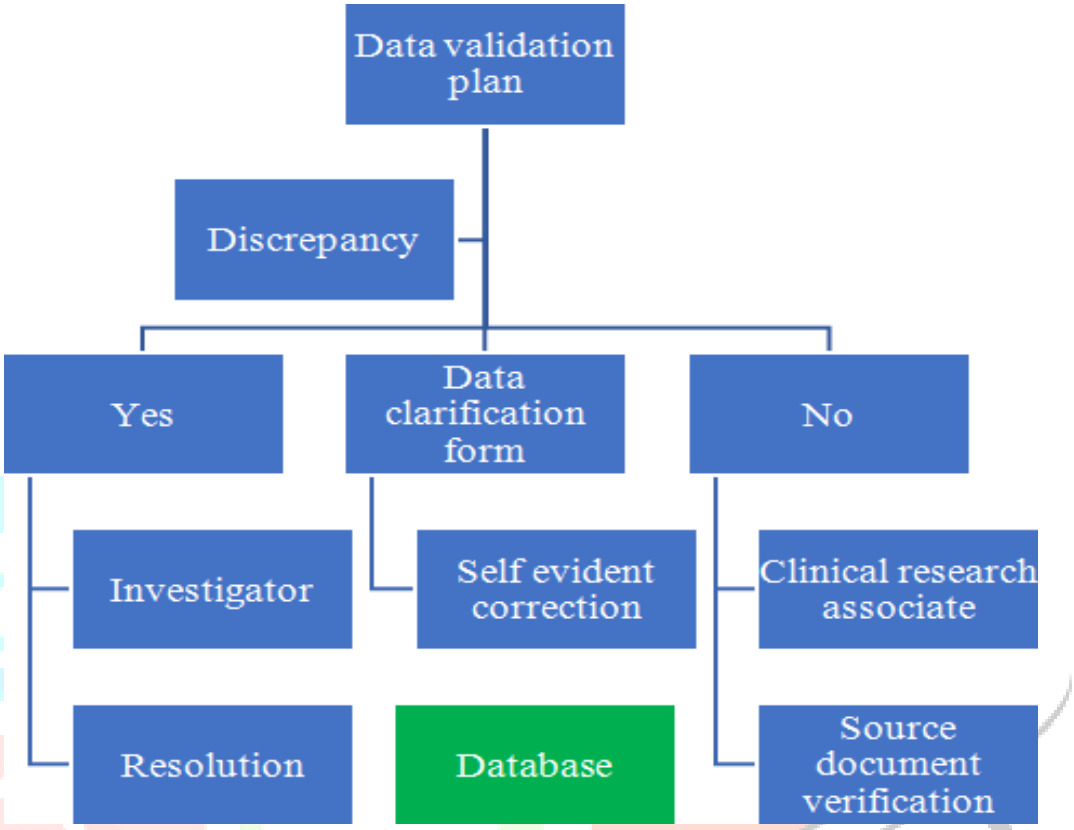

Fig 2. : Flowchartdepictingthedata validationplan.

Pre-clinical studies:

Pre-clinical studies involve in vitro (i.e., test tube or laboratory) studies and trials on animal populations. Wideranging dosages of the study drug are given to the animal subjects or to an in-vitro substrate in order to obtain preliminary efficacy, toxicity and pharmacokinetic information and to assist pharmaceutical companies in deciding whether it is worthwhile to go ahead with further testing.

Phase 0:

Phase 0 is a recent designation for exploratory, first-inhuman trials conducted in accordance with the U.S. Food and Drug Administration's (FDA) 2006 Guidance on Exploratory Investigational New Drug (IND) Studies Phase 0 trials are designed to speed up the development of promising drugs or imaging agents by establishing very early on whether the drug or agent behaves in human subjects as was anticipated from preclinical studies.

Phase 1:

Phase I trials also normally include dose-ranging, also called dose escalation, studies so that the appropriate dose for therapeutic use can be found. The tested range of doses will usually be a fraction of the dose that causes harm in animal testing. Phase I trials most often include healthy volunteers.

