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ROLE OF BIOSTATISTICS AND RESEARCH METHODOLOGY IN PHARMACEUTICAL SCIENCES

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ABSTRACT

Clinical Research is a systematic study for new drugs in human subjects to generate data for discovering or verifying the Clinical, Pharmacological (including pharmacodynamic and pharmacokinetic) or adverse effects with the objective of determining safety and efficacy of the new drug. Clinical Research is conducted in 4 Phases. Phase I trials - the new drug is administered to a small number, around 20-80 healthy, informed volunteers under the close supervision of a doctor is to determine whether the new compound is tolerated by the patient's body and behaves in the predicted way. Phase II trials – the medicine is administered to a group of approximately 100-300 informed patients to determine its effect and also to check for any unacceptable side effects. Phase III trials - between 1000 and 5000 patients use statistics to analyze the results. Statistics is a major tool in pharmacological research that is used to sum up experimental data in terms of central tendency like mean or median and variance like standard deviation, standard error of the mean, confidence interval or range but more importantly it authorize us to managing hypothesis testing. It is the science that helps in control medical uncertains. It is consist of different steps like generation of hypothesis, collection of data and importance of statistical analysis in medical reasearches and experimental pharmacologyClinical Trial Methodology emphasizes the importance of statistical thinking in clinical research and presents the methodology as a key component of clinical research. Selection of the proper statistical test depends on the type and number of variables and whether parametric conditions are met. Thus Biostatisticians are those who perform statistical programming, design, and analysis for clinical trial projects. Planning, coordinating and providing statistical analyses, summaries and reports of studies is also a part of their job profile. They are also responsible for New Drug Applications and Biological License Applications submissions.

KEYWORDS: Biostatistics, Clinical research, ANOVA, Research methodology.

INTRODUCTION

Biostatisticians are in high demand due to their various responsibilities in scientific data. They also collaborate with informatics, experts, scientists, and researchers for various functions. They consider the variables in subjects like patients, communities, or population to understand them and also make sense of different sources of variation. It is to achieve their ultimate goal of solving problems in public health by disentangling the received data and make valid inferences. It is the reason they are in demand in government agencies and legislative offices. Their research is used often to influence changes at the policy-making levels. The responsibilities of Biostatisticians are To determine the ways to utilize the vast information and statistics obtained through various sources like genomics, clinical trials, experimental studies and observational and longitudinal studies for public health, Being specialists of data evaluation, they take complex and mathematical findings of clinical trials and research related data.[1] They then translate them into variable information to make public health decisions. Biostatisticians are required to develop statistical methods for the following are Clinical trials to study and evaluate treatments, screening and prevention methods in the population (e.g. Evaluating protocol in terms of study rationale, study objectives, study design, sample size calculation, statistical analysis of primary endpoints, statistical analysis of secondary endpoints, treatment of missing data, informed consent, insurance issues, economic issues), Epidemiological studies of the origins of disease in humans, Spatial studies of the geographical distribution of disease and risk factors, Genomics which is the study of the biological activity of genes as they relate to disease and treatments, Human genetics a study of the genetic differences among diseases and disease states. Many students studying medicine find it unnecessary in their initial years of study to learn

statistics. But the reality is many profound doctors feel the need biostatistics since in the time of their study it was not in the medical study curriculum.[2] The doctors need to study biostatistics not only for researchers but also to enhance their reading capability of medical literature. Only with the introduction of evidence-based medicines as a cornerstone for medical management, biostatistics came into vital prevalence.

All systematic researches carried out on human beings to generate data for discovering or verifying the pharmacological, clinical or adverse effects with the objective of determining efficacy and safety of the new drug are called clinical researches. They bring in the following benefits to humankind are Assess the relative benefits of competing therapies, Investigating proposed medical treatments, Establishing optimal treatment combinations, Improving knowledge of disease, Developing diagnostic methods, New treatments & medical devices. Guidelines of evidence-based medicine are squarely depended on meta-analysis. It is, in turn, is based on many randomized controlled clinical types of research. Only this will provide rock-solid evidence to help doctors in making decisions on the best management options for patients. A firm understanding of statistical methods only will facilitate the understanding of the randomized clinical research methods and results. Hence biostatistics plays an important role in evidence-based medicine, which is the base for doctors to recommend treatments for patients now. Biostatistics has an important role in both designing a pharmaceutical experiment and evaluating its result. Randomization techniques are essentially important in designing an experiment. The goal of randomization is transforming systematic errors into random errors and confirming comparability among experimental groups. Randomization also provides a rationale for applying statistical tests. Combining randomization techniques with blinding and local control enables us to construct a scientifically reliable and effective experiment. An appropriate statistical analysis absolutely depends on the method of randomization. In order for a pharmacological study to be successful, it is very important to consider statistical aspects in the designing stage.[3]

