BJMHR
British Journal of Medical and Health Research
Journal home page: www.bjmhr.com

Biostatistical Methods in Contemporary Medical Research: Research Methodology, Clinical Trial Design and Emerging Applications

Tapan Kumar Mahato*
Ranchi College of Pharmacy, Namkum, Ranchi, Jharkhand – 834010, India

ABSTRACT

Statistical analysis forms the basis of evaluating biomedical research. Medical research has flourished over recent decades leading to continued advancements in understanding of theoretical and applied statistical methods in biomedicine and related fields. This article reviews and provides practical understanding of various theoretical statistics and research methodology and designs. The review deals with measures of central tendency and variability, confidence intervals, p-values, risk factors, correlation and regression, randomization, sample size, bias and errors, and reporting. Other methodologies and techniques of clinical research and trial designs, such as, blinding, missing data, sensitivity analysis and trial adaptations, are reviewed. The review considers diverse emerging research methods, including Bayesian and other innovative research paradigms, to test medical hypotheses. It reviews methods to exploit digital and other pioneering biomarkers, as well as integrated research and evolution of the biomedical sciences. The focus of this review is to maintain the central role of theory, practice, and methods of medical statistics to research and advances in biomedicine and other related disciplines. The role of technology is to facilitate medical research and provide a framework for scientific inquiry and disciplined pursuit of new knowledge.

Keywords: Biostatistics; Medical statistics; Clinical trial design; Research methodology; Statistical inference; Bayesian methods; Artificial intelligence

*Corresponding Author Name: Tapan Kumar Mahato
Received 25October 2026, Accepted 3 November 2026

Please cite this article as: Mahato TK., Biostatistical Methods in Contemporary Medical Research: Research Methodology, Clinical Trial Design and Emerging Applications. British Journal of Medical and Health Research 2026.

INTRODUCTION

Research generates data in several formats including text, tables, or graphs. However, research data are often meaningless until analyzed, and interpreted within the scope of an established methodological and theoretical framework. Various branches of statistics assist researchers to analyze data, draw scientifically valid conclusions, and communicate research findings with integrity, accuracy, and transparency. Biostatistics and other cognate disciplines sharpen researchers' focus to estimate and interpret the effects of biomedical interventions and build evidence to inform policies [1,2].

Other areas of biostatistics include the formulation of a research question, the planning of a study, selecting variables to be studied, choosing the best method of sampling, deciding the sample size, the presentation of data, selection of appropriate statistical tools, evaluation of results, and interpretation and communication of results of scientific research. The above mentioned steps are important in biostatistics in all areas of research including the health and pharmaceutical sciences. It is important to appreciate that the correct application of biostatistics in health and drug research can help determine the probable effectiveness, safety and other clinical implications of a health intervention.

Biostatistics enables researchers to see data and helps researchers build inferences beyond what the data and sample examined can directly establish. The role of software such as Excel and other statistical packages, and their ease of use, has increased the ability of researchers to implement complex statistical methodologies. Nonetheless, researchers must determine the appropriate statistical methods and appreciate the underlying theory.[5,6].

Biostatistics helps design clinical trials. Well-defined clinical-trial protocols specify relevant inclusion/exclusion criteria, comparators (if any), endpoints, sample size, and a statistical analysis plan. Designing a clinical trial involves planning the analysis and integration of different elements of the trial. Deficiencies in design of a trial cannot be addressed by employing advanced statistical methods of analysis.

This article provides an approach to an integration of various segments of medical statistics, biostatistics, clinical research methodology, and trial design. The application of these elements is demonstrated with some illustrative examples. The review intends to create understanding of some crucial elements of statistics and their role in advancement of knowledge in the field of clinical medicine. The review also aims to enhance the ability of clinicians and researchers to appreciate the importance of various aspects of clinical research and their role in evidence based clinical practice.

Literature search and evidence selection

The author extensively researched literature relating to health, medical, and pharmaceutical statistics, clinical research, and related biostatistics to formulate this narrative review. Primary sources were well-established textbooks, peer-reviewed literature, and articles covering recent methodological advances. They included relevant publications of the World Health Organization, U.S. Food and Drug Administration, and the International Council for Harmonization. To enrich the article, the author used relevant sources describing innovations in statistical methodology of clinical trials, modern developments and trends in clinical trial research, such as use of Artificial Intelligence (AI) and real-world data (RWD), Bayesian and Decentralized Clinical Trials. This article is not a systematic review or meta-analysis.

Medical Statistics and Biostatistics: Definition, Scope and Significance in Research

All types of research, especially those in medicine, health and allied sciences, deal with patients, diseases, treatments, clinical outcomes, and risk factors. For analysis of research data, in addition to core scientific knowledge and understanding, it is imperative to know and understand the principles and techniques of organization, interpretation, and analysis of statistical data. Medical Statistics provides the required framework and knowledge, while biostatistics provides a more generalized statistical outlook for research in biological and pharmaceutical sciences. Understanding both these domains of knowledge and research helps in application of evidence in healthcare and other allied professions. Moreover, both these domains help to explore the inherent research questions, clinical/trial outcomes, and clinical/biostatistical variations, especially in the context of distinguishing signal from noise.[1,2].

Biostatistics plays a pivotal role in research as it aids in the interpretation of research data in a quantitative manner. It assists in each step of the research process from framing the research question and identifying the research variables to planning the research design, collecting and analyzing research data and drawing inferences from the research data. It plays an important role in health and pharmaceutical research as the efficacy, safety and risks associated with diagnostic and other health interventions need to be evaluated in a quantitative manner.[3].

