*Biological Forum – An International Journal* **15(5a): 377-387(2023)**

**ISSN No. (Print): 0975-1130**
**ISSN No. (Online): 2249-3239**

# A Comprehensive Review of Innovative Clinical Trial Strategies

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*(Received: 03 April 2023; Revised: 25 April 2023; Accepted: 03 May 2023; Published: 15 May 2023)*
*(Published by Research Trend)*

**ABSTRACT: The federal government emphasizes clinical trials in evidence-based medicine and healthcare reform for improved patient care and quality. However, these trials can pose risks and produce inaccurate information. A well-designed trial requires ethical oversight. Phases I involve safety and general effects studies in volunteers Phase II evaluates the drug in a small group of selected patients. Phase III expands the study to hundreds of patients, and doctors provide feedback on adverse drug reactions (ADR) and effectiveness in phase IV. Clinical trials are increasingly under pressure to enroll patients rapidly and effectively, sometimes with very few resources. Safety data from meta-analyses is challenging to assess and interpret due to the lack of access to individual participant data, the varied nature of safety data, and the statistical difficulties of studying rare incidents. Clinical trial administration practices have evolved, with more adaptable designs emerging. These designs allow for multiple sub studies with different objectives, interventions, and subgroups within a larger master protocol structure. This study reviews existing master protocol studies such as umbrella trials, basket trials, platform trials and statistical methods like Bayesian analysis. Bayesian statistics provides a formal framework for combining information at all stages of clinical trial administration, including design, execution, and analysis. Clinical studies use biostatistics techniques to account for patient response to therapy and draw accurate conclusions, preventing fraud and inadvertent mistakes. Adaptive trial designs offer flexibility and effectiveness, but concerns about quality, validity, and trial integrity persist. However, adaptable clinical designs are increasingly discussed due to their ability to identify potential therapeutic benefits and reduce clinical development length. Adopting adaptive trial designs is expected to enhance clinical development success.**

**Keywords:** Pre-clinical trials, Clinical trials, Traditional clinical trials, Adaptive clinical trials, randomized clinical trials, Master protocols, Bayesian analysis.

## INTRODUCTION

What we know, what we believe, and our curiosity about events all have an impact on how we behave. Patients and doctors and researchers who take part in randomized controlled trials (RCTs) are unavoidably going to be curious about the treatment they were given or assigned in experimental settings. When possible and appropriate, it is crucial to maintain blindness among key parties (such as patients, doctors, and/or data analysts) throughout the trial in order to ensure the internal validity of the study results. However, this can be challenging to do for a number of different reasons. RCT investigators frequently come across as being excessively kind or careless when it comes to blinding, in contrast to the extremely strict requirements of clinical trial planning and execution (Bang *et al.*, 2010). Clinical trials are implemented using a strict methodology supported by scientific, statistical, ethical, and legal considerations. Therefore, in order to preserve a relationship with patients and industry in search of the safest, most effective, and most efficient remedies, it is imperative for health care professionals to comprehend the tenets on which well-conducted clinical trials hinge (Umscheid *et al.*, 2011). Within the last ten years, significant technical and analytical advancements have made it possible to perform "genomic profiling," or high-throughput examination of clinical specimens for patterns of genomic expression. The discovery of multigene indicators that predict clinical prognosis more precisely than conventional clinicopathologic features has been aided by comparing the genomic expression patterns of breast cancer specimens from relapsing and nonrelapsing patients. The benefits and drawbacks of creating such indicators have been discussed elsewhere, and specific standards for the quantity of data needed to define and justify their clinical utility have been proposed (Sparano and Paik 2008). The use of Bayesian analysis techniques is being made easier by improvements in processing capacity and methodology. At the University of Texas M. D. Anderson alone, over 100 active clinical trials have been planned or are being followed from a Bayesian perspective. Furthermore, compared to none ten years ago, 10% of recent medical device approvals by the US FDA's Center for Devices and Radiological Health are based on Bayesian designs and analyses (Berry, 2006). It is critical to understand the significance of biomarkers and how they are employed in clinical research to create targeted medicines, especially in light of the growing interest in and efforts toward precision

care. The development of basket and umbrella design trials within the master protocol framework is one of the notable methodological developments that have recently been made toward biomarker-guided clinical trials (Park *et al.*, 2020). The heterogeneity that exists not only between patients with the same tumor type (inter-patient heterogeneity) but also within a single person (intra-patient heterogeneity), as shown by the molecular evolution of a tumor through time (through sequences of therapy) and space (from primary tumor to metastasis), presents a challenge for the development of novel therapeutics. Thus, the development of oncology-related drugs has changed as a result of the notions of "oncogenic driver" and "oncogene addiction." Parallel to this, the widely held belief that multiple targeted therapeutics will likely be necessary to overcome tumor resistance is based on an increased understanding of the complex structural paradigm of genetic alterations activating intracellular proteins along multiple pathways, as well as several years of early clinical experience with the success of (and subsequent resistance to) single-target therapies (Renfro and Sargent 2016).