Scope and Direction

The focus of this guidance is on statistical principles. It does not address the use of specific statistical procedures or methods. Specific procedural steps to ensure that principles are implemented properly are the responsibility of the sponsor. Integration of data across clinical trials is discussed, but is not a primary focus of this guidance. Selected principles and procedures related to data management or clinical trial monitoring activities are covered in other ICH guidelines and are not addressed here. This guidance should be of interest to individuals from a broad range of scientific disciplines. However, it is assumed that the actual responsibility for all statistical work associated with clinical trials will lie with an appropriately qualified and experienced statistician, as indicated in ICH E6. The role and responsibility of the trial statistician (see Glossary), in collaboration with other clinical trial professionals, is to ensure that statistical principles are applied appropriately in clinical trials supporting drug development. Thus, the trial statistician should have a combination of education/training and experience sufficient to implement the principles articulated in this guidance. For each clinical trial contributing to a marketing application, all important details of its design and conduct and the principal features of its proposed statistical analysis should be clearly specified in a protocol written before the trial begins.[4] The extent to which the procedures in the protocol are followed and the primary analysis is planned a priori will contribute to the degree of confidence in the final results and conclusions of the trial. The protocol and subsequent amendments should be approved by the responsible personnel, including the trial statistician. The trial statistician should ensure that the protocol and any amendments cover all relevant statistical issues clearly and accurately, using technical terminology as appropriate. The principles outlined in this guidance are primarily relevant to clinical trials conducted in the later phases of development, many of which are confirmatory trials of efficacy. In addition to efficacy, confirmatory trials may have as their primary variable a safety variable (e.g. an adverse event, a clinical laboratory variable or an electrocardiographic measure), a pharmacodynamic or a pharmacokinetic variable (as in a confirmatory bioequivalence trial). Data are the first thing which pops out on the head when we talk about any kind of analysis. Since we are dealing with data for analysis, we should know the basic concepts of it. Data are the actual pieces of information that we collect through our process or experiment. It can be categorized into categorical and numerical data. Categorical data are defined in categories or groups. For e.g. Male or Female, Yes or No, etc. Numerical data are further classified into Discrete and Continuous data. Discrete data are the data which take certain values. For e.g. No of patients, Devices, etc. Continuous data are the data which can take any values either fractional or decimal. For e.g. Blood pressure level, Height and Weight of the patient, etc.[5]

Sampling is a method used in Statistical Analysis of a data where a specific number of samples are taken from a population for a study. For e.g. Health Ministry wants to know the opinion or suggestions of recently implemented health programme in Karnataka. Here the population – Karnataka and sample – Bangalore, Mysore, Mangalore, Hubli, etc. Hypothesis testing is a method to determine whether the results are statistically significant or not. In simpler words, the process of drawing inferences (making decisions) about the sample with regards to the population as a whole is known as Hypothesis Testing. Measurement System Analysis helps us to detect the amount of variation exists within a measurement system. Suppose during the initial clinical trial phase of a particular medicine, "If the data are not taken properly?" And move forward for

further analysis. Then "What would be consequences of it?" Obviously, it may fail later on final phases.[6]

Considerations for Overall Clinical Development
Development plan

The broad aim of the process of clinical development of a new drug is to find out whether there is a dose range and schedule at which the drug can be shown to be simultaneously safe and effective, to the extent that the risk-benefit relationship is acceptable. The particular subjects, who may benefit from the drug, and the specific indications for its use, also need to be defined. Satisfying these broad aims usually requires an ordered programme of clinical trials, each with its own specific objectives (see ICH E8). This should be specified in a clinical plan, or a series of plans, with appropriate decision points and flexibility to allow modification as knowledge accumulates. A marketing application should clearly describe the main content of such plans, and the contribution made by each trial. Interpretation and assessment of the evidence from the total programme of trials involves synthesis of the evidence from the individual trials. This is facilitated by ensuring that common standards are adopted for a number of features of the trials such as dictionaries of medical terms, definition and timing of the main measurements, handling of protocol deviations and so on.[7] A statistical summary, overview or meta-analysis may be informative when medical questions are addressed in more than one trial. Where possible this should be envisaged in the plan so that the relevant trials are clearly identified and any necessary common features of their designs are specified in advance. Other major statistical issues (if any) that are expected to affect a number of trials in a common plan should be addressed in that plan.