Medical statistics, biostatistics and clinical trial statistics:

Although, Medical Statistics, Biostatistics and Clinical Trial Statistics have overlapping domains, they differ in their scopes. Medical Statistics focuses on research and statistical analysis of data generated from the field of Clinical Medicine. Biostatistics, on the other hand, encompasses statistics related to various fields of biological and health related research including Epidemiology and Pharmaceutical research. Clinical Trial Statistics focuses on planning, design, conduct, and analysis of clinical and other health interventional research and trials.

Table 1: Distinction among medical statistics, biostatistics and clinical-trial statistics [1, 2, 4]

Aspect	Medical statistics	Biostatistics	Clinical-trial statistics
Primary focus	Medical and clinical data	Biological, pharmaceutical, epidemiological and health data	Data generated during clinical trials
Typical applications	Patient characteristics, diagnosis, prognosis, treatment outcomes	Experimental biology, epidemiology, pharmacy, public health and clinical research	Randomized trials, treatment comparisons, safety and efficacy evaluation
Common methods	Mean, median, percentages, confidence intervals, correlation and regression	Descriptive statistics, probability, hypothesis testing, risk measures and modelling	Sample-size calculation, randomization, effect estimation, interim and final analyses
Example	Comparing mean blood pressure before and after treatment	Estimating relative risk of disease among exposed and unexposed persons	Comparing a new antihypertensive drug with standard therapy

Significance of biostatistics in research: Statistical analysis is an essential and integral part of any research, and often forms the final step in the research process. However, thorough understanding of statistics and research methodology is vital for designing an effective research study. A deficiency in the research methodology and design, including inadequate and defective sample size, sampling strategy and research instrument and variables can render even the best research study unproductive and ineffective. Thus, the role of statistics and research methodology during the development and design of the research study is vital and essential in ensuring the integrity and correct interpretation of research study.

From calculation to research interpretation:

In research, statistical calculations are only meaningful when they answer relevant research questions. A statistically significant difference doesn't mean the difference is clinically significant. Also, a clinically significant difference may be an important outcome of research, yet the study may not be significant statistically because of a small sample size. Interpreting research should be done based on the effect size, as well as the research population and the bias associated with the research. The context of the research should also be taken into account, and a p-value should not be the only consideration.

Therefore, the proper application of biostatistics should not be the sole concern of a researcher to evaluate the mathematics of the research. Rather, the focus should be on improving the research and strengthening the conclusions with respect to the area of research interest. This, combined with the overall structure of the research, should ensure the conclusions are valid.[1,3].

Research methodology:

Linking research questions with statistical evidence:

Research methodology encompasses a set of procedures and techniques to create a framework that helps answer a research question through evidence. These procedures vary from planning the study to data collection and analysis. The type of evidence required is determined by nature of the research. In clinical and pharmacological research, adequate planning and strategy are essential to eliminate bias, and the evidence collected should be able to answer the research question. Therefore, research methodology and biostatistics are interrelated. Reliable research methodology along with pertinent biostatistics help draw pertinent and valid conclusions that affect the practice of medicine [1, 2, 3].

Core Statistical Measures and Practical Calculations in Medical Research

Usefulness of data in medical and related fields is determined by their analysis and interpretation. Data analysis and its interpretation is done by applying and interpreting the results of the statistics computed from the data. Frequency distribution, variation, standard deviation, standard error, and confidence intervals, along with probability and epidemiological risk, are some of the statistical tools used in medical and pharmaceutical research [1, 2].

Measures of central tendency:

Measures of central tendency identify a representative or central value within a dataset. The three commonly used measures are the mean, median, and mode.

The arithmetic mean is calculated as:

$$\bar{x} = \frac{\sum x}{n}$$

Illustrative example: Suppose systolic blood pressure values of five patients are 118, 122, 126, 130, and 134 mmHg.

$$\bar{x} = \frac{118 + 122 + 126 + 130 + 134}{5} = \frac{630}{5} = 126 \text{ mmHg}$$

Therefore, the mean systolic blood pressure is 126 mmHg.

The median is the middle value in a set of ordered data. In the example, the median is 126 mmHg. The mode is the most frequently occurring value in a set of data. In the case where the observed values are pulse rates of 72, 76, 76, 80 and 84, the mode is 76.

The mean is best used to summarize data that is almost symmetrical. The median is best used to summarize data that contains outliers or extreme values. Rapid calculation of the mean and median is made possible by software programs such as MS Excel, SPSS and Minitab. However, interpretation of the results remains the responsibility of the user [5, 6].

Measures of dispersion:

The variation in the collection of observations may be large even if the data is centered. Measures of dispersion show how data is spread out in a dataset.

The range is the difference between the highest and lowest observations:

$$\text{Range} = \text{Maximum value} - \text{Minimum value}$$

Using the previous blood-pressure dataset:

$$134 - 118 = 16 \text{ mmHg}$$

Thus, the range is 16 mmHg.

Low variance indicates relatively little variability on the squared measurement scale; the standard deviation expresses little variability. dispersion in the original units. A low variance doesn't always indicate data is clustered; it may also mean the observations have little variability. A low standard deviation suggests that the data is clustered. The smaller the standard deviation, the more data is clustered around the mean [1].