A patient and public participation (PPI) approach to the trial creation process, from the generation of research questions through the distribution of results, may assist staff in developing relationships of trust and mutual commitment with potential participants. If it can be shown that taking part in RCTs improves health, this will motivate volunteers to participate in research and give medical practitioners the confidence to ask patients to participate in trials. Evidence supporting the advantages of RCT participation may aid in the interpretation of study findings' generalizability, facilitating the introduction of novel therapies into clinical practice and healthcare policy. In this comprehensive evaluation, we sought to ascertain if participating in RCTs (the intervention) had any positive effects on health (the outcome) among the population that was eligible (Hajjaj *et al.*, 2022). Platform trials are a brand-new kind of clinical study in which numerous therapies can be assessed concurrently in comparison to a single control group under a single master protocol. Comparing platform trials to more widely used traditional designs (such as two-arm trials), there may be some special benefits. Platform trials are more "disease-focused" than "intervention-focused" designs because they enable the more effective evaluation of numerous interventions over time, producing data that may be applied to both internal and external scientific discoveries. There are additional difficulties when trying to identify what would be the optimal therapeutic choice for a given condition across several trials because these trials frequently use varied, non-standardized trial data gathering and processing methodologies. Platform trials are becoming more popular because of their ongoing, disease-specific examination. The United States Food and Drug Administration (FDA) has shown their support for a wider dissemination of platform trials and master protocols, as evident by their recently released (September 2019) draft guidance on master protocols and a 2017 editorial published by the Directors of Drug Evaluation and Research in the New England Journal of Medicine. Important methodological advancements have been made in platform trial designs (Park *et al.*, 2020).

## MATERIAL AND METHOD

**Overview of Clinical Trials:** A clinical trial is a research project that tries a novel medical procedure or a novel application of an already-proven procedure to see if it will be a more effective means of disease prevention, detection, diagnosis, or treatment (Thorat *et al.*, 2010). Clinical trials, as their name indicates, are a collection of tests and observations performed on human participants in clinical research (Tiwari *et al.*, 2016). It is a methodical procedure designed to determine the safety and effectiveness of a medicine or technology in treating, preventing, or diagnosing a disease or other medical condition (Kandi *et al.*, 2021). Clinical trials are used to test new interventions to see if they are safe, effective, and superior to currently used therapies (Tiwari *et al.*, 2016).

**Pre-clinical studies**: Pre-clinical research includes tests on animals and in vitro (also known as test tube or laboratory) research. To obtain preliminary information on the study drug's efficacy, toxicity, and pharmacokinetics and to help pharmaceutical companies decide whether it is worthwhile to move forward with further testing, a variety of dosages of the study drug are administered to the animal subjects or to an in-vitro substrate (Thorat *et al.*, 2010).

In clinical trials phase 0 (micro-dosing studies), phase 1, phase 2, phase 3, and phase 4 of clinical study are included. Phases 0 and 2 of a study are referred to as exploratory phases, whereas phases 1 and 3 are referred to as therapeutic and confirmatory phases, respectively. Phase 4 is sometimes known as the post-approval or post-marketing monitoring phase. Phase 0, also known as the micro-dosing phase, was once carried out in animals but is currently done on healthy human volunteers to determine the dose tolerability (pharmacokinetics) prior to being delivered as part of the phase 1 study (Kandi and Vadakedath 2023).

**Table 1: Table consisting of description of different phases involved in clinical trials.**

| Phase | Objective | Sample Size | Duration | Key Features | Reference |
|---|---|---|---|---|---|
| Phase 0 | Exploratory pharmacodynamics or pharmacokinetics | Very small (10-15 participants) | Short (a few days) | Determines how a drug is metabolized and how it affects the body. | (Tiwari *et al.*, 2016) |
| Phase 1 | Assess safety, dosage range and side effects | Small (20-80 participants) | Several months | Determines the maximum tolerated dose, optimal dosage, | (Thorat *et al.*, 2010) |