Confirmatory trial

A confirmatory trial is an adequately controlled trial in which the hypotheses are stated in advance and evaluated. As a rule, confirmatory trials are necessary to provide firm evidence of efficacy or safety. In such trials the key hypothesis of interest follows directly from the trial's primary objective, is always pre-defined, and is the hypothesis that is subsequently tested when the trial is complete. In a confirmatory trial it is equally important to estimate with due precision the size of the effects attributable to the treatment of interest and to relate these effects to their clinical significance. Confirmatory trials are intended to provide firm evidence in support of claims and hence adherence to protocols and standard operating procedures is particularly important; unavoidable changes should be explained and documented, and their effect examined. A justification of the design of each such trial, and of other important statistical aspects such as the principal features of the planned analysis, should be set out in the protocol. Each trial should address only a limited number of questions. Firm evidence in support of claims requires that the results of the confirmatory trials demonstrate that the investigational product under test has clinical benefits. The confirmatory trials should therefore be sufficient to answer each key clinical question relevant to the efficacy or safety claim clearly and definitively. In addition, it is important that the basis for generalisation to the intended patient population is understood and explained; this may also influence the number and type (e.g. specialist or general practitioner) of centres and/or trials needed.[8] The results of the confirmatory trial(s) should be robust. In some circumstances the weight of evidence from a single confirmatory trial may be sufficient.

Exploratory trial

The rationale and design of confirmatory trials nearly always rests on earlier clinical work carried out in a series of exploratory studies. Like all clinical trials, these exploratory studies should have clear and precise objectives. However, in contrast to confirmatory trials, their objectives may not always lead to simple tests of pre-defined hypotheses. In addition, exploratory trials may sometimes require a more flexible approach to design so that changes can be made in response to accumulating results. Their analysis may entail data exploration; tests of hypothesis may be carried out, but the choice of hypothesis may be data dependent. Such trials cannot be the basis of the formal proof of efficacy, although they may contribute to the total body of relevant evidence. Any individual trial may have both confirmatory and exploratory aspects. For example, in most confirmatory trials the data are also subjected to exploratory analyses which serve as a basis for explaining or supporting their findings and for suggesting further hypotheses for later research. The protocol should make a clear distinction between the aspects of a trial which will be used for confirmatory proof and the aspects which will provide data for exploratory analysis.[9]

In the earlier phases of drug development the choice of subjects for a clinical trial may be heavily influenced by the wish to maximise the chance of observing specific clinical effects of interest, and hence they may come from a very narrow subgroup of the total patient population for which the drug may eventually be indicated. However by the time the confirmatory trials are undertaken, the subjects in the trials should more closely mirror the target population. Hence, in these trials it is generally helpful to relax the inclusion and exclusion criteria as much as possible within the target population, while maintaining sufficient homogeneity to permit precise estimation of treatment effects. No individual clinical trial can be expected to be totally representative of future users, because of the possible influences of geographical location, the time when it is conducted, the medical practices of the particular investigator(s) and clinics, and so on.[8,9] However the influence of such factors should be reduced wherever possible, and subsequently discussed during the interpretation of the trial results.

