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Article

Clinical Research in Ayurveda – Can statistics as A Scientific Discipline Help the Cause?

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Abstract: Ayurveda as a healthcare system has survived for thousands of years but continues to be dogged by reported lack of efficacy of the treatments in clinical trials. The reported lack of efficacy could be due to a real lack of efficacy (which then contradicts the survival of Ayurveda as a functional medical system enjoying considerable public patronage) or could be attributed to inadequacies in the efforts towards evidence generation or in a larger context the overall scientific conduct of research in Ayurveda. In an effort towards better evidence generation, there is an immediate need for standardizing the design, conduct and reporting of clinical trials of Ayurvedabut it is a daunting task. For this effort to benefit the scientific endeavors of Ayurveda researchers, it should allow the researchers to be able to apply Ayurveda's multi-component, individualized and inherently holistic approach. Statistical principles can benefit this effort. Statistical hypothesis testing (SHT) is central to these statistical principles and alsoaligns well with conventional scientific principles of evidence generation. Although there are challenges with SHT, good practitioners engaged in it do much more than just apply the mathematical theory behind it. As a particular example, lot of time in clinical trial designing is spent in addressing biases and designing trials prudently by minimizing the effect of such biases. SHT can benefit such an effort objectively. There is a need for Ayurveda researchers to engage deeply and mindfully about biases in study designin order to gain scientific validity and acceptability. The article highlights issues that arise in Ayurveda research, and discusses few ways of dealing with these issues using statistical principles.

Keywords: Ayurveda research; good research; hypothesis generation; hypothesis testing; managing bias and sample size

1. Introduction

Scientific research is considered to be legitimate by how it is planned and performed and not merely by its outcomes. The study design, sample size, and statistical analysis must be able to suitably assess the hypothesis set by the clinical investigator. An effective research plan requires firm, reproducible science and sound statistical methodology. Authoring the statistical component of a research plan is a multidisciplinary task. The clinical researcher, pharmacologist (if any), epidemiologist (if any) and statistician on the research team need to wisely assess the final research proposal to confirm that the science and statistics match up to each other properly. The after-effects of a defectively developed statistical methodology may result in a flawed clinical study that cannot sufficiently examine the chosen hypotheses. Statisticians offer design advice and develop the statistical methods that match to the research hypothesis [1]. The clinical researcher may not have to know how to execute complex analyses but does need to grasp the broad statistical logic behind the proposed statistical design and analysis. This leads to a more efficient and meaningful research thereby increasing the productivity of the entire research team. Collaborating with a statistician early and often,will help strengthen the study proposal and increase opportunities for scientific peer-acceptance and funding[1].

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It is important to remember that only good research can lead to good publications, which can only happen with due enquiry, methodical investigation, innovation, and hard work. Although journals on Ayurveda research have been in existence for many years, peer review process, as practiced in conventional medical research, is a relatively recent development. In academic publishing, the goal of peer review is to assess the quality of articles submitted for publication in a scholarly journal [2][3]. While there are a huge number of journals publishing research on Ayurveda, they are still believed to be in their stage of infancy. There is a need to create awareness among Ayurveda Researchers regarding these challengesand alsoto upskill them on research methodology and scientific writing skills. Overall, it has been observed that, there aren't standard/uniform guidelines that are applicable for Ayurveda journals. Though certain efforts have been attempted earlier, there is a need for streamlining these strategies [4].

The western biomedical scienceevolved by using a method that can be referred to as a*hierarchical method*, where it constructs theories to uncover new knowledge through a sequential process of answering specific questions e.g. what is the efficacy of a particular drug or what is the safety profile of a drug?[5]This method assumes a step wise approach and deals with the problem in successively conducted clinical trials in a specific sequence. The pharmacology of the molecule is ascertained at the very beginning through various studies on 'in-vitro and in-vivo' experimental models. These studies are followed by clinical trials in humans, majority of which are randomized clinical trials (RCTs) designed to study and test a specific hypothesis. The RCTs are considered to provide data which is least biased and allows for maximum generalizability. These studies could be complemented by case studies, case series, observational studies and real-world studies. This 'one step at a time' approach has worked very well in the western medicine framework.