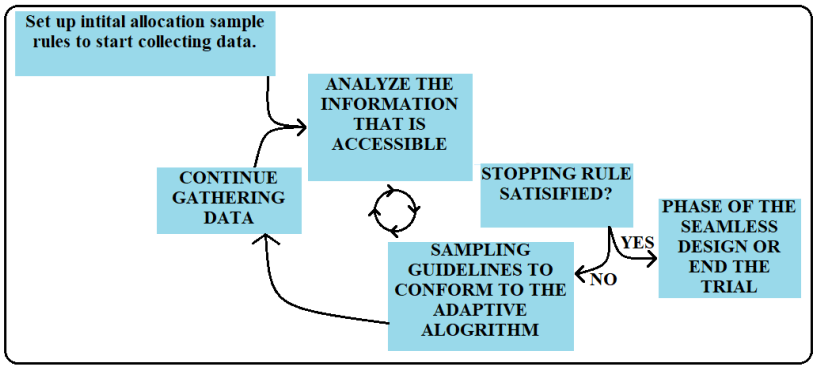
| | | | | | |
|---|---|---|---|---|---|
| | | | | and potential side effects, pharmacodynamics, pharmacokinetics | |
| Phase 2 | Assess efficacy and further evaluate safety. | Moderate (20-300 participants) | Several months to a year. | Determines if the drug works as intended, further investigates side effects, and explores appropriate dosing regiments. | (Thorat *et al.*, 2016) |
| Phase 3 | Confirms efficacy and monitor adverse drug reactions | Large (300-3000 participants) | Several years | Confirms drug's effectiveness, monitors side effects in a larger patient population, and compares it to standard treatments. | (Thorat *et al.*, 2010) |
| Phase 4 | Post-marketing surveillance and long-term safety. | Varies (thousands or more) | Ongoing (years or decades) | Monitors long-term safety, evaluates the drug's use in specific populations or combinations, and collects additional information on effectiveness and side effects once the drug approved and available on the market. | (Thorat *et al.*, 2010) |

**Problems faced in traditional clinical trials:** Clinical trials are the most thorough method of comparing innovative therapies to current treatments for a specific result. Clinical trials that are well-conducted have the potential to have a major influence on patient care; as a result, they should be planned and carried out with this objective in mind. One method to do this is to guarantee that trial results are pertinent, suitable, and significant to patients in actual clinical settings. However, only a small number of studies really have a significant impact on patient care, frequently as a function of how the trial findings are selected, gathered, and reported (Heneghan *et al.*, 2017). But there are several chances for failure in clinical trials for drugs and medical devices. Failures can be caused by a lack of efficacy, problems with safety, or a lack of financing to finish a study, as well as other things like failing to uphold proper manufacturing practices, failing to abide by FDA directives, or difficulty with patient recruiting, enrollment, and retention. At each stage of the clinical trial procedure, it is crucial to provide precise and enough findings to decide whether or not it is worthwhile to continue (Fogel, 2018). Additionally, clinical studies are very expensive and time-consuming to perform. Clinical trials are expensive, which greatly raises the final price of new drugs and medical equipment. The transition of promising novel therapeutics from the bench to the bedside can be delayed, often indefinitely, as a result of inefficient trial design delays (Methodol, 2014).

- **Failing to show effectiveness or safety:** Failure to show efficacy has been and continues to be the main cause of trial failure. According to an analysis of 640 phase 3 studies using new treatments, 54% of those failed due to poor clinical development, with 57% failing due to insufficient effectiveness. Potentially effective drugs may still fail to show efficacy for a variety of reasons, such as a poor study design, an inappropriate statistical endpoint, or a clinical trial that was underpowered (i.e., had a sample size that was insufficient to reject the null hypothesis due to patient dropouts and insufficient enrolment (Hwang *et al.*, 2016).
- **Influence on the economy-** Hwang et al. noted that 22% of the failed phase 3 studies they examined failed due to lack of funding. The costs required to complete the entire development process from discovery to bringing a drug to market vary, and so do estimates of these costs (Fogel, 2018).
- **Obstacles in the legal and ethical systems**-Most publications highlighted regulatory and ethical review delays.The period of time between the start of all regulatory processes and the trial's actual launch was unusually long. Although it was unusual to give an explicit time frame, one research noted that funding frequently ended before all necessary permissions were obtained (Alemayehu *et al.*, 2018). Clinical trials can be more adaptable using adaptive designs by using trial outcomes to change the trial's path in line with pre-established rules. Since they frequently make better use of resources like time and money and may need fewer participants, trials with an adaptive design are frequently more efficient, informative, and ethical than trials with a typical fixed design (Pallmann *et al.*, 2018).