Primary and secondary variables

The primary variable ('target' variable, primary endpoint) should be the variable capable of providing the most clinically relevant and convincing evidence directly related to the primary objective of the trial. There should generally be only one primary variable. This will usually be an efficacy variable, because the primary objective of most confirmatory trials is to provide strong scientific evidence regarding efficacy. Safety/tolerability may sometimes be the primary variable, and will always be an important consideration. Measurements relating to quality of life and health economics are further potential primary variables. The selection of the primary variable should reflect the accepted norms and standards in the relevant field of research. The use of a reliable and validated variable with which experience has been gained either in earlier studies or in published literature is recommended. There should be sufficient evidence that the primary variable can provide a valid and reliable measure of some clinically relevant and important treatment benefit in the patient population described by the inclusion and exclusion criteria. 8 The primary variable should generally be the one used when estimating the sample size. In many cases, the approach to assessing subject outcome may not be straightforward and should be carefully defined.[10] For example, it is inadequate to specify mortality as a primary variable without further clarification; mortality may be assessed by comparing proportions alive at fixed points in time, or by comparing overall distributions of survival times over a specified interval. Another common example is a recurring event; the measure of treatment effect may again be a simple dichotomous variable (any occurrence during a specified interval), time to first occurrence, rate of occurrence (events per time units of observation), etc. The assessment of functional status over time in studying treatment for chronic disease presents other challenges in selection of the primary variable. There are many possible approaches, such as comparisons of the assessments done at the beginning and end of the interval of observation, comparisons of slopes calculated from all assessments throughout the interval, comparisons of the proportions of subjects exceeding or declining beyond a specified threshold, or comparisons based on methods for repeated measures data. To avoid multiplicity concerns arising from post hoc definitions, it is critical to specify in the protocol the precise definition of the primary variable as it will be used in the statistical analysis. In addition, the clinical relevance of the specific primary variable selected and the validity of the associated measurement procedures will generally need to be addressed and justified in the protocol. The primary variable should be specified in the protocol, along with the rationale for its selection.[11] Redefinition of the primary variable after unblinding will almost always be unacceptable, since the biases this introduces are difficult to assess. When the clinical effect defined by the primary objective is to be measured in more than one way, the protocol should identify one of the measurements as the primary variable on the basis of clinical relevance, importance, objectivity, and/or other relevant characteristics, whenever such selection is feasible.

Composite variables

If a single primary variable cannot be selected from multiple measurements associated with the primary objective, another useful strategy is to integrate or combine the multiple measurements into a single or "composite" variable, using a predefined algorithm. Indeed, the primary variable sometimes arises as a combination of multiple clinical measurements (e.g. the rating scales used in arthritis, psychiatric disorders and elsewhere). This approach addresses the multiplicity problem without requiring adjustment to the type I error. The method of combining the multiple measurements should be specified in the protocol, and an interpretation of the resulting scale should be provided in terms of the size of a clinically relevant benefit. When a composite variable is used as a primary variable, the components of this variable may sometimes be analysed separately, where clinically meaningful and validated. When a rating scale is used as a primary variable, it is especially important to address such factors as content validity, inter- and intra-rater reliability and responsiveness for detecting changes in the severity of disease.

Global assessment variables

In some cases, 'global assessment' variables (see Glossary) are developed to measure the overall safety, overall efficacy, and/or overall usefulness of a treatment. This type of variable integrates objective variables and the investigator's overall impression about the state or change in the state of the subject, and is usually a scale of ordered categorical ratings.[12] Global assessments of overall efficacy are well established in some therapeutic areas, such as neurology and psychiatry. Global assessment variables generally have a subjective component. When a global assessment variable is used as a primary or secondary variable, fuller details of the scale should be included in the protocol with respect to:

The relevance of the scale to the primary objective of the trial; The basis for the validity and reliability of the scale; How to utilize the data collected on an individual subject to assign him/her to a unique category of the scale; How to assign subjects with missing data to a unique category of the scale, or otherwise evaluate them. If objective variables are considered by the investigator when making a global assessment, then those objective variables should be considered as additional primary, or at least important secondary, variables. Global assessment of usefulness integrates components of both benefit and risk and reflects the decision making process of the treating physician, who must weigh benefit and risk in making product use decisions. A problem with global usefulness variables is that their use could in some cases lead to the result of two products being declared equivalent despite having very different profiles of beneficial and adverse effects. For example, judging the

global usefulness of a treatment as equivalent or superior to an alternative may mask the fact that it has little or no efficacy but fewer adverse effects11. Therefore it is not advisable to use a global usefulness variable as a primary variable. If global usefulness is specified as primary, it is important to consider specific efficacy and safety outcomes separately as additional primary variables.

Multiple primary variables

It may sometimes be desirable to use more than one primary variable, each of which (or a subset of which) could be sufficient to cover the range of effects of the therapies. The planned manner of interpretation of this type of evidence should be carefully spelled out.[13]