Table 2: Common statistical measures and their research interpretation [Source: 1, 2, 5, 6]

Measure	What it describes	Simple medical interpretation
Mean	Arithmetic average	Average blood pressure in a group
Median	Middle observation	Typical value when data are skewed
Mode	Most frequent observation	Most common blood group or symptom category
Range	Difference between maximum and minimum	Overall spread of glucose values
Variance	Squared variability around the mean	Mathematical measure of dispersion
Standard deviation	Typical spread around the mean	Variability of body weight or laboratory values
Standard error	Precision of an estimated mean	How precisely the sample mean estimates the population mean
Confidence interval	Plausible range for a population parameter	Precision surrounding a treatment effect
p value	Compatibility of observed data with a specified null hypothesis	Statistical evidence against the null hypothesis

Standard error and precision of the mean:

The standard error of the mean (SEM) estimates the precision with which a sample mean represents the corresponding population mean.

$$SEM = \frac{SD}{\sqrt{n}}$$

Suppose the mean fasting blood glucose level in 25 patients is 110 mg/dL with an SD of 15 mg/dL.

$$SEM = \frac{15}{\sqrt{25}} = \frac{15}{5} = 3 \text{ mg/dL}$$

In general, a smaller SEM indicates greater precision of the estimated sample mean and, thus, greater precision of the mean. The SEM describes the precision of the mean, whereas the SD

describes the dispersion of individual observations, but the SD measures how spread out the observations are. Therefore, low SEM and low SD may both lead to a conclusion that the mean is clustered, but SD should not be interchanged with SEM.

Confidence interval:

A confidence interval provides an estimate of the uncertainty surrounding a sample statistic. For a sufficiently large sample, an approximate 95% confidence interval for a mean can be expressed as:

$$\bar{x} \pm 1.96 \times SEM$$

Using the previous example:

110 ± 1.96(3) = 110 ± 5.88 mg/dL; approximate 95% CI: 104.12–115.88 mg/dL.

SD should not be interchanged with SEM.

Understanding the p value:

The p value is used in hypothesis tests to evaluate how consistent the data is with the assumptions of a hypothesis when the null hypothesis is being tested. A small p value usually provides evidence to reject the null hypothesis. However, a p-value does not express the size of an effect, the probability that the null hypothesis is correct, or the medical significance of the result. Therefore, the p value, in isolation, should not be used to draw a conclusion in a statistical test.

Applying the p value to medical research, if an experiment to compare two different antihypertensive drugs reports a p value of 0.03, the researcher may say that the data is statistically significant and provides evidence to support that a difference in the two drugs exists at the 5% level. However, the researcher should consider other variables to assess medical significance, including the absolute and relative decrease in blood pressure, adverse effects, other analyses, and the clinical judgment of the researcher [18].

Relative risk: Practical epidemiological example:

Relative risk demonstrates the probability of an occurrence among exposed/group 1 versus group 2 (unexposed). Example: Among 200 people in group 1 (the exposed), 40 people developed the disease. Among 200 people in group 2 (the unexposed), 20 people developed the disease.

Risk among exposed:

$$R_e = \frac{40}{200} = 0.20$$

Risk among unexposed:

$$R_u = \frac{20}{200} = 0.10$$

Relative risk:

$$RR = \frac{R_e}{R_u} = \frac{0.20}{0.10} = 2.0$$

Interpretation: People in group 1 developed the disease at a rate that is twice as high as people in group 2.

Attributable risk:

The attributable risk reflects the additional risk among exposed individuals.

$$AR = R_e - R_u$$

Using the same data:

$$AR = 0.20 - 0.10 = 0.10$$

or

$$AR = 10\%$$

Interpretation: In the case of the observed relationship, among 100 individuals in the exposed group, approximately 10 more individuals developed the disease, when compared to the group that was not exposed [4].

Practical role of statistical software:

While statistical software facilitates the analysis of data and determines statistical significance, the researcher needs to comprehend statistics and make a judgment to select the most appropriate method to analyze the data and draw the right conclusions [5, 6].

Clinical Trial Design: from Research Question to Reliable Clinical Evidence

Clinical trials aim to investigate the impacts of interventions on health and disease to provide evidence to healthcare policy and practice. Designing a clinical trial requires the integrated planning of research questions and their components, including the definition of the population, the interventions to be tested and the comparators, the outcomes, sample size, allocation, follow-up, and statistical analysis as well as of the ethical considerations of the research. Scientifically, a good clinical trial should be ethical and aligned with research priorities. Reliability, value and impact of clinical research are intertwined with the focus on the needs of the targeted population[7].

The recently updated ICH E6(R3) guideline on Good Clinical Practice makes similar considerations and proposes to improve the representativeness and generalizability of study populations[8].

Essential components of clinical trial design:

The design of a trial is based on a relevant clinical question. A useful approach to developing a statistical plan is to elaborate on the population, intervention, comparison, and outcome (PICO). For example, a research question may be formulated as follows: “In the case of hypertensive adults, does the use of Drug A compared with Drug B, in a blinded manner,

reduce systolic blood pressure by more than 10 mmHg at the end of 12 weeks?" In this example, the population is "adults with hypertension," the intervention is "Drug A," the comparison is "Drug B," and the outcome is the change in systolic blood pressure.

The protocol of a clinical trial should be transparent regarding its objective, eligibility, interventions, assessments, measurement, sample size justification, randomization, blinding, analyses, ethics, and other considerations. The recently developed SPIRIT 2025 statement defines 34 key elements of a clinical trial protocol, and emphasizes the description of interventions and trial implementation, as well as the inclusion of research participants, the public and harmonization in clinical research, and research transparency[9].

Phases of Drug Clinical Trials:

Traditionally, the development of a new drug has been considered to involve successive steps starting with evaluating the safety of the drug and ending with large-scale post-marketing surveillance. Recently, the U.S. Food and Drug Administration (FDA) has provided a different perspective by describing the various phases of clinical trials based on their objectives and the populations of interest[10].