Phase II:

Once the initial safety of the study drug has been confirmed in Phase I trials, Phase II trials are performed on larger groups (20-300) and are designed to assess how well the drug works, as well as to continue Phase I safety assessments in a larger group of volunteers and patients. When the development process for a new drug fails, this usually occurs during Phase II trials when the drug is discovered not to work as planned, or to have toxic effects.

Phase III:

Phase III studies are randomized controlled multicentre trials on large patient groups (300–3,000 or more depending upon the disease/medical condition studied) and are aimed at being the definitive assessment of how effective the drug is, in comparison with current 'gold standard' treatment. Because of their size and comparatively long duration, Phase III trials are the most expensive, time-consuming and difficult trials to design and run, especially in therapies for chronic medical conditions.

Phase IV:

Phase IV trial is also known as Post Marketing Surveillance Trial. Phase IV trials involve the safety surveillance (pharmacovigilance) and ongoing technical support of a drug after it receives permission to be sold. Phase IV studies may be required by regulatory authorities or may be undertaken by the sponsoring company for competitive (finding a new market for the drug) or other reasons. [9]

Phases of clinical trials:

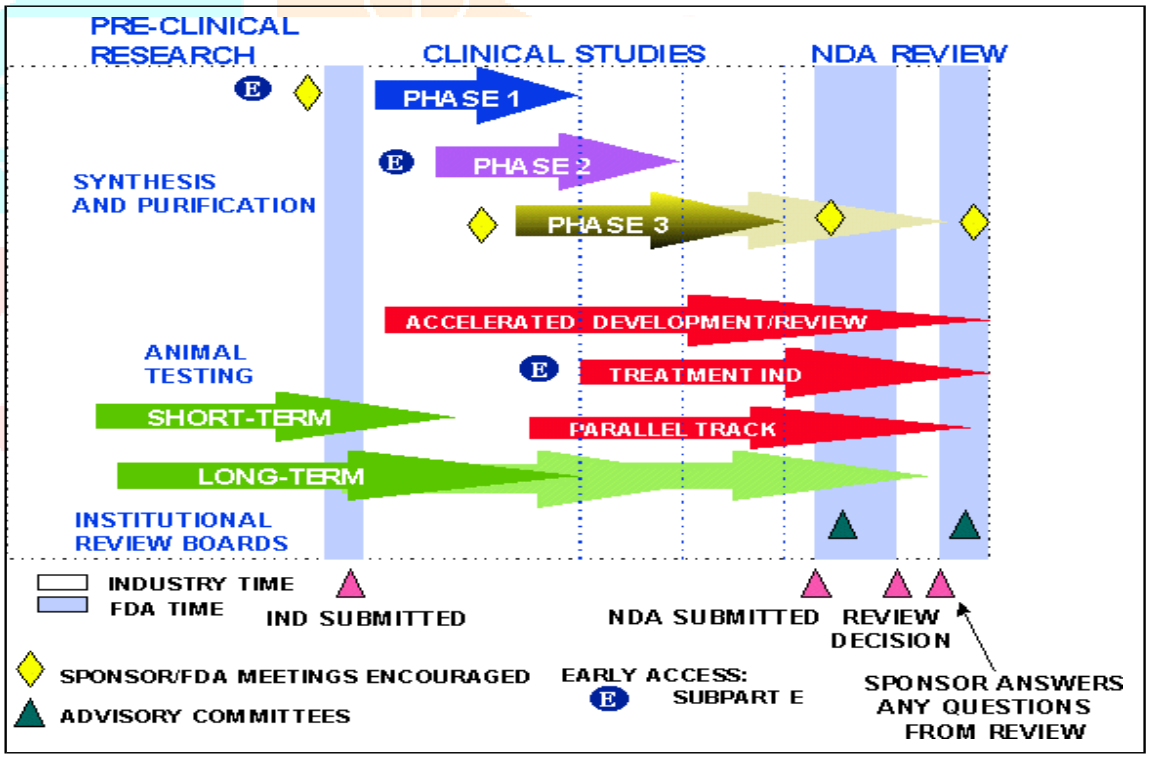

Fig 3. : Phases of Clinical Trial.