Surrogate variables

When direct assessment of the clinical benefit to the subject through observing actual clinical efficacy is not practical, indirect criteria (surrogate variables - see Glossary) may be considered. Commonly accepted surrogate variables are used in a number of indications where they are believed to be reliable predictors of clinical benefit. There are two principal concerns with the introduction of any proposed surrogate variable. First, it may not be a true predictor of the clinical outcome of interest. For example it may measure treatment activity associated with one specific pharmacological mechanism, but may not provide full information on the range of actions and ultimate effects of the treatment, whether positive or negative. There have been many instances where treatments showing a highly positive effect on a proposed surrogate have ultimately been shown to be detrimental to the subjects' clinical outcome; conversely, there are cases of treatments conferring clinical benefit without measurable impact on proposed surrogates. Secondly, proposed surrogate variables may not yield a quantitative measure of clinical benefit that can be weighed directly against adverse effects. Statistical criteria for validating surrogate variables have been proposed but the experience with their use is relatively limited. In practice, the strength of the evidence for surrogacy depends upon (i) the biological plausibility of the relationship, (ii) the demonstration in epidemiological studies of the prognostic value of the surrogate for the clinical outcome and (iii) evidence from clinical trials that treatment effects on the surrogate correspond to effects on the clinical outcome. Relationships between clinical and surrogate variables for one product do not necessarily apply to a product with a different mode of action for treating the same disease.[14]

Categorized variables

Dichotomization or other categorization of continuous or ordinal variables may sometimes be desirable. Criteria of 'success' and 'response' are common examples of dichotomies which require precise specification in terms of, for example, a minimum percentage improvement (relative to baseline) in a continuous variable, or a ranking categorized as at or above some threshold level (e.g., 'good') on an ordinal rating scale. The reduction of diastolic blood pressure below 90mmHg is a common dichotomization. Categorizations are most useful when they have clear clinical relevance. The criteria for categorization should be pre-defined and specified in the protocol, as knowledge of trial results could easily bias the choice of such criteria. Because categorization normally implies a loss of information, a consequence will be a loss of power in the analysis; this should be accounted for in the sample size calculation.

Design techniques to avoid bias

The most important design techniques for avoiding bias in clinical trials are blinding and randomization, and these should be normal features of most controlled clinical trials intended to be included in a marketing application.[15] Most such trials follow a double-blind approach in which treatments are pre-packed in accordance with a suitable randomization schedule, and supplied to the trial centre(s) labeled only with the subject number and the treatment period so that no one involved in the conduct of the trial is aware of the specific treatment allocated to any particular subject, not even as a code letter.

Applications

Biostatistics is the application of statistics in the development and use of therapeutic drugs and devices in humans and animals. Simply it is the science of data. It has huge application in pharmaceutical science and in medical technology.

In Pharmacology

To find the action of drug, a drug is given to animals or humans to see whether the changes produced are due to the drug or by chance. To compare the action of two different drugs or two successive dosages of the same drug. To find the relative potency of a new drug with respect to a standard drug.[16]

In Medicine

To compare the efficacy of a particular drug, operation or line of treatment-for this, the percentage cured, relieved or died in the experiment and control groups, is compared and difference due to chance or otherwise is found by applying statistical techniques. To find an association between two attributes such as cancer and smoking or filariasis and social class-an appropriate test is applied for this purpose. Cough in typhoid is found by chance and fever is found in almost every case. The proportional incidence of one symptom or another indicates whether it is a characteristic feature of the disease or not, to identify signs and symptoms of a disease or syndrome.[17]

In community medicine and public health

To test usefulness of sera and vaccines in the field, percentage of attacks or deaths among the vaccinated subjects is compared with that among the unvaccinated ones to find whether the difference observed is

statistically significant. In epidemiological studies, the role of causative factors is statistically tested. Deficiency of iodine as an important cause of goiter in a community is confirmed only after comparing the incidence of goiter cases before and after giving iodized salt. In public health, the measures adopted are evaluated. Lowering of morbidity rate in typhoid after pasteurization of milk may be attributed to clean supply of milk, if it is statistically proved. Fall in birth rate may be the result of family planning methods adopted under National Family Welfare Programmed or due to rise in living standards, increasing awareness and higher age of marriage.[18]

Statistical expertise in drug discovery

Researchers all over the world are searching for the next generation of drugs to combat some of the greatest health threats we face in the 21st century. The biggest problem is often finding the right molecule to fight a disease with; many of our existing drugs have been discovered more or less by accident. It can be enormously time-consuming and expensive to test new drug candidates systematically in the lab to identify the ones with promising therapeutic properties to take forward into clinical trials. A new initiative in the department of statistics offers pharmaceutical companies the tools they need to make this process dramatically quicker and more efficient. One class of proteins, antibodies, is of particular interest. Antibodies are an essential part of the immune system, since they bind to antigens (proteins or sugars) on the surface of a bacteria or virus and so mark it out as an invader. They are now being investigated for a range of uses including cancer treatment. As with other drug candidates, there are vast numbers of antibodies that could be considered. Statistical software developed by the Deane group is able to model antibodies in three dimensions and predict what properties they will have. The software helps companies to priorities which antibodies they should investigate further, and even to design entirely new antibodies.[19]