**Adaptive Clinical Trials:** The idea of adaptive design first originated in the 1970s, and adaptive randomization and a class of designs for sequential clinical trials were first created in that decade. As a result, adaptive randomization, group sequential designs with the flexibility to terminate a trial early for reasons of safety, futility, and/or efficacy, and sample size re-estimation at intervals to achieve the desired statistical power make up the majority of adaptive design techniques used in clinical research. Clinical

research has been modifying the trial and/or statistical procedures of ongoing clinical trials based on acquired data for many years. Recent years have seen a significant increase in interest in the possible use of adaptive design techniques in clinical trials. The Biotechnology Industry Organization (BIO) and Pharmaceutical Research and Manufacturers of America (PhRMA) have created working groups on adaptive design and recommended strategies, approaches, and implementations for regulatory consideration (Chow and Chang 2008). Sample size reassessment, response adaptive randomization and discarding of inferior treatment arms, adaptive enrichment, and "seamless" designs are a few examples of common types of adaptive clinical trials. Actual power is determined by a sample size reassessment using event-based assessments made during the experiment. Response adaptive randomization enables adjustments to the randomization ratio throughout the course of the study, increasing the likelihood that newly enrolled patients will be assigned to the treatment arm if interim results are positive. A trial can be "enriched" by changing its eligibility criteria to either exclusively or primarily enroll patients from a given subgroup if interim analysis reveals that this subgroup has a more favourable response. Adaptive enrichment is the modification of the trial's eligibility criteria or outcome evaluations. The relevance, scope, or likelihood of success of the experiment may also be increased by enhancing clinical and biochemical results. Continuous adaptive trial designs enable progression from one phase to the next, typically from phase II to phase III trials. The initial allocation ratio, the intended total sample size, and a possible enriched population for the ensuing phase III can all be determined using the findings from the phase II trial (Thorlund *et al.*, 2018).




**Basic Outline of Adaptive Clinical Trial**

**Fig. 1.** Flowchart showing overall adaptive process.

**Randomized Clinical Trial: A part of Adaptive Clinical Trials:** Clinical trial participants are frequently randomly assigned to different therapies on an individual basis. When individual allocation is either difficult or undesirable, cluster or group randomization is the process of allocating numbers to groups of people. The use of cluster allocation has numerous benefits. For instance, whether assessing clinical recommendations or the benefits of medical education on patient outcomes, healthcare professionals must almost always be the "unit" of allocations (Puffer *et al.*, 2003). Clinical research can be divided into observational and experimental studies, such as RCTs. Research that is not experimental includes case reports, case series, cross-sectional studies, and prospective observational studies, including case-control and cohort studies. Although they cannot offer causal inferential value, these research investigations frequently yield significant insights. Evidence-based medicine is based on RCTs because they can produce high-quality data that can be used to describe causal links. In RCTs, the target population (e.g., patients with the appropriate diagnosis) are constructed from the research sample and then randomly assigned to various groups (e.g., standard treatment or placebo vs. new treatment). Predetermined end points are the effects of investigational treatments that can be examined at particular times (Spieth *et al.*, 2016).

Strong evidence suggests that inflammatory states may be linked to specific subgroups of major depressive illness. Investigating the antidepressant impact of anti-inflammatory therapy and evaluating the potential negative consequences of these interventions in individuals with depressive symptoms or depression were the goals of this systematic review and meta-analysis. Anti-inflammatory drugs, in particular NSAIDs, are frequently used by people taking antidepressants, likely because of the bidirectional relationship between depression and pain. This raises serious public health concerns about the concurrent use of antidepressants and anti-inflammatory drugs. (Köhler *et al.*, 2014).

A thorough examination of randomized controlled trials published in the New England Journal of Medicine (NEJM), the Lancet, and the Journal of the American Medical Association (JAMA) turned up 396 instances of medical reversals. Many of these 396 reversals were the focus of systematic reviews: in 209 cases (53%), the systematic review verified that the medical practice in question was indeed a medical reversal; in 109 cases (28%), the results of the systematic review were inconclusive; and in 78 cases (20%), there was no systematic review. JAMA reported 154 of the reversals (or 39%), NEJM reported 129 (or 33%), and Lancet reported 113 (or 29%) (Perez *et al.*, 2019).