Table 3: Simplified characteristics of clinical-trial phases [10]

Phase	Main purpose	Typical participants	Simple example
Phase I	Initial safety, tolerability, dose and pharmacokinetics	Small number of healthy volunteers or selected patients	Determining the tolerated dose of a new drug
Phase II	Preliminary efficacy with continued safety assessment	Patients with the target disease	Assessing whether a new antidiabetic drug lowers glucose
Phase III	Confirm efficacy, characterize safety and compare with standard treatment/placebo	Larger patient population	Comparing the new drug with standard therapy in several centres
Phase IV	Post-marketing effectiveness and safety surveillance	Broader real-world population	Detecting uncommon adverse effects after approval

Randomization and control groups:

Randomization helps to balance known and unknown prognostic factors and reduces selection bias. It is a way of assigning participants to groups in a clinical trial. Using a random procedure (flipping a coin for example), a 1:1 ratio would aim for balance, but in truth, complete balance cannot be certain. With 100 potential participants, randomization might assign 50 to each group.

In a clinical trial, a control group is required to evaluate the intervention. The comparator for the control group may be placebo, usual care, standard care or treatment, or any other treatment. In the case of a clinical trial, the most common design is a randomized parallel group design. Other designs may include a crossover, factorial, cluster-randomized, pragmatic, multi-arm, or an allowable adaptive design. The 2025 revision to the CONSORT

statement recognizes the necessity for extension of the core reporting standard for specific designs[11].

Blinding:

Blinding helps to prevent those involved in a study from knowing the treatment being given to the study participants. Personnel can be divided into groups, such as participants, health care personnel, persons determining the end point of the study, and persons analyzing study data. The degree of blinding used in a study is determined by what is feasible. For example, in a study of the efficacy of an antihypertensive agent, placebo can be used along with the actual drug, and the tablets can be coded, so that the persons determining the end point of the study do not unmask the treatment being given. Blinding is also important in studies of preventative measures. When blinding is not possible, for example, in a study of a new physical therapy, the assessor determining the outcome should be blinded to reduce bias.

Sample size and statistical power:

When there is inadequate sample size, large differences among groups may go unmeasured. On the other hand, if sample size is too large, it would be a waste of time and resources. The ICH guidelines state that for clinical trials, the sample size should be determined based on the expected effect of the treatment and variances in the study [12]. For two groups comparing a continuous outcome, an illustrative sample-size formula is:

$$n = \frac{2\left(Z_{\alpha/2} + Z_{\beta}\right)^2 \sigma^2}{\Delta^2}$$

where n is the approximate number required per group, σ is the expected standard deviation, and Δ is the clinically meaningful difference.

Practical example: Suppose a trial is designed to detect a 5-mmHg difference in systolic blood pressure, assuming SD = 10 mmHg, two-sided α = .05 and power = 80%.

$$n = \frac{2(1.96 + 0.84)^2(10)^2}{(5)^2}$$

$$n = \frac{2(7.84)(100)}{25} = 62.72$$

Therefore, approximately 63 participants per group are required.

If a 10% dropout rate is anticipated:

$$n_{adjusted} = \frac{63}{1 - 0.10} = 70$$

Therefore, to estimate statistical power for 80% statistical power, a total of approximately 140 participants should be enrolled, with 70 participants in each group.

Statistical analysis plan and outcome interpretation:

The finalization of the statistical analysis plan (SAP) should precede the evaluation of results for any comparisons across treatment groups. There are several aspects of the SAP that should be prespecified, including the analysis population and the primary estimands. Prespecified SAPs help decrease the likelihood of employing post-hoc analyses and drawing post-hoc conclusions. Although the objective of the trial may be prespecified, the estimation of the treatment effect of interest may be prespecified or post-hoc. If post-hoc, this creates the risk of selectivity, especially if the treatment effect of interest aligns with the prespecified objective of the trial. ICH E9(R1) recommends that the treatment effect of interest should be defined and articulated prior to choosing the estimator and analysis strategy. It is ideal that both treatment effect estimates and their corresponding confidence intervals are communicated [14,19].

Estimands articulate the treatment effects of interest. These effects are contextualized in consideration of the specific population, treatment, variables, events, and levels of interest. Articulating these components aids in the convergence of the analysis, sensitivities, and the clinical and statistical elements of a trial [14,19].

For example, suppose systolic blood pressure decreases by 12 mmHg with Drug A and 7 mmHg with Drug B. The estimated treatment difference is:

$$12 - 7 = 5 \text{ mmHg}$$

From a clinical perspective, a difference of 5 mmHg is likely clinically important. However, from a statistical perspective, the 95% confidence interval may range from 2 mmHg to 8 mmHg. The results of a clinical trial should inform the clinical team of the potential benefits and risks of a treatment.

From protocol to publication:

In the context of a clinical trial, the same principles and standards should govern the research question, development of the study protocol, clinical trial conduct and analysis, and publication of the results. SPIRIT 2025 and CONSORT 2025 provide relevant guidelines for protocols and completed clinical trials, respectively [9, 11].

The emphasis in this section is on the importance of incorporating statistics at the design stage of the clinical trial rather than considering statistics after the data collection stage. Accomplishing a trustworthy clinical trial requires evaluation and analysis of a broad spectrum of factors, including pre-specification of the trial, type of randomization, sufficient sample size, assessment of the outcomes, integrity of the trial, and interpretation of the results.