The Ayurvedic system of medicine has been in existence for over a millennium and there isarguably a huge amount of empirical evidence base. Ayurveda uses complex treatment regimens which can consist of drugs, detox therapies, diet, exercise, etc.[6]One of the characteristics of an Ayurveda intervention is its complexity[7]. The intervention is complex due to various reasons amongst which multiple component intervention and adjustment of the components depending on the individual being treated [8]are two which make designing of Ayurvedic clinical trials a complex task. Ayurveda continues to be a popular healthcare system, which is widely used in India and the neighboring countries [9]. Clinical end points in Ayurveda are specific states of homeostasis or physiological equilibrium[10]. In contrast, in western biomedicine to a large extent, the interventions have been 'simple' which have allowed double-blind RCTs. Due to this, biases associated with selection of patients/subjects and with performance/evaluation of interventions are minimized. However there are many situations, even in the western biomedicine where these 'ideal' trials are infeasible and in these cases non randomized un-blinded trials, observational studies, case studies and case series have been used. Some examples which come to mind are evaluation of public health interventions, trials in therapeutic areas such as oncology and psychiatry, medical device trials and trials which involve invasive interventions like surgery[11]. It is now accepted that trials in these areas have biases[12] associated with them and a goal for these trials is as much about understanding the efficacy of the intervention as it is about understanding the limitations and biases associated with the trial itself. Ayurveda can learn and adapt from existing examples in the fields mentioned above, which have used non-randomized trials.Design, conduct, analysis and reporting of trials in Ayurveda using interventions that are -holistic, not reductionist is difficult and as a result calls for some sort of guidance and standardization [9]. This need is further enhanced by the sheer number of Ayurveda trials being reported in the recent past as can be verified by using any medical databases and using 'Ayurveda' or 'Ayurvedic' as a search criterion. These reports could be using case series methodology or be reported as pure observational studies with the aim of understanding, evaluating and quantifying the effects of the Ayurvedic interventions. As such there would biases associated with these trials. Guidance and standardization including use of appropriate statistical methodology should beapplied to acknowledge these biases and minimize it.

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2. Types of biases

Bias is defined as any tendency which prevents unprejudiced consideration of a question. In research, bias occurs when 'systematic error is introduced into sampling or testing by selecting or encouraging one outcome or answer over others'[9]. Understanding bias allows readers to critically and independently review the results of the study and avoid treatments that are suboptimal or potentially harmful[9]

Various kinds of biases can arise pre-trial, during trial or post-trial and can occur at various phases of the design, conduct and analyses of a clinical trial. These have been summarized in **Table 1**, which is not exhaustive but only illustrative. Certain biases are scientific in nature whereas others exist due to human behavioral factors. While some biases such as flawed design, selection bias etc. can be avoided or minimized through scientific means whereas some others such as interviewer bias, performance bias etc. can only be acknowledged and mitigated. Managing bias is a key element in designing a fit-for-purpose trial that can help us arrive at meaningful conclusions. As can be noted from the table, these biases if not acknowledged can result in conclusions that will not be reliable.

Table 1. Types of Bias[11].

Phase	Type of bias	Meaning	How to avoid
Pre-trial	Flawed design	Inappropriate study and data collection design to answer a specific scientific question	Clearly defined risk and outcome, preferably with objective or validated methods. Standardized and blinded data collection
Pre-trial	Selection bias	Systematic differences between baseline characteristics in multiple intervention arms	Select patients using rigorous criteria to avoid confounding results. Patients should originate from the same general population
Pre-trial	Channelling bias	Influence of prognostic factors or severity of illness influencing intervention assignment More problematic for non-randomized trials	Assign patients to study cohorts using rigorous criteria
During trial	Interviewer bias	Systematic difference between how information is solicited, recorded, or interpreted	Standardize interviewer's interaction with patient. Blind interviewer to exposure status
During trial	Chronology bias	Historic controls could cause this bias, if they are used as comparators A study recruits patients over a period of time, and due to this, there is a chance that patients recruited earlier and later may have differences due to changing clinical practices or new scientific knowledge which has been gained	Adjust for this bias using statistical methodology
During trial	Recall bias	The good or bad outcomes from earlier experiences tamper the patients' recollections during the treatment process	Use objective data sources whenever possible. When using subjective data sources, corroborate with medical record
During trial	Transfer bias	Unequal loss to follow up patients across intervention arms cause this bias	Carefully design plan for loss-to-follow up patients prior to the study
During trial	Exposure misclassification	Exposure is rarely continuous in real-life and intermittent drug intake is common practice and exposure misclassification can result in biased effect estimation,	Clearly adherence and compliance to drug intake needs to be planned and tracked