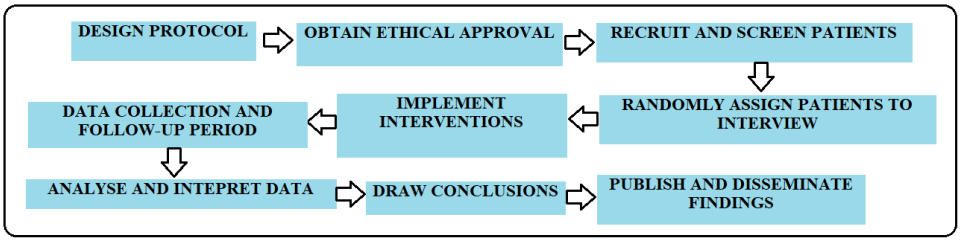



**Fig. 2.** A flowchart describing the process of Randomized Clinical Trials in a nutshell.

Creating a study topic that is clinically pertinent is the first step in designing an RCT. According to the study question, the underlying hypothesis will frequently aim for superiority (a comparative trial) or noninferiority (an equivalence trial) of one intervention over another. A superiority trial aims to demonstrate that Intervention A is better than Intervention B, whereas noninferiority trials aim to demonstrate that the new treatment is at least as effective as the standard therapy but offers additional benefits such as lower costs, lower toxicity, a better side effect profile, or improved
methods of administration when compared to the standard of care. The two common designs for RCTs are parallel and crossover. Following randomization, subjects will either be randomized to receive Intervention A or B (or C, D, E, etc.) for the duration of the trial (parallel design) or to get Intervention A first, followed by Intervention B, and then Intervention B last (crossover design). Since each person acts as their own control in a crossover trial and interindividual variability is thereby eliminated, these studies can be quite effective (Spieth *et al.*, 2016).

To find all significant headings pertinent to the core specialties of internal medicine, the MEDLINE (2002) medical subject heading (MESH) tree structure was employed. Eight areas of internal medicine were specifically searched using the single broadest heading in the MeSH structure (cardiology: "cardiovascular diseases"; endocrinology: "endocrine diseases"; immunology: "immunologic diseases"; nephrology: "kidney diseases"; rheumatology: "musculoskeletal diseases"; oncology: "neoplasms"; neurology: "nervous system disease"; respiratory medicine: "respiratory tract (Strippoliv *et al.*, 2004).

**Master Protocols, A Part of Adaptive Clinical Trials:** Master protocols are innovative methods that simultaneously study several hypotheses (e.g., different populations or treatments, or allowing adding deleting arms throughout the trial) with the goal of improving efficiency and evaluating trials in a more moral manner. These designs are rarely adopted in spite of their many benefits (Mills *et al.*, 2019). A master protocols is a research protocol that includes several sub-studies. These studies may all have distinct goals, but they all work together to assess one or more investigational medications in one or more disease subtypes as part of the overall umbrella trials, and platform trials, are cutting-edge designs that simultaneously examine several hypotheses. Several populations or treatments, or the ability to add or remove arms during the study, trial framework. The sponsor has the option to include or exclude specific sub-studies from the master protocol by designing the protocol with a fixed or adaptive design purpose. These master protocols include medicines with various modes of action, the discovery of biomarkers, and genetic subtyping into distinctive and adaptable designs (Park *et al.*, 2019). Master protocols classified as basket trials, for instance. These provide trial evaluation with increased efficiency and a more moral attitude. Many different diseases may be studied using these methods, which are often employed in cancer studies (Mills *et al.*, 2019).

**Table 2: A comparative study between different types of master protocols in clinical trials.**

| | **Umbrella Trials** | **Basket Trials** | **Platform Trials** | **References** |
|---|---|---|---|---|
| **Definition** | A master protocol is frequently used to assess the effectiveness of many investigational treatments provided as single medications or as medication combinations in a particular disease group known as an umbrella trial. | A basket trial is a master protocol that is intended to assess a single experimental medicine or therapeutic combination in several disease populations defined by disease stage, histology, number of prior treatments, genetic or other biomarkers, or demographic variables. | Platform trials are master protocols that combine elements from basket and umbrella trials, focusing on permanent experiments. They can be continuously conducted for research on various medications and disease populations at different periods, allowing for continuous improvement in | (Mills *et al.*, 2019; Renfro and Sargent 2017) |

| | | | | |
|---|---|---|---|---|
| | | | research outcomes. | |
| **Advantages** | 1. Allows for personalized medicine by targeting specific subgroups or biomarkers | 1. Efficiently tests the efficacy of a treatment across different diseases. | 1. Enables simultaneous evaluation of multiple treatments in multiple patient populations. | (Renfro and Sargent 2017) |
| | 2. Reduces the time and cost required for evaluating multiple treatments. | 2. Provides an opportunity to identify rare patient populations that respond to the treatment. | 2. Increases the likelihood of identifying effective treatments in a shorter time frame. | |
| | 3. Maximizes patient recruitment as it includes a larger patient population. | 3. Enables the evaluation of targeted therapies for specific genetic mutations. | 3. Allows for adaptive trial design, allowing modifications based on accumulating data. | |
| **Disadvantages** | 1. Requires identification of biomarkers or subtypes and their association with treatment response. | 1. Limited understanding of the treatment's mechanism of action across different diseases. | 1. Complexity in trial design and execution due to multiple treatments and patient populations. | (Cunanan *et al.*, 2017 ; Mills *et al.*, 2019) |
| | 2. Potential difficulty in obtaining sufficient patient numbers for each subgroup. | 2. Limited availability of patients with specific genetic mutations. | 2. Statistical challenges in analyzing data from multiple treatment arms and patient groups. | |
| | 3. Treatment effects may be diluted if the disease subtypes or biomarkers are not well-defined. | | 3. Requires strong coordination and collaboration among multiple stakeholders. | |