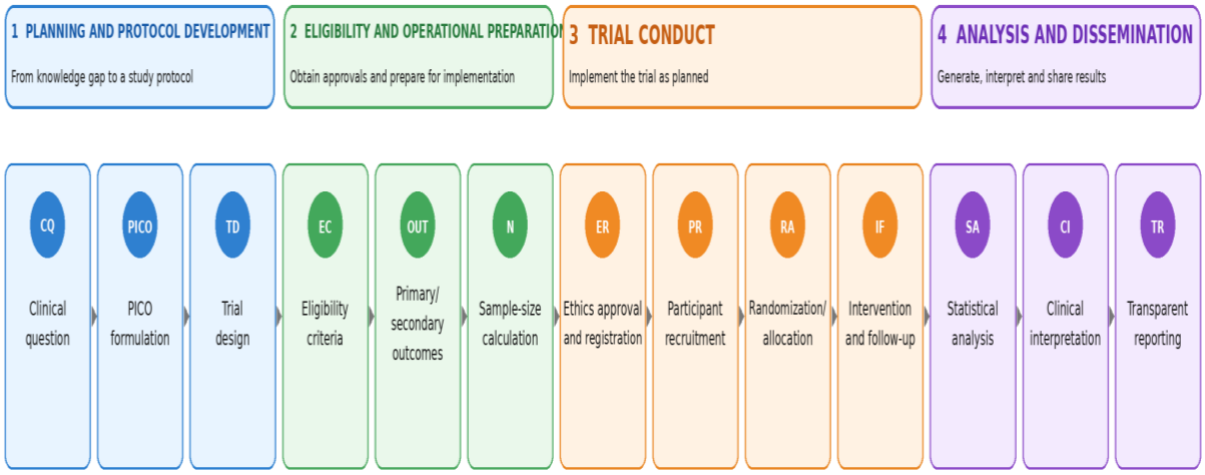


Figure 1: Simplified pathway of clinical-trial design [7, 8, 9, 11]

Selection of appropriate statistical tests and interpretation of clinical data

Various considerations affect the choice of statistical method, for example, study objective, type of outcome, number of study groups, dependence of study observations, the nature of the data distribution, research study design, and assumptions of the statistical method. Although advanced statistical software may be able to perform analysis of very large data sets in a short time, making inference about data sets still requires selecting a statistical method consistent with the design and process that generated the data set, and interpreting the output in the context of the clinical study [1,5,6].

Prior to data analysis, the researcher may want to determine the nature of study observations, i.e., continuous, count, time to event, or ordinal, and the type of relationship, if any, between the study observations. The Researcher may also want to consider and justify plausible parameters of the study population. The Researcher may need to take other study design aspects, such as covariance and study interactions, into account.

There are numerous techniques to analyze repeated observations, long-term or interval-censored outcomes, and clustered outcomes. Furthermore, the researcher must define the analyzable unit to select the appropriate statistical method. It is important to analyze a given unit of interest from multiple, complementary perspectives.

Table 4: Selection of commonly used statistical tests in medical research [1, 2, 5, 6, 18]

Research situation	Appropriate test	Simple medical example
Compare mean of two independent groups	Independent *t*-test	Mean blood pressure in Drug A vs. Drug B groups
Compare mean before and after treatment in same patients	Paired *t*-test	Fasting glucose before and after 8 weeks of therapy
Compare means of three or more groups	One-way ANOVA	Mean cholesterol levels in placebo, low-dose and high-dose groups
Compare categorical proportions	Chi-square test	Adverse-event occurrence in treatment vs. control groups
Measure linear association	Pearson correlation	Relationship between BMI and

between two continuous variables		systolic blood pressure
Predict outcome from one or more variables	Linear or logistic regression	Predicting blood pressure from age, BMI and treatment
Compare two independent groups when data are non-normal	Mann–Whitney U test	Pain scores between two treatment groups
Compare paired non-normal observations	Wilcoxon signed-rank test	Symptom score before and after intervention
Compare three or more non-normal independent groups	Kruskal–Wallis test	Median biomarker level across three treatment groups

Continuous data are often analyzed using parametric statistical methods. An independent samples t-test is used to analyze means from two different sample populations, and a paired t-test is used to evaluate means from the same sample population on two different occasions. The use of one-way ANOVA is comparable to that of the independent samples t-test. It involves the comparison of means from 3 or more sample populations. When there is a need to make several comparisons, the potential for a type 1 error needs to be considered in the analysis. A properly prespecified confirmatory analysis should control the Type I error rate; exploratory analyses require cautious interpretation.[28].

The chi-square test is used in the analysis of the relationship between categorical variables. When the cell count in the contingency table is small, the Fisher exact test may be used. If one wishes to determine whether the difference in the proportion of adverse events observed between patients receiving Drug A and Drug B is statistically significant, the Fisher exact test may be appropriate. Logistic regression may also be used in a similar fashion.

Correlation and regression analyze different types of questions. Correlation quantifies how linearly associated two continuous variables are and can be done using the Pearson correlation coefficient. Just because two variables have a correlation, it does not mean that one variable causes the other to occur. In regression, the goal is to describe or explain an occurrence of a variable using one or more other variables. This is also called an adjusted or estimated association. The treatment effect is the change in the outcome of an association. If the outcome of the occurrence is continuous, then a regression model can estimate the associated treatment effect. A similar regression model can also be created to explain a binary outcome.

Regression models are created using various assumptions which are not always true in the real world. The adequacy of a regression model should be tested using different methods such as diagnosis and model validation. Calibration and other tests should also be performed to ensure that a regression model is behaving as expected. Additionally, assessment of a statistically significant result should depend on other factors such as the size of the effect of the association, the confidence of the result, how robust the model is, the baseline risk of the

group, whether there are adverse events, and other assumptions and considerations of the regression model [18].

