Bias in Dental Research / Dentistry.

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ABSTRACT

Bias is an inevitable part of study designs. Despite best efforts of research, scholars and authors biases are bound to occur in research methodology. The aim of this review article is to acquaint the dental authors with various types of bias and methods to reduce these in dental research. To understand the basics of different biases in dental research is hence essential to keep it to minimum in any research for the effectiveness of the study.

Keywords: Bias, Dental Research, Study designs.

INTRODUCTION

Bias in statistics means '*a tendency of an estimate to deviate in one direction from a true value.*'[1] It is a form of systematic error that can affect scientific investigations and distort the measurement process. Biased study loses its validity according to the degree of the bias.[2] Some study designs are more prone to bias. e.g. Retrospective study.

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In research there are two types of bias observed: Random bias and Systemic bias. Random Biases are those which results due to sampling variability or measurement precision. Usually occur in quantitative studies. It is very difficult to avoid it completely in precision. It can only be minimized. e. g. Antenatal vaccination may be sometimes used by some investigators as a criteria to sample pregnant females in a given population. A simple random sample may be chosen from the sampling frame consisting of a list of vaccinated expectant mothers in the area being surveyed. This method does involve taking a simple random sample, but it is not an actual simple random sample of the target population (pregnant females in the area being surveyed). It will miss females who are not vaccinated, also include some females of reproductive age group getting vaccinated because of reasons other than pregnancy (i.e. post exposure prophylaxis of tetanus) thus affecting sample. Thus, the method systematically excludes certain types of females in the area.

Systemic bias is not due to technical error, but a human error, for example, because of the improper case selection method for different groups. Not all individual get an equal chance of getting selected in either group. e. g. Suppose in an institution the head of department believes in naturopathies and for mouth ulcer he/ she usually advice some naturopathies medicine, in favourable cases to prove that naturopathy is better. Another similar bias of systemic bias is a systematic bias, so many a times it is confused with systemic bias, but the systematic bias is an error due to mathematical problems that occur randomly in research methodology.

There are different types of bias, which have an effect on the validity of research methodology. Among them the most commonly found are: Selection bias, detection bias, measurement bias, intervention bias etc.

Selection bias is likely to occur in the early stages of the trial during participant recruitment. Suppose a trial is assessing the effect of deciduous canine extraction vs. non-extraction for alleviating permanent canine impaction. If an investigator favours deciduous canine extraction, he or she might consciously or subconsciously select, for the extraction group, participants with canines in a more favourable position for eruption and vice versa. Selecting patients to include in the extraction group who are more likely to show canine eruption introduces bias by overestimating the effect of deciduous canine extraction (the intervention) on the resolution of canine impaction (the outcome).[15]

Selection bias can also occur in terms of A) Volunteer or referral Bias, B) Non respondent Bias.

Volunteer or Referral Bias: Volunteer or referral bias occurs because people who volunteer to participate in a study (or who are referred to it) are often different than non-volunteers/non-referrals. This bias usually, but not always, favours the treatment group, as volunteers tend to be more motivated and concerned about their health. E.g. people with lifestyle disease, who are volunteer for yoga & have a strong faith in it, cannot be compared to controls. It is of the high possibility that these cases will favour the treatment and create bias in the study.

Non Respondent Bias: Chances of non respondent bias to occur in a study is commonly observed in prospective study or longitudinal study where due to any reason patient does not respond to a survey, opinion of non responders may differ significantly from the people who are participating in the study.

HOW TO REDUCE SELECTION BIAS?

In research to reduce selection bias randomization should be done. The blinding process should be maintained throughout the study with best possible efforts. *e.g.* Information sent by soft copy or hard copy should be highly protected and should not be readable. Soft data should be accessible only through multiple highly secured passwords with OTP (one time password), hard copies of data should be sent to investigators through tamper proof envelope.

We should not get a false sense of security with RCTs regarding randomization. Investigators in some cases may exaggerate the effect of new interventions, allocation concealment was not carried out in most cases in which it was not reported, the majority of RCTs are at risk of exaggerating the effects of the interventions they in sealed opaque envelopes, for instance, investigators can (and sometimes do) look through the envelopes using powerful lights or even open the envelope using steam and reseal it without others noticing. [3] Despite its simplicity as a manoeuvre and its importance to reduce bias, allocation concealment is rarely reported, and perhaps rarely implemented in RCTs. Allocation concealment was reported in less than 10% of articles describing RCTs published in prominent journals in five different languages.[4]

Other biases are-
Publication bias: Investigators and sponsors are more likely to write and submit, and peer-reviewers and editors to accept, Manuscripts with positive results are generally submitted for publication. This tendency has been called *publication bias*.[5,6] There is about 80% of the published articles in general medicine with positive outcomes[7] 53%–72% in anaesthesiology,[8] 82% in dental journals,[9] and 50%–76% in alternative medicine.[10] The research

studies giving highly positive results of a new medicine, technique or investigation should be thoroughly investigated and reviewed. e.g. A large-scale trial of deworming and vitamin A that included one million children in India was completed in 2005, but was published for the first time many years later in 2013. [11] The results indicated that the deworming program was not effective in improving weight gain or reducing mortality, which is at odds with policies endorsed by powerful institutions, including the World Health Organization, the World Bank, and the Gates Foundation. Therefore, the investigators spent several years checking the trial data to ensure "the credibility of the study." [12]