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		wrong conclusions and contradictory irreproducible results	
During trial	Outcome misclassification	Due to incorrect categorization of the outcome a patient gets misclassified into incorrect category	Use objective diagnostic studies or validated measures as primary outcome
During trial	Performance bias	This bias mainly occurs in surgical settings, where a surgeon's skills play an important role in the outcome	Use blinded evaluators to assess performance
After trial	Citation bias	Only submitting studies having positive results getting published and studies with negative results not getting published causes this bias This is detrimental in many ways, valuable information carried in the failed studies could be a great source for furthering the science which is denied due to this bias	Register trial with an accepted clinical trials registry. Check registries for similar unpublished or in-progress trials prior to publication
After trial	Confounding	Confounding occurs when an observed association is due to three factors: the exposure, the outcome of interest, and a third factor which is independently associated with both the outcome of interest and the exposure	Known confounders can be controlled with study design (case control design or randomization) or during data analysis (regression). Unknown confounders canbe controlled with randomization. If this is not possible, use statistics methods to match the confounders

3. Statistics as a scientific tool

In general, the framework for taking decisions while interpreting observations can be represented using a 2x2 table (**Table 2**).

Table 2. Decision making matrix.

		What decision was taken?	
		Correct	Incorrect
How decision was taken?	Knowingly	Good Science	Fraud
	Un-knowingly	Luck	Bad Science/Bad Luck–Unknown

We want to be in a situation where all our decisions are taken knowingly and turn out to be correct. We already have police and policies basedprocesses in place to deal with situations where people knowingly take incorrect decisions. Unknowingly taking the incorrect decision adds to inefficiencies and is based on luck. Health of people cannot rely on luck. The problem of un-knowingly takingdecisions, both correct and incorrect, is a difficult one to solve but that isthe problem we can attempt to solve by enhancing knowledge base of all decision makers. Standardization and use of established scientific methodology will ensure that instances of un-knowingly taking an incorrect decision would be minimized.

Many problems in research including in Ayurveda have been tackled incorrectly, possibly un-knowingly, and has resulted in sub-optimal and biased solutions. Many clinical researchers un-knowingly assumed that the best design for any clinical trial is a randomized clinical trial resulting in trials which have been reductionist in nature. They abandoned the multi-component, holistic approach of Ayurveda and blindly aped the much simpler single drug-single disease intervention models used in western medicine. The end-result of this approach has resulted in trials having interventions which are not

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used in normal clinical practice anduse of clinical end-pointswhich are not defined in terms of Ayurvedic clinical management principles [9].

One could argue that one of the major problems that is facing the Ayurveda research fraternity is the role of Type I and Type II errors and how the - the hypothesis for testing is articulated. For negative clinical trials, since most of the times a reductionist approach was used, the practitioners ignore the result stating that the full holistic treatment was never used and as such the results are biased. This basically questions the role of Type I error. Clinical intervention giving rise to the negative clinical trials continues to be used in general practice, albeit in a form as given in classical texts and not based on a reductionist approach as was tested.

Statistical principles allows us to summarize data, and using SHT, make inferences about hypotheses that have been pre-defined. Using these inferences, which come with associated errors, decisions can be taken. In other words, statistical principles aid in decision making, especially when data analyses is involved with the decision making. Bedrock of good science includes the three pillars of ethics, transparency and scientific validity. Statistical principles lend themselves towards each of these three pillars[13]. Just as an illustration, the list below provides a connection between the three pillars and some commonly used statistical principles.

Table 3. Statistical programing principles and Good Science.

Statistical Programming Principles	Clinical Research Principles
Hypotheses Testing	Scientific validity and Transparency
Confidence Intervals	Scientific validity
Sample Size	Scientific validity and Ethics
Randomization and Blinding	Scientific validity and Transparency
Bias and Bias reduction	Scientific validity and Transparency
Statistical interpretation of data	Scientific validity and Transparency
Meta-analyses	Scientific validity
Design of experiments	Scientific validity, Transparency and Ethics
Good programming principles	Scientific validity and Transparency
Validation and Quality Assurance	Transparency

In western biomedicine, statistics has played a pivotal role in better understanding of themedical phenomenon, the conduct of clinical trials and interpretation of clinicaldata; it may be desirable that these statistical principles are used for Ayurveda clinical research.