Common Statistical Errors, Bias, Missing Data and Good Reporting Practices

There are numerous ways medical research can be designed or conducted so that even the most appropriate statistical methods will not avert erroneous or misleading conclusions. Examples of such methods and practices are failure to recognize bias and confounding; unwarranted assumptions regarding data; inadequate attention to the adequacy of the study design, the method of data analysis, and the kind of data to be analyzed; and lack of adjustment for multiplicity of testing.[3-5] These aspects and others need to be carefully considered and addressed prior to performing the research rather than at the end of the research after data have been collected [1, 2].

Common Statistical Errors in Medical Research:

Statistical errors in research can occur at many stages including the choice of an inappropriate method of analysis, neglect of assumptions of the methods used, the use of inappropriate descriptive methods, placing unwarranted emphasis on P values, and the lack of justification for the performance of multiple tests of significance. Sometimes an erroneous conclusion of statistical significance leads to the premature acceptance of a new research hypothesis.

Table 5: Common statistical problems and recommended practice [1, 2, 11, 14, 18, 21, 22]

Problem	Possible consequence	Recommended approach
Wrong statistical test	Invalid inference	Select test according to outcome type, groups and distribution
Reporting only *p* values	Magnitude of effect remains unclear	Report effect size and 95% CI
Confusing SD with SEM	Misrepresentation of variability	Use SD for data variability and SEM for precision of the mean
Multiple unplanned comparisons	Increased false-positive findings	Prespecify analyses and address multiplicity
Ignoring missing data	Biased treatment estimates	Describe extent, reasons, assumptions and analytical method
Post-hoc subgroup analysis	Spurious associations	Distinguish prespecified from exploratory analyses
Correlation interpreted as causation	Incorrect causal conclusion	Consider design, temporality and confounding
Selective outcome reporting	Distorted evidence	Report prespecified outcomes transparently

Bias and confounding:

Bias is a systematic deviation from the truth introduced during study design, conduct, analysis, or reporting. Major forms include:

- Systematic differences in the members of comparison groups due to the way the members are selected or the way the members remain in the comparison groups.

- Systematic differences in measurement of exposure or in measurement of outcome due to inadequacy in the research design.
- Systematic differences in members of comparison groups due to the way the members are lost to follow up.
- Systematic differences in the members of comparison groups due to the way research outcomes are reported.
- Differences in intervention delivery among the comparison groups due to the way members of the comparison groups are selected to receive an intervention.

Confounding occurs when an observed relationship between an exposure and an outcome is explained by a separate, related, and previously unaccounted for variable. There are several design-based and analytical methods that can be used to deal with confounding. Design-based methods include randomization, restriction, matching, and sampling. Analytical methods include stratification, standardization, regression and adjustment, and use of propensity scores. Methods of adjustment may lead to a more precise estimation of the effect of an exposure of interest, but a causal interpretation can not always be made.

A causal interpretation of an adjusted relationship may not always be adequate. Researchers should consider a number of things in the context of causal interpretation. These may include, but are not limited to, defining the causal contrast of interest, considering confounding based on prior knowledge, and considering different scenarios based on unmeasured confounding. To make assumptions about unmeasured confounding and to consider different scenarios, researchers may use target-trial thinking and/or trust their a priori knowledge about the causal structure of the system of interest. As another example, consider an observational study that finds a relationship between consumption of coffee and risk of developing cardiovascular disease. Smoking is a confounder in this example because smokers may consume more coffee and because, independently, smoking increases the risk of cardiovascular disease. Other design and analytical methods that may help adjust for this confounding may include stratification, matching, and regression.

Missing data:

Missing data can complicate clinical and epidemiological studies, including biases introduced by participants dropping out or not showing up for scheduled appointments, study intervention or treatment being stopped, side effects, and loss to follow-up. The impact of missing data depends on the amount of data missing, reason for the data to be missing, and the assumptions that will be made for the data analysis. A 2024 review of methodology emphasized the need to evaluate and understand the reasons data are missing and how the

data are missed (for example, missing data may be presumed to be random or may not be random) within the context of clinical research and randomized controlled trials [13].

Several methods, including multiple imputation, are available to address missing data and other forms of incomplete data. Multiple imputation is generally considered to be a useful method. However, several aspects of multiple imputation should be carefully evaluated before use and transparently reported, and the method must be interpreted and applied within the context of the study. Other methods, including extreme cases analysis, should also be considered [11].

Multiple imputation should be considered prior to other methods of analysis because, under certain conditions and assumptions, it is a valid method. Other methods, including extreme case analysis, should be considered as part of sensitivity analysis [14,21].

Sensitivity analysis:

A sensitivity analysis involves exploring the effect of changes to the study design and analysis on the main results. An example of where sensitivity analysis is applicable is on a clinical trial to assess the effect of an imputation strategy for missing outcome data. If the conclusions of the analysis are insensitive to the imputation method, then the analysis is evidence of a well-behaved trial. The ICH E9(R1) states that sensitivity analysis is of key importance, and should be conducted by the trial sponsor to assess the effects of missing data and other assumptions beyond the control of the trial [14].

Good statistical reporting practice:

There are several reporting standards for different study designs. The main example is the CONSORT (2025) and STROBE standards. The RECORD (2015) standard provides an extension to the above-mentioned standards and recommends transparency in reporting the methodology of studies that utilize routinely collected health data [23].

In addition, it is important that the statistical methods and assumptions are stated. Other details that are important in statistical reporting include sample size, effect size estimates, type of analysis performed, and explanatory statements that provide justification for the findings. Model-based analyses require the same detail, as well as assumptions regarding the reasons for model mis-specification, validity of the model, and performance of the model. Additional information regarding the sources of data, algorithms to determine eligibility of the study population, and variable definitions should be reported for observational and real-world data studies [22,23].