Assay data in drug discovery

As one might expect, there are usually a large number of assays used to optimize molecules and these vary in complexity and type. The primary pharmacology assays are usually related to potency against the target or phenotype. In traditional target-based projects, initial potency measurements are from simple biochemical ligand-binding assays. Compounds that show sufficient activity against the target are then run against some type of functional assay to verify the relevance of the hit.[20] The initial screen for potency is often conducted at a single concentration; molecules that prove interesting might then be followed by a dilution series of the concentration to verify that a dose-response relationship exists. To do this, the assay value is determined over a range of concentrations and a statistical dose- response model is fit to the data.[21]

Computers in medicine

The computers can be used and are used now in solving various problems in biostatistics for;

1. Collection, compilation, tabulation and diagrammatic presentation in the manner required for any size of data for completeness and accuracy.
2. Finding averages; coefficient of variation, standard deviation and standard error and percentiles, etc. of any size of data simultaneously.
3. The application of tests of significance such as 'Z', 't' and $\chi 2$, correlation and regression coefficients and other tests to find probability (P values), necessary in practice of medicine, public health and in research.
4. Construction of life tables to find longevity of life at birth and at any age such as on retirement for budgeting pension and other old age problems.
5. Probability of length of life after cancer without or after operation.
6. Chances of survival and period of survival after operation on heart such as bypass, closure of foramen ovale, repair and replacement of valves of heart, etc.
7. Successful chances of grafting of tissues such as cornea and parts of liver.
8. Survival after transplantation of heart, kidney and removal of brain tumor, etc. World Registry of such surgical operations helps in above applications.

The MINITAB, SPSS, SAS and STATA are some of the well-known statistical software packages for the personal computer, which are used for the tabulation and statistical analysis of data.[22] This software are further categorized on the basis of task performing by the software and their working principle like software assessing pharmacokinetic parameters, ligand interactions and molecular dynamic, molecular modeling and structural activity relationship, image analysis and visualizes, data analyzer and behavior analysis software. Simply they analyses data and further proceed.

SPSS

Excellent graphic user interface makes statistics analysis easier, including many most complex models. SPSS is a Windows based program that can be used to perform data entry and analysis and to create tables and graphs. SPSS is capable of handling large amounts of data and can perform all of the analyses covered in the text and much more.[23]

Minitab

A statistics package developed by some researchers to help six sigma professionals analyze and interpret data to help in the business process is called Minitab. The data input is simplified so that it can be easily used for statistical analysis and it also helps in manipulating the dataset. If trends, patterns and charts are given, those are analyzed and interpreted so that final conclusion can be made. The answers are given and those are magnified with the given products or services to help in the

business. Problem-solving is made easy and faster with the Minitab tool.[24]

It helps professionals in: Simplifying the data input for statistical analysis manipulating the dataset. Identifying trends and patterns. Extrapolating the answers to the existed problem with product/services.

STATA

Stata is powerful statistical software that enables users to analyze, manage, and produce graphical visualizations of data. It is primarily used by researchers in the fields of economics, biomedicine, and political science to examine data patterns. It has both a command line and graphical user interface making the use of the software more intuitive. This command-based statistical packages offers a lot flexibility for data analysis by just altering a different command options or writing a do-file.[25] Meanwhile, the program language keeps a simple structure, so easy to learn that the users can focus on the statistical modeling.

SAS

It is expanded as Statistical Analysis System. SAS was developed at North Carolina State University from 1966 until 1976, when SAS Institute was incorporated. SAS was further developed in the 1980s and 1990s with the addition of new statistical procedures, additional components. SAS provides a graphical point-and-click user interface for non-technical users and more through the SAS language. It is especially strong in Analysis of Variance (ANOVA), the general linear model, and their extensions.[26] These are the some software which used maximally in drug discovery and pharmaceutical industries which introduction discuss above.

CONCLUSION

Well designed and conducted investigation alone can prove or negate a hypothesis that is being tested. Statistical techniques cannot rectify mistakes due to careless or dishonest recording of data or faulty planning. The data should be collected honestly and sincerely without preconceived ideas about the outcome of interest. Biostatistician techniques can insure that the results found in the equivalent study are not only because of chance. In medical researches statistics plays an important role for superior and accurate results. A elegant and accurately conducted study is a basic requirement to achieve valid conclusion. Some methods and good practice in biostatistics must be learnt to understand their use and application in diagnosis.

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