Standardization of clinical research through development of guidelines like CONSORT[12] or STROBE [14] is an effort that some agencies working in the sector are involved with. The immediate benefit of such a guideline would be of enabling the reach of Ayurveda to a wider audience and reducing the skepticism arising due to lack ofa valid scientific process. Some high level problems that these guidelines could address from a statistical viewpoint couldinclude:

- Appropriate trial design which could include choice of control group, blinding, randomization (wherever feasible)and valid sample size calculations
- Statistical designs that can address the issue of complex interventions that render randomization or blinding infeasible
- Studying interventions which could have synergistic effects (statistical interactions) and are individualized to each patient/volunteer in a clinical study
- Role of Type I and Type II error and articulating an appropriate hypothesis for testing
- Identifying a suitable approach to designing the trial. Should equivalence approach be used instead of superiority? If equivalence is used, what should be the choice of equivalence margin? How do you do equivalence testing when endpoints are not

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exactly the same for the Ayurvedic intervention and the gold standard treatment as given in western bio-medicine?

- Defining and measuring complex endpoints as 'cure' in Ayurveda which may be a specific state of homeostasis, hence difficult to measure due to its multivariate and composite nature
- Aid the study of correlation between complex endpoints defined based on Ayurvedic principles and western bio-medicine endpoints
- Enable appropriate definition of disease and inclusion/exclusion criterion based on Ayurvedic principles and analyzehow it correlates to western bio-medicine definitions
- Analyze appropriately data from studies that are non-randomized and which can potentially result in 'biased' estimates

4. Leveraging effective use of Statistical Methods

Statistical methods which can be used to minimize biases could be at the analyses stage of the trial or at the designing stage. Ideally the analyses method should be driven by the statistical design used.

*Statistical Analyses Methods:*Trials which are non-randomized but have confounders which have been measured and have a control group, standard stratification and regression techniques will allow for assessment of the intervention which is adjusted for other confounders and strata rendering it lessbiased.For stratified analyses [15] study subjects are divided into strata with similar characteristics. Intervention effects are assessed within each stratum and then the overall effect can be calculated by averaging the within-strata estimates. Averaging is done using weighted average where some characteristic of the strata is used to determine the weight. Stratification is best used when there are only one or two confounders, for e.g. age, sex and/or in case of Ayurveda it could be the subject's *prakriti*.

In regression techniques (linear regression if the outcome is continuous, logistic regression if it is binary and Cox regression if censoring occurs) estimates of each confounder's relationship to outcome is estimated. For assessment of intervention effect, adjustments are added to or subtracted from intervention effect seen without the adjustments, to account for the impact of each of the confounders to the outcome or to account for the differences in the confounders between the treatment groups.

Another method which is very powerful is the propensity scores method [16] and is useful where many confounders need to be controlled for but the data is limited. The principle is based on the fact that propensity scores capture the information about the relationship between confounders and treatment allocation (not the outcomes as is the case in stratification and regression techniques), so that selection bias is removed when comparisons are made between groups with similar propensity scores. In many Ayurveda trials, selection bias could be a major component of the overall bias due to non-randomized nature of allocating the interventions. If confounding variables or characteristics which determine the allocation are captured correctly, then the bias associated with the selection -could be removed using the propensity score method[17].

The method involves calculation for each subject their chance of receiving the experimental intervention from their baseline characteristics or in other words estimates a subject's propensity of receiving the experimental intervention based on his or her characteristic. In a randomized trial with two equal sized treatment groups, the propensity will be the 0.5 for each subject and will not depend on his or her characteristic. In non-randomized trials, for example for an Ayurveda intervention where two treatment groups are Ayurveda whole system intervention and normal western biomedicine intervention, it is likely that treatment assignment will depend on baseline characteristics. It might be that patients with diagnoses of the disease which is closer to how it is described in traditional Ayurveda texts may be more likely to receive Ayurveda intervention. In this case the average propensity score in the Ayurveda intervention group will differ from the average in

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the western biomedicine group. In this case selection bias is a problem that needs to be addressed and propensity score method can be used to do that.

All of the methods mentioned above, namely stratification, regression and propensity score techniques require that key confounders are measured and are measured accurately. Irrespective of which method is used, investigators must include detailed description of the methods thoroughly and be conscious and critical of the assumptions they must make whenever they use these methods [18]. All these need to defined and described in the protocol before the trial is conducted.

Statistical Design Methods: Randomized clinical trials are a preferred method for assessing intervention effects and more generally assessing causality, especially when they can be implemented and all assumptions required for conducting these trials are met. When they are infeasible, alternative designs permit a wider range of research questions to be answered and permit more direct generalization of intervention effects; however, when using such designs, estimates of the magnitude of the effect may be overestimated and could result in biased conclusions.