A useful reporting principle is:

Research question → Prespecified analysis → Appropriate statistical method → Effect estimate → Confidence interval → Clinical interpretation → Transparent reporting

Using this principle will minimize the possibility that the statistical analysis will be performed to find the answer to the research question, and will promote the role of biostatistics as the means of deriving proper and precise clinical evidence.

Future Perspectives in Medical Statistics, Biostatistics and Clinical Trial Design

It is probable that clinical research will incorporate newer statistical approaches, artificial intelligence (AI) and machine learning, Bayesian statistics, real-world data and evidence, digital and remote health, and advanced integrations, simulation, modelling, and computing. Continuous advancements in clinical research will make it imperative to incorporate biostatistical considerations to design proper studies, understand and interpret research outcomes and facilitate reproducibility and clinical relevance.

Artificial Intelligence and Advanced Analytics:

The use of artificial intelligence (AI) and other advanced analytics to obtain clinical data and evidence is quickly advancing. The U.S. Food and Drug Administration has released a policy to assess and address the risk of artificial intelligence (AI) and machine learning (ML)-based software. TRIPOD+AI and PROBAST+AI are two recently released guidelines for reporting and assessing the quality of clinical prediction and other models [24,25].

In developing a prediction model, various parameters including age, blood pressure, lipid profile, diabetes, and smoking may be considered. The model should be validated using independent data, and should be evaluated in a representative sample of patients. Care should be taken to address missing data, and to avoid data leakage and over-fitting. In addition to assessing model fit, a range of other considerations should be evaluated including calibration and discrimination. From a fairness perspective, the model should be evaluated across different ethnic groups. Transportability, transparency, and interpretability should also be evaluated. Overall, performing predictive research requires integrating different skills including biostatistics, computer science, and clinical practice [24,25].

Bayesian and Adaptive Clinical-Trial Methods:

In clinical research, focusing on a priori defined parameters of interest is paramount. Prior knowledge, or evidence, is combined with newly generated data to formulate updated estimates of the parameters. The combined evidence is expressed in the form of probability distributions. For example, this method may be useful in defining the optimal dose in a clinical trial. The FDA has published guidelines on the use of Bayesian methods in clinical research.

Clinical trial adaptiveness encompasses a range of design features. For example, sample size may be modified based on emerging data. Adjustments in the allocation ratio of randomized arms may be warranted. The inclusion of multiple operating features results in increased

complexity. Simulation is often used to evaluate the impact of design features on key trial parameters [26].

Decentralized Trials, Digital Data and Real-World Evidence:

Decentralized clinical trials collect data from different locations (e.g. participant's home, local clinic) and use different methods (e.g. mobile apps, wearable devices, telemedicine). These trials attempt to eliminate the burden on the participant. This approach, however, creates challenges to study protocols and consistent measurement of data. The guidance from the FDA states that it is important to ensure oversight and integrity of study data, especially if the clinical trial's activities are decentralized [17].

Digital technologies make it possible to collect continuous data on clinical trial participants. Other data, e.g. data collected from wearable devices, can also be used in clinical trials. Real-world data have the potential to extend clinical trial data and increase the knowledge on clinical trials. However, when real-world data are used in clinical trials, it is important to understand the evidence on data, define the outcome, understand the measurement and reproducibility of the data, and address the bias and missing data in the studied population. It is important to ensure that studies using real-world data answer the research question with the data[27].

Precision Medicine, Reproducibility and Statistical Judgment:

Medical research is focusing on using different types of data and technologies to understand what would be the most appropriate treatment for a patient. This approach also uses regression modeling and analysis to understand treatment effect at the patient level. Given the large number of potential subgroup analyses and interactions, it is important that research questions and hypotheses addressing these interactions are prespecified [28].

Reproducible reporting is vital as analyses increase in complexity and number. Processes, procedures, and plans relevant to the analysis must be documented to support the analysis and findings (e.g. prespecified plans of analyses, protocols, assumptions, processing, and deviations). The focus on describing analyses and making them available to support transparency and integrity, including allowing others to reproduce the analysis and findings, continues to be the objective of ongoing initiatives and efforts. These initiatives include the updated version of the CONSORT statement (reporting guidelines and statements for randomized clinical trials) [11].

Auto-surrogate and other artificial intelligence and software programming innovation will continue to transform data processing and research. However, the above innovations and advances will not change or alleviate the responsibilities of the clinician or scientist to define the research question, design and conduct the research (including addressing bias and

challenges), implement and interpret research findings, and develop and support knowledge. It is likely and intended that deep and multidisciplinary collaboration across the biostatistics and clinical research spectrum including the domain of science, research and information technology will continue to take center stage in medical research and innovation.

Table 6: Emerging directions in medical statistics and clinical-trial methodology [11, 15, 16, 17, 24-27]

Emerging area	Potential contribution	Major statistical challenge
Artificial intelligence	Prediction, pattern recognition, trial optimization	Bias, interpretability and external validation
Bayesian methods	Use of prior evidence and flexible inference	Appropriate prior specification
Adaptive trials	More efficient decision-making during a trial	Control of statistical operating characteristics
Decentralized trials	Improved accessibility and reduced participant burden	Data consistency, monitoring and missingness
Digital biomarkers	Continuous and real-world measurement	Validation and high-frequency data analysis

CONCLUSION

Research in biomedicine and health sciences must be based on the right methodological and biostatistical foundations and clear clinical trial design. Statistical concepts help with every step of research from defining the question and designing the study to determining the number of subjects to sample and analyzing the data. Consideration of possible bias, estimating uncertainty and interpreting data in the context of clinical relevance also involve a statistical perspective. There are several other statistical methods and concepts including estimation, regression, and prediction and their Bayesian and other alternative statistical frameworks. In addition to the conventional ways of research, methods including adaptive and real-world clinical trials, digital biomarkers, and artificial intelligence in health and medicine are rising. Modern research is characterized by the integration of numerous and increasingly sophisticated methods. This calls for a higher standard and greater focus on missing data and confounding, and providing effect estimates and/or interval estimates of uncertainty. In research, nothing can take the place of collaboration among specialists with various backgrounds including medicine, science, and statistics. Such collaboration will help develop innovations in research, clinical practice, and scientific advancement that improve health.