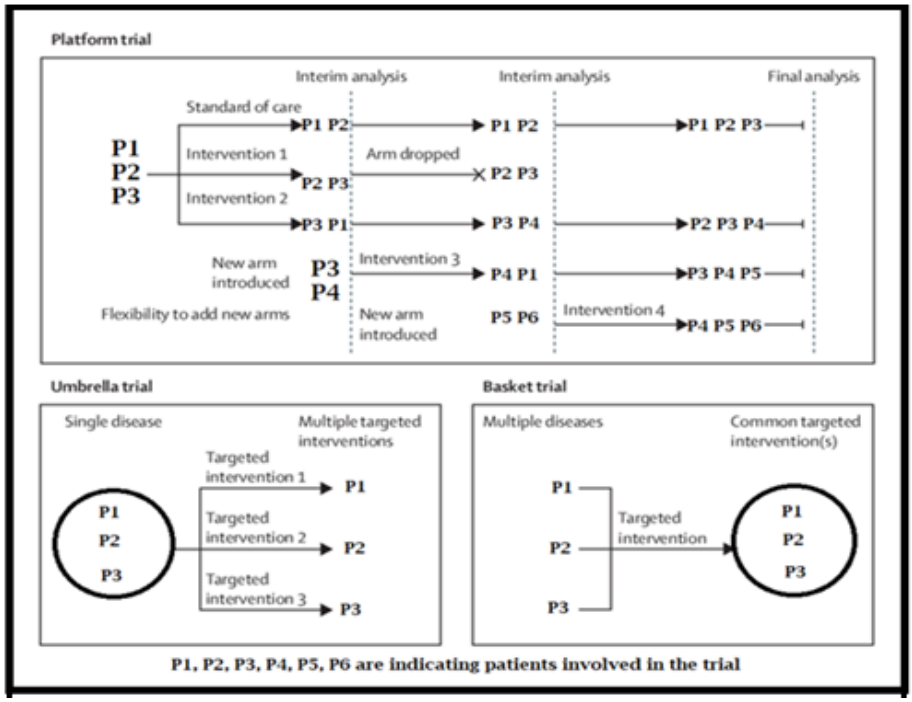



**Fig. 3.** Schematic presentation of platform trial, Umbrella trial and basket trial.

**Statistical methods in Clinical Trials:** Many nations implemented pharmacovigilance systems for marketed products in the wake of the thalidomide tragedy in the early 1960s. These systems included the systematic gathering of reports of suspected adverse events (AEs) and the dissemination of information regarding suspected adverse effects of drugs. 1 It is widely acknowledged that, for a variety of reasons, it is impossible to detect every safety risk connected to a pharmaceutical during the premarketing clinical trials. First off, the number of patients or human subjects who will have been exposed to a medicine at the time of first product registration, especially for a new chemical entity, is frequently insufficient to detect uncommon (incidence of 1 in 1,000) or rare (incidence of 1 in 10,000) adverse events (AEs) (Almenoff*et al.*, 2007). The major statistical methodologies involved in Clinical trials are Bayesian analysis, GENSTAT analysis, Computer aided multivariate analysis etc.

**Bayesian Analysis:** According to the historical record, Reverend Thomas Bayes' idea of the Bayesian methodology was published posthumously in 1763 (with the assistance of his friend Richard Price), a long time before frequentist techniques gained popularity. According to the now-famous Bayes theorem, Prob(|data) P() Prob(data|), the posterior probability of an event can be computed as being proportional to the product of the event's prior probability and data likelihood. With the notable exception of Pierre-Simon Laplace, this straightforward yet profound theorem was widely disregarded in the beginning. However, the work of Jeffreys, de Finetti, Good, Savage, de Groot, Lindley, Cornfield, and Zeller, among many others, helped to revive it in the mid-1900s. It should be noted that Jerry Cornfield played a significant role in introducing Bayesian thinking to clinical trial planning while working at the Public Health Service/National Cancer Institute from 1947 to 1958 and the National Heart Institute from 1960 to 1967 (Lee and Chu 2012).