The broad aim of clinical trials within the Ayurvedic context could be split into following types:

- Category 1: To provide evidence of effectiveness
- Category 2: To provide evidence of safety
- Category 3: To provide reference/evidence for existing practice
- Category 4: To enhance the existing knowledge base for a known intervention.
- Category 5: To further the science (in case of new or modified interventions or approach)

Afore mentioned aspects if stated clearly upfront will allow the choice of the right design which could very well be a non-randomized study. Some of the more popular designs which could help in answering anyone of the above mentioned objectives are being listed here.

5. Standard trial designsrelevant in the context of Ayurveda

Cluster trials: Contamination of the control group, leading to biased estimates of effect size, is often cited as a drawback of randomized trials of population level interventions, but cluster trials [19], widely used in health services research, is one solution. Here, groups such as all patients in a particular Ayurveda center are randomly allocated to the whole system intervention or a control intervention (standard care). Care should be taken that all characteristics of the centers,for e.g. size of the center, number of Ayurveda *vaidyas* in each center, nature of activity whether primarily research or clinical services etc. are similar. Randomization of the centers should take care of balancing the above mentioned characteristics, but in case it does not, or in case non-randomized cluster design is used, methods mentioned above (stratification, regression or propensity scores) could be used.

Preference trials and randomized consent designs: Practical or ethical obstacles to randomization can sometimes be overcome by the use of non-standard designs. Where patients have very strong preferences among treatments, basing treatment allocation on patients' preferences, or randomizing patients before seeking consent, may be appropriate. In Ayurveda trials, a subjects' preference for Ayurveda intervention could be very high or low. In this case allocating Ayurveda intervention to a subject with high preference for Ayurveda might be appropriate. Note that if the above policy of allocation is used, the trial is non-randomized. Comprehensive Cohort Designs, Two Stage Designs, Randomized consent designs are various modifications of adjusting the design according to the subject's preference and could be used [13][20][21].

Observational studies (also known as nonequivalent-control-group design) have subjects that are measured at baseline and then again after the intervention. Subjects can receive a control or experimental treatment, but the rule for assignment to (selection into) treatment conditions is unknown to the researchers[22][23]. The use of nonrandomized

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observational studies is an important tool for determining the effectiveness of an intervention in routine clinical practice. Such trials can have cohort or case-control designs, which will allow for the inclusion of broader populations of patients and providers than RCTs. Due to non-random nature or non-equivalent nature of these trials with respect to the treatment groups, participants in the two groups may have different histories, or baseline and outcome measures. As such confounders must be measured carefully and correctly to minimize the biases arising due to selection of subjects or performance bias due to non-blinded nature.

Before and After Clinical Trials measure performance before and after the introduction of an intervention in the same individual and any observed differences in performance are assumed to be due to the intervention [24]. An extension of this simple design is the interrupted time series (ITS) design where multiple measures before and after the intervention are made. In contrast to simple before and after designs, ITS designs allow for assessing intervention effects as compared to underlying time trends that might coincide with the before and after measurements[24]. Addition of a control group would make the before and after trial even more robust, so for e.g. before and after time series measurements in a control and intervention group would be a good robust design in-lieu of a randomized clinical trial.

6. Two illustrations that demonstrate the challenges in clinical research in Ayurveda

Example 1: During a review of a grant proposal for 'Integrative Research on Aging and Regenerative Biology', criticism was received on design of clinical trial for a specific disease, which was equivalent to Osteoporosis in modern medicine. The proposed design just said that a pragmatic clinical trial design which incorporates holistic intervention in about 500 patients would be used. The question or comment that was made on this was 'Nonspecific complicated and diffuse with respect to clinical trials…without any rationally designed protocols under the pretext of holistic approach … focusing on individualized medication'. The challenge in this case is how do you rationally design a study which gives statistically unbiased results especially in cases where randomized, double blind studies are not possible?

In this case designs such as cluster trials where Ayurveda centers are randomized, preference trials and randomized consent designs, observational studies and before and after designs could be used. Analyses of such trials using methods as adjusting for covariates or propensity scores method have been suggested. Sample size calculations for such designs is challenging and need to be resolved. Practical implementation of such trials including drug supply management and data management issues need to be worked out.

