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Review Article

Bias in Clinical Research: A Review Article

V Srujan Kumar[1], KVNR Pratap[2], T Madhavi Padma[3], V Siva Kalyan[4] and Tejaswi Kala[5]*

[1]*Senior Lecturer, Department of Public Health Dentistry, Mamata Dental College, Khammam, India*

[2]*Professor and HOD, Department of Public Health Dentistry, Mamata Dental College, Khammam, India*

[3]*Professor, Department of Public Health Dentistry, Mamata Dental College, Khammam, India*

[4]*Reader, Department of Public Health Dentistry, Mamata Dental College, Khammam, India*

[5]*Assistant Professor, Department of Public Health Dentistry, Tirumala Institute of Dental Sciences, Nizamabad, India*

***Corresponding Author:** Tejaswi Kala, Assistant Professor, Department of Public Health Dentistry, Tirumala Institute of Dental Sciences, Nizamabad, India.

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Abstract

Bias refers to any systematic deviation in the process of collecting, analyzing, interpreting, publishing, or reviewing data that can result in results that are consistently different from the actual truth. The concept of bias has traditionally been linked to three primary interpretations: a) Prejudice of the observer (including the impact of a theory on observation) b) Bias as a systematic error of an instrument c) Bias as a result of an incorrect study design. Biases, whether acquired consciously or absorbed from cultural surroundings, have been inherent in historical research since the early origins of the field. In our review, we have elucidated the several forms of bias that can arise in epidemiological studies and have also outlined strategies to mitigate its impact. Additional research is necessary to elucidate the phenomenon of bias in research.

Keywords: Bias; Review; Clinical Research; Types of Bias

Introduction

''Bias'' is a popular word in the research literature and beyond. Biases entail deviations that are beyond chance. Understanding the sources of bias, its impact, and how it has been handled and hopefully avoided is important for grading evidence. Over time, investigators have described a large number of different biases. A vast glossary of bias terminology has been formed by the creation of new concepts over time. Certain biases are applicable to a broad range of research methodologies, investigations, and locations, whereas others are limited to certain circumstances [1].

The concept of bias has traditionally been linked to three primary interpretations: a) the preconceived notions or prejudices of the observer (including the impact of a theory on the act of observation) b) bias as a consistent error in the measurement instrument c) bias resulting from a flawed study design [3].

Bias refers to the absence of internal validity or inaccurate evaluation of the relationship between an exposure and its impact on the target population. External validity refers to the ability to apply the findings obtained in one population to other populations, indicating generalization. External validity is contingent upon internal validity, but, the existence of the latter does not ensure the former. Bias should be differentiated from random error or imprecision. Occasionally, the term bias is also employed to denote the mechanism responsible for generating a deficiency in internal validity [3].

Biases, whether acquired consciously or absorbed through cultural environments, have been present in historical research since the earliest stages of the profession [4].

This article's goal is to provide a review of the literature on bias in epidemiological research.

Bias is a process at any state of inference tending to produce results that depart systematically from the true value (Fletcher et al, 1988) [5].

Bias in epidemiological studies [6]

- Selection bias
- Information bias
- Confounding bias
- Bias in specific trials

Selection bias

Nonrandom sampling refers to the process of selecting persons, groups, or data for analysis without achieving adequate randomization. As a result, the obtained sample is not representative of the intended population for research [6].

Selection Bias		
Case Control Studies	**Cohort Studies.**	**Randomized Controlled Trials.**
Selection bias is a particular problem inherent in case-control studies, where it gives rise to non-comparability between cases and controls. In case-control studies, controls should be drawn from the same population as the cases, so they are representative of the population which produced the cases.	Selection bias is less of problem in cohort studies compared with case-control studies, because exposed and unexposed individuals are enrolled before they develop the outcome of interest.	Randomized trials are theoretically less likely to be affected by selection bias, because individuals are randomly allocated to the groups being compared, and steps should be taken to minimize the ability of investigators or participants to influence this allocation process. However, refusals to participate in a study, or subsequent withdrawals, may affect the results, if the reasons are related to exposure status [7].

Table a

Types of selection bias

Type	Description	Example
1. Prevalence-Incidence bias (Neyman bias, Selective survival bias).	This type of bias is introduced into a case control study as a result of selective survival among the prevalence cases.	The high case fatality rate in the early stages of clinically manifested coronary artery disease may invalidate the study of possible etiological factors, since the persons available for study as cases are the survivors [8].
2. Admission rate (Berksons Berkesonion) bias 1946:	It is termed after Dr.Joseph Berkson who recognized this problem. This type of bias is due to selective factors of admission to hospitals, and occurs in hospital based studies.	This type of bias is more common in observational studies in particular case control studies [8]
3. Health care access bias:	It occurs when the patients admitted to an institution do not represent the cases originated in the community. This may be due to the own institution if admission is determined by the interestof health personnel on certain kind of cases (popularity bias) [5]	
4. Length time bias:	It is an apparent increase in survival due to detecting a health condition such as cancer, at an early stage, when there is no actual effect on survival, just a longer period with the diagnosis.	Even if treatments for people with cancer are not effective, people whose cancer is detected early by screening will appear to survive longer than people without screening, whose cancer is not detected until they have symptoms [5].
5. Spectrum bias:	It is produced in the assessment of validity of a diagnostic test, when researchers included only ‘‘clear’’ or ‘‘definite’’ cases, not representing the whole spectrum of disease presentation, and/or ‘‘clear’’ or health controls subjects, not representing the conditions in which a differential diagnosis should be carried out.	
6. Survivor treatment selection bias:	In observational studies patients who live longer have more probability to receive a Certain treatment and those who die earlier may be untreated by default. These facts are the essence of an often overlooked bias, termed “survivor treatment selection bias,” which can erroneously lead to the conclusion that an ineffective treatment prolongs survival.	
7. Exclusion bias:	It occurs when controls with conditions related to the exposure are excluded, whereas cases with these diseases as comorbidities are kept in the study.	This was the explanation given for the association between reserpine and breast cancer, controls with cardiovascular disease(a common comorbidity and related to the use of reserpine) were excluded but this criterion was not applied to cases, thus yielding a spurious association between reserpine and breast cancer [5].