We use a clinical trial and the introduction, methodology, results, and discussion (IMRAD) format to apply the Bayesian technique. Open prospective randomized controlled study 25 IMMERSION had parallel groups. Non-pregnant women were given the choice of resting in bed for the same amount of time at a neutral temperature (bed group) or immersing themselves in water for two hours in a bathtub (bath group). Vacuum volume was measured in order to assess diuresis (the primary endpoint). The results of a Bayesian statistical analysis were used. The mean difference, its 95% credible interval (CrI), and the associated posterior probability were estimated for the primary outcome. The primary analytical goal was to compare the levels of diuresis, or q, between the intervention group (partial immersion, or "bath") and the control group (bed rest). In order to conduct an equitail test, a sample size of 20 participants per group was needed with an expected mean diuresis difference of 100 ml, a standard deviation (SD) of 100 ml, a Type I error rate of 5%, and a Type II error rate of 20% (Ferreira *et al.*, 2020).

We take a basic look at how Bayesian statistics can be used in paediatric Type-2 diabetes (T2D) trials to show how this strategy might improve the viability of those studies. Bayesian statistics incorporate prior knowledge or beliefs regarding the impact of a treatment into the study's overall conclusions. This is done by employing an assumed distribution for the model parameters, which are then combined with the posterior distribution, which is derived using the study's data (Huff *et al.*, 2017). A collection of data of the same is presented in below Table 3.

**Table 3: Data from adult T2D clinical trials summarized for prior distribution generation.**

| Drug used | Dose (mg) | duration of treatment (in days) | Mean decrease in HbA1c% (treatment placebo) | Standard Deviation | Reference |
|---|---|---|---|---|---|
| **GLP-1 Antagonists** | | | | | |
| Liraglutide | 1.2 | 182 | 1.1 | 1.55 | (Nauck *et al.*, 2009) |
| Dulaglutide | 0.75 | 182 | 1.05 | 1.03 | (Nauck *et al.*, 2014) |
| **SLGT-2 Inhibitors** | | | | | |
| Dapagliflozin | 5 | 168 | 0.36 | 0.84 | (Bailey *et al.*, 2013) |
| Canagliflozin | 100 | 182 | 0.62 | 0.78 | (Lavalleetal, 2013) |
| **DPP-4 Inhibitors** | | | | | |
| Sitagliptin | 100 | 168 | 0.65 | 1.46 | (Charbonneletal, 2006) |
| Linagliptin | 5 | 168 | 0.66 | 0.85 | (Taskinenetal, 2011) |

With respect to the data, the alternative hypothesis—that a treatment effect exists—was directly quantified using Bayesian statistical inference. Bayesian parameter estimates are derived from the posterior distribution, which encapsulates the uncertainty about an effect's magnitude (Gelman and Hill 2007). Examining the

correlation between clinical and experimental pain measures involved the use of Bayesian GLMM. Clinical pain and function measurements have undergone adjustments, with specific results published and previously discussed (Ahn *et al.*, 2017). With the exception of the PPT quadriceps test and cold pain, there is evidence to suggest a link (posterior probability 75%) between at least one of the two clinical measures and each of the experimental pain measures. According to these findings, improvements in experimental pain measurement were linked to decreases in clinical pain (Ahn *et al.*, 2018). Bayesian inference has been useful for making decisions in the context of ongoing research into treatment effects discovered in pilot studies (Schmitz *et al.*, 2017). For a wide range of readers, the current study also includes a primer on Bayesian inference. The benefit of this method lies in how it is to be interpreted: when researchers utilize P-values from frequentist inference, they are frequently attempting to address the posterior likelihood that the alternative hypothesis exists. The spread of Bayesian methods may be advantageous for researchers in this field in particular since they may be better suited to analyzing topics with small sample sizes, as was the case in the current study (Gelman, 2006; Mcneish, 2016).