Example 2: A recent preliminary abstract on a study on lower back problem was written as such. It is estimated that approximately 80% of the human population will suffer from lower back pain, at some point of their lives. Back ache symptoms are the most common cause of disability in those in the age group above 45 years. Modern medical treatment has its limitations in managing lower back pain. Ayurveda adopts the whole system approach and different treatment measures are planned to disrupt the pathology. Internal medications (individualized), external therapy, diet and regimens are employed. To create an evidence base, determination of optimal Ayurveda treatment, documentation of cases using standard diagnostic and assessment procedures has been taken up.Based on an open label prospective study with 54 patients getting treated for lower back pain, it was seen that 27 patients responded and 27 were non-responders which included patients who dropped out or had missing data. More chronically ill patients (17 of 29 [58%] responded compared to acutely ill patients (10 of 25 [40%]). The median duration of treatment was 4.57 vs. 3.14 weeks for responders vs. non-responders, (4.57 chronic vs. 4.14 acute). 11 responders were given physiotherapy vs. 4 for non-responders (7 chronic vs. 4 acute). Responders were suffering from lower back problem for more time compared to the non-responders (median of 12 months vs. 3 months, 24.00 months chronic vs. 1.00 month acute). The drop-out patients who did not come after baseline visit were more ill

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than any other group with median at 15.00 months. The median improvement for responders on a Quality of Life questionnaire was 50% vs. 16% for non-responders (median 56% chronic vs. 40% acute). There are a lot more patients treated in acute category who are treated for longer period but have failed to respond'.

As can be seen from the abstract, the results are complicated and difficult to summarize for recommending an optimal Ayurvedic intervention. The problem becomes more complicated as the internal medicine that is used is also individualized. Based on Ayurvedic principles they can be classified into certain categories. How do these categories influence the results needs to be determined. This is a case of complicated statistical analyses which is needed for a small experiment. In such complex scenarios, the validity of the results is largely determined by the size of the sample being tested. Sample size calculation is a key step in designing a clinical study. It is critical to understand that different study designs need different methods of sample size estimation. There is a considerable amount of literature examining sample size estimation. A lot of premier universities across the world have made free tools available online for researchers to use. These applications can be utilized by the teams while developing Ayurvedic clinical trials. These approaches would allow for better quality of clinical trial designs. A few online sample size calculators which are free and simple to use:

- http://riskcalc.org:3838/samplesize/
- https://sample-size.net/
- https://biostat.app.vumc.org/wiki/Main/StatCalc
- https://www.openepi.com/Menu/OE_Menu.htm
- More sources of free software are available elsewhere [25][26][27][28][29].

Cluster randomized controlled trials (CRCTs) are regularly used in health service assessment. Assuming an average cluster size, required sample sizes are readily computed for both binary and continuous outcomes, by estimating a design effect or inflation factor [30]. A well defined CRCT can provide answers to certain types of intervention such as those used in health promotion and educational interventions. Cluster randomization is often used to avoid 'contamination' between those receiving the intervention and those who are not[31][32][33].

In a preference clinical trial (PCT), two or more health-care interventions are compared among several groups of patients, at least some of whom have purposefully chosen the intervention to be administered to them. When blinding of interventions is difficult or impossible then the use of PCT should be considered. Researchers normally want to know whether an intervention can work for the patients who choose it. To answer the question, researchers must let patients choose[31]. Two stage PCT design allows appropriate analysis of the data from both arms of the study allows investigators to estimate the impact on study outcomes of treatment preferences that patients may have, in addition to evaluating the usual direct effect of treatment[32].

The propensity score is the probability of treatment assignment conditional on observed baseline characteristics. The propensity score allows one to design and analyze an observational (nonrandomized) study so that it mimics some of the particular characteristics of a randomized controlled trial[33].

The ideas presented above and the freely available calculators for sample size calculations provide fundamental and practical solutions for the researchers who are not aware of these avenues.

6. Conclusion

Clinical research methods in Ayurveda need to be standardized. Statistics as a science and statisticians as partners can play a significant role in this endeavor. The statistical principles that are alluded to and problems that are highlighted - Are they new or theoretically difficult to solve? The answer is clearly no. The issue is of creating a standardization framework which utilizes all the existing statistical techniques and computing power

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to move Ayurveda research forward. The framework should be such that the Ayurveda researches feel fully empowered to do a trial as they see is the best for their interventions and do not do trials which are forcibly fit into the framework of randomized clinical trials. Statisticians through their consulting skill and their ability of going into the fundamental details lend themselves as key partners in progressing Ayurvedic clinical research. Let us move towards turning the famous Mark Twain quote 'Lies, Damned Lies, Statistics' into 'Lies, Damned Lies and thereforestatistics'. This hopefully will ensure that instead of getting a correct answer for the wrong question, an approximate answer to the right question for Ayurvedic trials would be is obtained.

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