MATERIALS AND METHODS:

Search Strategy:

Articles in English-language medical literature we identified by a computer-aided search of the National Library of Medicine Medline from 1966 to August 2004. The search strategy used the exploded “clinical trials” and “participation or inclusion or willingness.” Related articles were also reviewed. Next, we manually searched reference sections of the electronically identified articles in an attempt to identify any articles missed by the electronic search. [10]

Literature search:

The publication selection and review process are described in Fig. 1. A systematic search of Pubmed and Scholar Google was undertaken using a combination of the following MESH terms or keywords: "Clinical trial"; and "patient selection" or "recruitments" or "enrollement" with "decision support system" or "medical records systems, computerized". For instance, for Pubmed, we used the following query: ("Clinical Trials as Topic"[Mesh] and ("Patient Selection"[Mesh] OR "recruitment" OR "enrollement")) AND ("Decision Support Systems, Clinical"[Mesh] OR "Medical Records Systems), Computerized[Mesh]). We searched CTRSS publications from 1998 to October 2009.

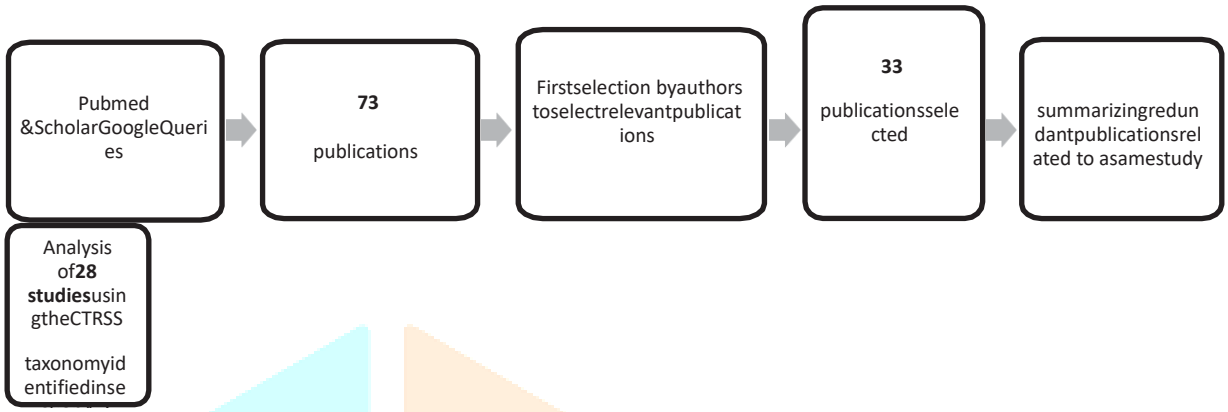

Fig 4. : Flow chart of the publications selection and review process.

Analysis axes:

A systematic review was carried out of both research and industrial CTRSS systems along with a brief review of the decision support methods and interoperability standards employed in the field. Once the publications had been identified, they were classified according to a simplified version of the Clinical Decision Support Systems Taxonomy (CDSS Taxonomy) proposed by Berlin et al, which addresses the technical, workflow, and contextual features of any kind of CDSS. [11]

Clinical trials: true experiments:

In accordance with the revised schedule "Y" of the Drugs and Cosmetics Act (DCA) (2005), a drug trial may be defined as a systematic study of a novel drug component. The clinical trials aim to evaluate the pharmacodynamic, and pharmacokinetic properties including ADME, efficacy, and safety of new drugs. According to the drug and cosmetic rules (DCR), 1945, a new chemical entity (NCE) may be defined as a novel drug approved for a disease/condition, in a specified route, and at a particular dosage. It also may be a new drug combination, of previously approved drugs. A clinical trial may be performed in three types; one that is done to find the efficacy of an NCE, a comparison study of two drugs against a medical condition, and the clinical research of approved drugs on a disease/condition. Also, studies of the bioavailability and BE studies of the generic drugs, and the drugs already approved in other countries are done to establish the efficacy of new drugs. Apart from the discovery of a novel drug, clinical trials are also conducted to approve novel medical devices for public use. A medical device is defined as any instrument, apparatus, appliance, software, and any other material used for diagnostic/therapeutic purposes. The medical devices may be divided into three classes wherein class I uses general controls; class II uses general and special controls, and class III uses general, special controls, and premarket approvals. [12]

Data sources and searches:

We conducted systematic searches of EMBASE, PubMed, Cochrane Registry of Controlled Clinical Trials and Web of Science databases in September 2014 using phrases in English derived from descriptions of the 10 most common forms of adaptive designs: adaptive hypothesis, adaptive treatment-switching, biomarker adaptive, adaptive dose-finding, pick-the-winner/droptheloser, sample size re-estimation, adaptive randomisation, adaptive group sequential, adaptive seamless and multiple adaptive.Table 1 includes definitions for each of these types of adaptive designs. We also included

adaptive designs that did not seem to fit any of these specific categories, but that fit the FDA's definition of adaptive designs as prospectively planned modifications to study design or hypotheses based on analysis of interim data from subjects in the study.5 We did not limit the searches to any specific date ranges and included all available adaptive trials for our study at the time of our research.

Table 1. Definitions oftypesof adaptivedesigns:

Sr. No.	Typeofadaptivedesign	Definition
1.	Adaptivedose-finding	These trials allocate patients to multiple different treatment doses and patient responses areassessedatinterimanalyses.Trialdesignisthenadaptedtoallocatemorepatientsto the treatment doses of interest, reducing allocation of patients to doses that appear non- informative. These studies usually occur in early-phase research to identify doses used in subsequent studies.
2.	Adaptivehypothesis	A study design in which trial hypotheses are adapted in response to interim analysis results. For example, adaptive hypothesis trials could involve a preplanned shift from a single hypothesis to multiple hypotheses, preplanned switching between the null hypothesis and the alternative hypothesis or preplanned switching between the primary and secondary study endpoints.
3.	Adaptivegroupsequential	In these variants on classical group sequential studies, results are analysed at interim analyses, with prespecified options of making adaptations such as sample size re-estimation, modification/deletion/addition of treatment arms, changing study endpoints, modifying dose and/or treatment duration or adapting randomisation schedules.
4.	Adaptiverandomisation	A study design in which accumulating results are observed and the randomisation scheme is adjusted so that patients enrolled later in the trial have a higher probability of being randomised to the treatment arm that was more effective among earlier patients in the trial.
5.	SeamlessPhaseII/III	A study design that combines the objectives of the Phase II investigational stage with the Phase III efficacy or confirmatory stage into a single study protocol moving from one stage to the second stage without stopping the patient enrolment process.
6.	Adaptive treatment-switching	A study design allowing the investigator to switch a patient's treatment from an initial assignment to an alternative treatment due to apparent lack of efficacy, disease progression or safety issues associated with the initial treatment.
7.	Biomarker adaptive	This method allows adaptations to trial design based on interim analysis of the treatment responses of biomarkers, such as genomic markers. This design can be used to select patient populations for subsequent trials, identify the natural course of a disease, achieve early detection of a disease and/or help in developing personalised medicine.
8.	Pick-the-winner/drop-the- loser	A study design that allows for dropping the inferior treatment group(s), modifying treatment arms and/or adding additional arms based on the review of accumulating data at interim analysis.
9.	Samplesizere-estimationMultipleadaptive	A study design using a flexible sample size adjustment or re-estimation based on interim analysis of accumulating data.Thisreferstoatrialthatincorporatesmultipleadaptivedesignsintoasinglestudy. [13]