To reduce publication bias methods for locating unpublished studies need to be built. These can include searching trial registers for completed and ongoing studies, searching informal publication sources, including meeting abstracts (included within Cochrane trial registers) and PhD theses, searching regulatory bodies (such as the US Food and Drug Administration (FDA) database), contacting the authors of included studies, and contacting pharmaceutical or medical device companies for further studies. Data retrieved this way can be in the form of complete manuscripts, simple data tables, answers to specific queries, study protocols, and/or full data sets from completed studies. [13]

Chronology bias: Chronology bias occurs when comparing any intervention with historic controls. Historic control are not the present data, but are used as control from past data. In chronology bias the presently collected data are compared historic control, but the result may be affected because data was collected in different time frames. The skills and experience of the operator varies may improve with time. Secular trends within the medical system could affect how the disease is diagnosed, how treatments are administered, or how preferred outcome measures are obtained. [14] e.g. To know the effect of the advanced radiological imaging system (CBCT) on morbidity and follow up of orthodontic treatment as compared to conventional x-rays (IOPA, OPG, LATERAL CEPHALOMETRY), if we analyze the data of a particular institute in different time frames then reduction in morbidity and follow up time after CBCT may be simply because of increased skill & experience of orthodontist rather than advanced radiological imaging (CBCT). Chronology bias can be minimized by conducting a prospective cohort or randomized control trials, or by using historical controls from only the very recent past.

Recall bias: It is due to the patient's inability to recall previous events properly turn effecting outcome. e.g. Many a patient complains of open bite in adult age, but they forget about the thumb sucking habit which was carried by them in early age. Due to

prolong gap between action and outcome, so many a times the real aetiology may not be clarify. Another example, in patient with high caries risk (multiple lesions ≥ 2 developed within the previous 2 yrs) the dietary intake of any refined carbohydrate or sugar level is assessed by asking the patient to fill up the diet analysis sheet of previous 3 days at least. The patient is advised to write down everything like intake of water, number of spoons of sugar in a tea or coffee, type of food and when they brush their teeth. So many a time patients not able to recall past events and the result is compromised.

Detection bias: Detection bias can occur during outcome recording and might be related to both investigators and participants. e.g. Investigators favouring 1 type of bracket compared with the other might consciously or subconsciously round up or down the plaque and periodontal index scores, depending on their preconceptions. At the participant level, observer bias is of particular importance when the outcome to be recorded is subjective and involves a response from each participant. Outcomes such as reporting of pain levels on a visual analogue scale after placement of different wire types or after taking pain medication could be modified if the patient knows the treatment group that he or she belongs to and if for some reason believes that 1 therapy is superior to the other.[15]

Measurement Biases: Measurement biases involve systematic error that can occur in collecting relevant data. Common measurement biases include instrument bias, insensitive measure bias, expectation bias, attention bias and verification or work-up bias.[16] e.g. In Orthodontics before any treatment lateral cephalometry tracing is done, angles and linear measurement are done by conventional method. This measurement quality depends on physicians, x-ray quality, and different malocclusions. 100% accuracy is rarely achieved. This type of error is very difficult to correct.
It can be sub – divided into: a) Instrument bias; b) Insensitive measure bias; c) Expectation bias; d) Attention bias

Instrument Bias: This type of bias can occur if instrument are not properly calibrated, this results in inaccurate measurements. e.g. Apex locator.

Insensitive measure bias: If instrument being used are not sensitive enough to detect important differences in the variables of interest. e.g. weighting in micrograms & fractions of micrograms accurately may have significance in some studies, but instrument used may not be sensitive to accurately measure in fractions of microgarms. e.g. Dontrix gauge which is used to measure elastic force.

Expectation bias: This bias usually occurs in the absence of blinding. Due to any reason when the observer favours the treatment outcome or any product, it usually favours whatever expectation he or she is having in their mind. e.g. If a Dentist is chosen as an investigator to study the oral hygiene between dental and medical student, Since oral hygiene is a province of the dentist, so due to expectation bias results will be altered.

Attention bias: Attention bias occurs because of an involved people's desire to perform better than others to gain attention; they may give more favourable responses thus affecting study.