## DISCUSSION

Our intervention successfully managed to achieve an imbalance in the opinion of the discussion initiators across conditions However, the difference in the acceptance rates across conditions is not statistically significant, and the change in the mean scores of all the reviewers, and the set of reviewers that participated in the discussion before and after the discussion is small. We thus find no evidence of herding in peer review (Stelmakh *et al.*, 2023). In this study, we concentrated on the herding effect's manifestation in conversations about peer reviews. It will be interesting to see if the individual cognitive biases associated with herding behaviour, such as anchoring bias, are still present in future research (Epley and Gilovich 2006; Epley and Gilovich 2001; Lieder *et al.*, 2018; Strack and Mussweiler 1997; Mussweiler and Strack, 2001), in peer-reviewed conversations, primacy and recency effects each have a b*unique role to play (Glanzer and Cunitz 1966). We gathered and assessed comments from interested medical researchers in order to acquire an understanding of the obstacles to applying Bayesian approaches in clinical research as well as prospective pathways that could, in some cases, enhance uptake. The poll gave useful information on potential explanations for the clinical development community's sluggish adoption. The key benefits of Bayesian methods include formal mechanisms for incorporating prior knowledge into the current trial analysis (thus, not ignoring what is already known about a disease state and an intervention) and for calculating the likelihood of a pre-specified treatment effect size, both of which are very helpful in clinical research (Clark *et al.*, 2022). We found five major obstacles to patients of different races and ethnicities participating in clinical trials using a multi-step approach that included a thorough literature review, gap analysis, and expert interviews: mistrust, lack of comfort with the clinical trial process, lack of information about clinical trials, time and resource constraints related to participation, and lack of awareness of the existence and significance of clinical trials (Clark *et al.*, 2019).Clinical trials can explicitly target seniors and focus on issues that are important to the geriatric oncology community. The Cancer and Leukaemia Group B (CALGB) 49907 phase 3 RCT (ClinicalTrials.gov identifier NCT00024102) illustrates this by contrasting routine adjuvant polychemotherapy vs. mono-chemotherapy in patients with breast cancer under the age of 65 (Sedrak *et al.*, 2021). Several authors with expertise as clinical investigators in underdeveloped nations have written about the difficulties they faced when conducting clinical trials. These authors' perspectives are based on their own experiences. The main impediments were problems with ethics and regulations, administration, finances, infrastructure, poor data quality, and a lack of training curricula that focused on clinical research (Mbuagbaw *et al.*, 2011). It could be advantageous to study and apply best practices at all levels (systemic, organizational, and individual). Establishing a national-level support group is necessary to address the various difficulties encountered when conducting trials, to provide mentoring assistance throughout the trial process, from grant acquisition to final report writing, and to act as an advocate for the simplification of funding and regulatory procedures (Alemayehu *et al.*, 2018).

## CONCLUSIONS

Human volunteers participate in clinical trials to verify the new drug's beneficial qualities. Investigational novel drugs through clinical stages I, II, III, and IV following preclinical development. These phases include a thorough discussion of pharmacokinetics, pharmacodynamic profile, side effects that may be detrimental or advantageous, adverse impact, and post-marketing surveillance. But traditional clinical trials have several drawbacks. They are slower, more expensive, and less efficient compared to alternative approaches. These trials create time and financial barriers for patients who wish to participate, making it difficult for some individuals to join. Additionally, traditional trials tend to limit overall participation and take a longer time to enroll and complete. Trials with an adaptive design are frequently more effective, instructive, and moral than trials with a typical fixed design because they frequently make better use of resources, such as money and time, and may even need fewer participants. Adaptive clinical trials, such as master protocols (umbrella, platform, and basket trials), offer greater flexibility, efficiency, and cost-effectiveness in drug development. Utilizing statistical methods like randomized clinical trials ensures rigorous evaluation of treatments, enhancing the reliability and validity of clinical trial outcomes for improved patient care and medical advancements.

## FUTURE SCOPE

Decentralized trials allow participants to complete their study activities remotely, using digital tools and devices. This can make trials more convenient and accessible for participants, and it can also help to reduce costs. Digital biomarkers are data points that can be collected through digital devices, such as wearable sensors or smartphones. Digital biomarkers can be used to track patient health and response to treatment, which can help to improve the efficiency and effectiveness of clinical trials. Real-world evidence is data collected from patients in the real world, outside of clinical trials. Real-world evidence can be used to supplement data from clinical trials, and it can also be used to track the long-term safety and effectiveness of treatments.

Patient-centered design is an approach to trial design puts the patient at the center of the process, and it seeks to ensure that trials are conducted in a way that is ethical, efficient, and patient-friendly. Precision medicine approach to medicine uses genetic and other data to tailor treatments to individual patients. Precision medicine has the potential to revolutionize clinical trials by making them more targeted and effective. Regulatory convergence is the trend towards harmonization of regulatory requirements across different countries. Regulatory convergence could make it easier to conduct clinical trials across borders, which could lead to faster drug development and access to new treatments for patients.

**Acknowledgement.** We are extremely grateful to our beloved parents. There constant motivation and support helped us to complete this review article in a stipulated period of time.

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**How to cite this article:** Anwesha Bhattacharya and Ritobrata Chandra (2023). A Comprehensive Review of Innovative Clinical Trial Strategies. *Biological Forum – An International Journal*, *15*(5a): 377-387.