REFERENCES

1. Singh G, Mahato TK. Biostatistics & Research Methodology. 1st ed. Technical Publications; Pune. 2022.

2. Mahato TK, Agrawal S. Introduction. In: Biostatistics and Research Methodology. Swalife Foundation-BioPress Division; 2025. doi:10.5281/zenodo.15821997.
3. Mahato TK. Biostatistics and research methodology: pillars of evidence-based pharmaceutical and health sciences. International Journal of Pharmaceutical Medicinal Research. 2025;1(1):1-7.
4. Mahato TK, Patel AP, Sharma S, et al. Biostatistical methodologies in epidemiology: importance, distinction and computation of relative risk and attributable risk. International Journal of Pharmaceutical Science and Research. 2024;9(4):9-14. doi:10.5281/zenodo.14008151.
5. Mahato TK. Biostatistical software: Microsoft Excel, SPSS and Minitab make finding central tendency and dispersion easy and effective. Paripex - Indian Journal of Research. 2023;12(4).
6. Mahato TK. Biostatistics: simple practical way to use Microsoft Excel. World Journal of Biology Pharmacy and Health Sciences. 2023;13(3):150-155.
7. World Health Organization. Guidance for Best Practices for Clinical Trials. Geneva: World Health Organization; 2024. Available from: https://www.who.int/publications/i/item/9789240097711
8. International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use. ICH Harmonized Guideline: Guideline for Good Clinical Practice E6(R3). 2025. Available from: ICH_E6(R3)_Step4_FinalGuideline_2025_0106.pdf
9. Chan AW, et al. SPIRIT 2025 statement: updated guideline for protocols of randomized trials. BMJ. 2025;389: e081477. doi:10.1136/bmj-2024-081477.
10. U.S. Food and Drug Administration. Step 3: Clinical research. Drug Development Process [Internet]. Accessed 11 September 2026. Available from: https://www.fda.gov/patients/drug-development-process/step-3-clinical-research
11. Hopewell S, et al. CONSORT 2025 statement: updated guideline for reporting randomized trials. BMJ. 2025;389: e081123. doi:10.1136/bmj-2024-081123.
12. International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use. E9: Statistical Principles for Clinical Trials. 1998.
13. Medcalf E, Turner RM, Espinoza D, et al. Addressing missing outcome data in randomized controlled trials: a methodological scoping review. Contemp Clin Trials. 2024;143:107602. doi:10.1016/j.cct.2024.107602.
14. International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use. E9(R1): Addendum on Estimands and Sensitivity

Analysis in Clinical Trials to the Guideline on Statistical Principles for Clinical Trials. 2019.

15. U.S. Food and Drug Administration. Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products: Draft Guidance for Industry and Other Interested Parties. 2025.
16. U.S. Food and Drug Administration. Use of Bayesian Methodology in Clinical Trials of Drug and Biological Products: Draft Guidance for Industry. 2026.
17. U.S. Food and Drug Administration. Conducting Clinical Trials with Decentralized Elements: Guidance document. 2024.
18. Wasserstein RL, Lazar NA. The ASA statement on p-values: context, process, and purpose. Am Stat. 2016;70(2):129-133. doi:10.1080/00031305.2016.1154108.
19. Kahan BC, Hindley J, Edwards M, et al. The estimands framework: a primer on the ICH E9(R1) addendum. BMJ. 2024;384:e076316. doi:10.1136/bmj-2023-076316.
20. Hernán MA, Robins JM. Causal Inference: What If. Boca Raton: Chapman & Hall/CRC; 2020.
21. Sterne JAC, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ. 2009;338:b2393. doi:10.1136/bmj.b2393.
22. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ. 2007 Oct 20;335 (7624):806-808. doi:10.1136/bmj.39335.541782.AD.
23. Benchimol EI, Smeeth L, Guttmann A, et al. The Reporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. PLoS Med. 2015;12(10):e1001885. doi: 10.1371/journal.pmed.1001885.
24. Collins GS, Moons KGM, Dhiman P, et al. TRIPOD+AI statement: updated guidance for reporting clinical prediction models that use regression or machine learning methods. BMJ. 2024;385:e078378. doi:10.1136/bmj-2023-078378.
25. Moons KGM, Damen JAA, Kaul T, et al. PROBAST+AI: an updated quality, risk of bias, and applicability assessment tool for prediction models using regression or artificial intelligence methods. BMJ. 2025;388:e082505. doi:10.1136/bmj-2024-082505.
26. U.S. Food and Drug Administration. Adaptive Designs for Clinical Trials of Drugs and Biologics: Guidance for Industry. December 2019.

27. U.S. Food and Drug Administration. Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products: Guidance for Industry. August 2023.
28. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc Series B Stat Methodol. 1995;57(1):289-300. doi: https://doi.org/10.1111/j.2517-6161.1995.tb02031.x