Several methods to estimate treatment effects are applied to depression severity data measured by the 17-item Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) from a double-blind randomized study comparing nortriptyline and paroxetine over 12 weeks (Mulsant et al., 2001). The sample comprised 116 geriatric inpatients and outpatients at Western Psychiatric Institute and Clinic who met DSM-IV criteria (First et al., 1997) for a major depressive episode, without psychotic features or a past history of bipolar or schizoaffective disorder. An entry HRSD score of 15 or above and a Mini-Mental State Examination (MMSE; Folstein et al., 1976) score of 15 or above were required for study entry. Subjects with contraindication to treatment with either medication were excluded. Qualified patients who consented to participate were randomly assigned to either nortriptyline (n=54) or paroxetine (n=62) and dosing was titrated according to protocol. Depression severity was assessed weekly with the HRSD for 12 weeks. Patients who failed to tolerate the randomized treatment or did not show satisfactory progress were terminated from the randomized portion of the study and were treated openly with the other protocol drug or augmented or replaced by other drugs, determined by the treating physician. Monitoring depression severity was continued during the open treatment. [14]

Selection Criteria:

Registered trials are considered eligible if they meet all of the following inclusion criteria: (i) each study must include Ayurveda treatment or intervention strategy for COVID-19 and (ii) each study should be either an interventional (clinical trials) or an observational study. No restrictions were set on participant age, trial design, and types of interventions in the experimental and control groups. Data extraction was done by using a predesigned spreadsheet to collect study data. All the following information is extracted from each study: (1) administrative informationtrial registry number and sponsorship;2 descriptive informationstudy type and length of study time; (3) study designinterventional study (randomization, allocation, intervention type, masking), observational study (time prospective), sample size, number of arms, trial medications (single herb/multiple drugs/compound formulation), medicine duration, disease severity and comparator agent; (4) tracking informationregistration date and actual start date of the study; and (5) recruitment informationage of the target population, study centre, and setup. [15]

Randomized controlled trials

Randomised controlled trials (RCTs) are trials in which the subjects are randomly assigned to experimental and control groups. The experimental group is given the treatment that is being tested and the control group is given an alternative treatment or a placebo or no treatment at all. Most experimental clinical studies are RCTs, and the subjects are either healthy volunteers or patients. After a new drug passes a pre-clinical trial, it is tested via RCTs.

Non-randomized studies

In non-randomised studies, the study population is selected on the basis of pre-determined selection criteria; it is not randomized with respect to treatment(s) but is prescribed treatment based on the course of the disease. In many experimental studies involving surgical intervention which is only appropriate for particular patient groups, randomization is either not possible or not ethical. Generally, phase IV of a clinical trial has non-randomized design. [16]

Design And Content of Approach:

The FMA consists of 33 items for the upper extremity and 17 for the lower extremity. Each item is scored on a 3-point ordinal scale (0, 1, or 2), with 0 generally corresponding to no function, 1 to partial function, and 2 to perfect function. The items are summed to provide a final score, with maximum score (no impairment) of 66 points for the upper extremity and 34 points for the lower extremity.

In the FMA testing approach presented herein, one side of the body is tested/scored, and then the other body side is tested/scored. For each test item, the initial subject limb position is described, testing materials are listed, specific instructions to be read to the patient are provided, specific assessor movements and amount of assistance that may be provided are outlined, then the specific details by which each item is scored are provided. The score is based on best performance. The task is to be performed within a reasonable time frame, with 20 seconds per attempt used as a cutoff based on experience, and a maximum of 3 attempts per test item. No special considerations in scoring are made for presence of amputation, contracture, prosthesis, aphasia, or orthopaedic problems. [17]

Data extraction:

The contents that were extracted mainly included registration number, project name, research leader, research type, study design, sponsor, implementation unit, start time, completion period, research site, research institute, stage, research object, inclusion standard, exclusion standard, sample size, setting, location, recruitment period, intervention group measures, control group measures, random methods, blind methods, distribution concealment, and measurement indicators. Literature evaluation was independently conducted by two researchers. [18]

Reporting guidelines :

Guidelines and checklists help individuals meet certain standards by providing sets of rules or principles that guide towards the best behaviour in a particular area. They are successfully and routinely used, often on a compulsory basis, in many areas of human activity to prevent errors and omissions (e.g. in aviation, hospitals, etc.). The World Health Organisation introduced its surgical checklist in 2008 [13] and piloted its implementation at eight diverse hospitals around the world [14]. The results of this study showed that implementation of the checklist was associated with a significant decline in the rate of post-surgical complications (from 11% before to 7% after the checklist introduction) and death from surgery (from 1Æ5% before to 0Æ8% after). [19]

Guideline content:

We itemized guideline content to compare recommendations across guidelines. This analysis was limited to evidence-informed guidelines, those with explicitly described methodology and those with either explicit or probable endorsement of the guideline by a recognized institution or organization. This subset was chosen to select guidelines that were potentially more rigorously developed (that is, those with methodology beyond the consensus of a few authors' opinions) or more widely acknowledged. To aid in this comparison, we referred to the 2005 version (PR spreadsheet of elements V2.0; David Gemzik, personal communication) of Clinical Data Interchange Standards Consortium's (CDISC) Protocol Representation Model [36], which aims to comprehensively list potential protocol concepts (to support the interchange of protocol information). Guideline content was mapped, where possible, to one of 264 concepts included in this model. Where no suitable concept existed or where the concept had a different level of granularity than the CDISC concepts, a new category was created. Content mapping was conducted by one reviewer (JT) and verified in full by a second reviewer (Jk). [20]

Clinical Trials AndPractice Guidelines:

The modern randomized clinical trial was invented in the middle of the twentieth century, but its prehistory dates back exactly 250 yearsto 1753when British naval surgeon James Lind showed that citrus fruit cured scurvy. Although it took two centuries for clinical trials to gain momentum, a few individuals along the way promoted quantification as a tool to evaluate treatments. For example, in the 1830s, French physician Pierre Louis (2) challenged those seeking new therapies to support their conclusions with statistics, not subjective impressions. He explained, "Let those who engage hereafter in the study of therapeuticsdemonstrate, rigorously, thedegree of influence of any therapeutic agent on the duration, progress, and termination of a particular disease." [21]

A Case Study of Ich Guideline:

The clinical programme was designed to satisfy CPMP guidelines for the indication of concern that were in force at that time. Five placebo controlled randomized studies were conducted looking at short-term efficacy. Four out of these studies used axed doses of 'synodrug', while used a variable dosing regimen. Two of the studies had a positive comparator. In total, ten direct yariables were used in these studies.

Several 'primary' variables were identied in the protocols in order to provide observer-rated assessments (rameters 1, 2 and 7), global clinical judgement assessments (parameters 3 and 4) and self-rated assessments (parameters 5,6 and 8). In addition to the eight parameters outlined in Table I, responder analyses where patients are considered to either have responded to treatment or not were planned and performed for two of the three primary variables used in all studies. For parameter 1 a patient was considered to have responded to treatment if the observer rated assessment decreased by 50 per cent from baseline. In order to be considered a responder for parameter 4, patients had to rate themselves as 'very much improved'. [22]

CONCLUSION:

Clinical trial process involved careful planning, implementing and analysing a clinical trial with a good practice.Involved 1-4 phases with specific objective and end result.A clinical trial must be planned in such a way that the prerequisites were ready in time.After careful planning, the studied must be implemented and data must be maintained with high accuracy for the subsequent analysis.Clinical trial must follow guidelines and protocol to ensure wellbeing of participants.Ensuring proper building both at randomisation and statistical analysis gives greater reliability.

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