Method to reduce Bias in Research is as follows:
Randomization: In a clinical, research, if treatment groups are systematically different, research results will be biased. Suppose that subjects are assigned to control and treatment groups in a study examining the efficacy of a medical intervention. If a greater proportion of subjects with co-morbidity are assigned to the control group, then the outcome of the medical intervention may be influenced by this imbalance. For proper randomization, it should be ensured that there is no prior knowledge of group assignment (i.e., allocation concealment). That is, researchers, subject or patients or participants, and others should not know to which group the subject will be assigned. If there is knowledge regarding group assignment, it will create a layer of potential selection bias that may taint the data. The basic benefits of randomization are as follows: It eliminates the selection bias, balances the groups with respect to many known and unknown confounding or prognostic variables, and forms the basis for statistical tests, a basis for an assumption of free statistical test of the equality of treatments. In general, a randomized experiment is an essential tool for testing the efficacy of the treatment.[17]

Blinding: Blinding refers to the concealment of group allocation from one or more individuals involved in a clinical research study, most commonly a randomized controlled trial (RCT). Although randomization minimizes differences between experimental and control group by equally distributing known and unknown confounding factors. It does nothing to prevent differences at treatment groups while conducting trial. This difference in treatment leads to biased estimation of results. So to optimize this bias incorporation of bias a strategy is followed, that includes blinding individual who are individual in the conduction of trial. e.g. blinding investigator, study subjects etc. Double blinding study is the best way to minimize bias in research.[18] A double blinding study refers to one in which both the investigator and the study subject are blinded to group assignment. Inappropriate blinding also leads to inaccuracy of the

results.[19] e.g. There was a study conducted in Serum IGF-1 levels as a clinical tool for optimizing orthodontic treatment timing. In this study, the observer was blinded about each patient's age and IGF-1 levels. In this study double blinding was done.[20]

Example of single blinding: There was a study which was conducted for Sellar dimension in skeletal class II subjects with different growth patterns, in this study to eliminate observer's bias all radiographs were coded. The allocated group was not known to the examiner at the time of evaluating the sellar parameters. This is a case of single blinding.[21]

Tips for blinding in trials
Blind as many persons as possible
Participants
- Practitioners (investigators, clinician, nurse, technician etc.)

- Data collectors
- Outcome adjudicators
- Data analysts

Blinding by using simple techniques
- Patients should not be informed of what group they are in, if possible
- Use independent outcome assessors

If blinding is not possible
- Standardize the treatment of the groups (apart from the intervention)
- Consider an expertise-based trial design
- Use objective, reliable outcomes if possible
- Consider duplicate assessment
- Acknowledge the limitation

BIAS AT A GLANCE

Pre Trial Bias			
Bias	Meaning	Example	How to avoid
Random Bias	Random Biases are those results which occur due to sampling variability or measurement precision.	To know expected pregnant lady from particular region, sample was selected from hospital vaccination list, there is a chance that who got vaccination rather than pregnancy might be included.	1) Large number of sample collection. 2) Investigators should be involved in collection of sample.
Selection bias	Selecting study subjects who will have better effect over comparison group.	Selection of twin block appliance for growing subjects and activator for non growing subjects for same problem.	1)Randomization 2)Allocation concealment
Bias During Study			
Volunteer Bias	Volunteers of any study cannot be the subjects of that same study.	People with lifestyle diseases, who are volunteer for yoga & have a strong faith in it, cannot be chosen as subjects.	1. Blinding
Non Response Bias	Response bias may occur when missing data are present non-randomly for study subjects.	Suppose 50 oral cancer patients were analysed and given new trial medications but only 40 patients turn out, so due to loss of data there will be disproportionate information regarding new medication effect on particular disease.	1. Blinding 2. Maintaining patient record (email ID, phone no, address)
Chronology bias	Bias occurring due to improvement of physicians owns work with time rather than any method.	If implant placement by using conventional IOPA is compared to advanced CBCT, in a particular department over a period of time by same physician than due to experience of the physician the quality will be improved over time rather than CBCT.	1. For comparison of any study it should be in same time frame.
Recall bias	Not able to remember past events where subjects opinion is prime concern.	Due to thumb sucking habit patient who have open bite in adulthood are usually not able to recall the habit due to long duration gap between habit and outcome.	1. Question should be in such way that it will be easy for patient to recall.
Expectation bias	To meet expectation change in the data.	If a dentist is chosen as an investigator to study the oral hygiene between dental and medical student, Since oral hygiene is a province of dentist, so due to expectation bias results will be altered.	Blinding
Attention Bias	Because of attention perform better than other group.	Suppose due to fewer subjects, volunteers of that study were chosen as subjects, because they know the outcome of that study they will perform better than other participants.	Blinding
Systemic Bias	It has tendency to support one outcome over other on the basis of previous perception.	Giving naturopathies medications for mouth ulcer rather than allopathic medicine due to his (physicians) believe in naturopathies.	Blinding
Instrument Bias	Difference in instrument sensitivity for same disease.	Apex locator.	1.Proper instrument selection of good quality.
Measurement Bias	Due to different view among investigator and difference in sensitivity of instrument this bias occurs.	For CVMI stages measurement CBCT is having better quality than lateral cephalometry. Improper selection of x- machine will lead to error in measurement.	1. Good quality instrument. 2. Proper knowledge about any disease 3. Randomization

Detection Bias	Recording any information the way investigator/ or participant want result.	In comparison of 2 type's bracket, investigators suppress the outcome of plaque index the bracket he/ she favours.	Blinding

Bias After Trial

Publication Bias	Publishing / supporting positive result, ignoring negative results.	A large-scale trial of deworming and vitamin A that included one million children in India was completed in 2005, but was published for the first time many years later in 2013.	1. The research should be thoroughly investigated and reviewed. 2. Methods for locating unpublished studies need to be built.

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