8. Friend control bias:	It was assumed that the correlation in exposure status between cases and their friend controls lead to biased estimates of the association between exposure and outcome.	In a matched study, with a matched analysis, there is no bias if the exposure induced risks of disease are constant over time and there are not gregarious subjects, individuals elected by more than one case [5].
9. Inclusion bias:	It is produced in hospital based case-control studies when one or more conditions of controls are related with the exposure. The frequency of exposure is higher than expected in the reference group, producing towards the null bias [5].	
10. Relative control bias:	It was assumed that the correlation in exposure status between cases and their relative controls yield biased estimates of the association between exposure and outcome.	In a matched study, with a matched analysis, there is no bias if the exposure induced risks of disease are constant over time [5].
11. Citation bias:	Articles more frequently cited are more easily found and included in systematic reviews and meta-analysis. Citation is closely related to the impact factor of the publishing journal. In certain fields, citation has been related to statistical significance [5].	
12. Dissemination bias:	When the findings of relevant studies are not disseminated, and are then not accessible, data within evidence syntheses may be considered inadequate. In addition, if non-dissemination is systematic rather than random, that is, disseminated studies and findings differ systematically from non-disseminated studies and findings, this will cause bias. Such bias could occur due to several mechanisms, and is referred to by the term dissemination bias.	The biases associated to the whole publication process, from biases in the retrieval of information (including language bias) to the way the results are reported.
13. Post hoc bias	The testing of hypothesis that the study was not designed to test, but that are suggested by the data has been referred to as Data Dredging. Finding an association by data dredging and then using the same data to test its significance may lead to unwarranted conclusions that had been termed post hoc bias [5].	
14. Publication bias:	It is regarding an association that is produced when the published reports do not represent the studies carried out on that association. Several factors have been found to influence publication, the most important being statistical significance, size of the study, funding, prestige, type of design, and study quality [5].	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 Laterin 2013 [9].
15. Response bias:	Cases with serious illness are likely to give more correct responses regarding history and current ailments compared to the controls. Some patients such as those of STDs may intentionally suppress sexual history and other information because of stigma attached to these diseases leading to response bias. Injury history may be distorted to avoid legal consequences.	If the subjects are able to exchange notes, the response to questions might alter, in some cases might even be uniform. An unsuspecting illness, death in the family, or any such drastic event may produce an extreme response. Response bias also comes under information bias [10].
16. Non-response bias:	Nonresponse bias is the bias that results when respondents differ in meaningful ways from non-respondents. The healthy volunteer effect is a particular case when the participants are healthier than the general population.	This is particularly relevant when a diagnostic manoeuvre, such as a screening test, is evaluated in the general population, producing an away from the null bias, thus the benefit of the intervention is spuriously increased [5].

Table b

Sources of selection bias are

- Paid participants may exhibit distinct characteristics compared to the general community.
- Hospital and clinical data are derived from a specific subset of the population.
- The disease or factor being investigated renders individuals unavailable for study [11].

Minimization of selection bias

- It is essential to properly identify the study population, including providing a precise definition of the study population.
- The selection of the reference group or comparison group (those not exposed or controls) is of utmost importance.

Information bias: (in measurement of exposure or outcome)

Information bias refers to the bias that occurs in a clinical study due to the incorrect classification of the level of exposure to the substance or factor being evaluated, as well as the misclassification of the disease itself.

Information bias, also known as measurement bias, occurs when crucial variables in a study (such as exposure, health result, or confounders) are measured or classified with inaccuracies [12].

Measurement errors are commonly referred to as misclassifications, and the impact of bias varies depending on the specific form of misclassification [10].

There are two types of misclassification bias.

- Differential misclassification bias
- Non differential misclassification bias

Differential misclassification bias:

Differential misclassification arises when there is unequal misclassification of exposure between individuals with and without the health outcome, or when there is unequal misclassification of the health outcome between exposed and unexposed individuals.

Non differential misclassification bias:

Non-differential misclassification refers to the situation when there is an equal misclassification of exposure across individuals with and without the health outcome, or an equal misclassification of the health outcome among individuals who are exposed and unexposed [12].

Sources of Information bias

- Subject variation
- Observer variation
- Deficiency of tools.
- Technical errors in measurement [13].

Various Information biases [14]:

- **Memory or Recall bias:** Recall bias is a type of information bias that arises from variations in the accuracy of remembering events or details between those who experienced a certain condition and those who did not, or from disparities in reporting a health outcome between individuals who were exposed to a certain factor and those who were not. Example: who have experienced a myocardial infarction may have a higher probability of retaining and recollecting specific habits or events compared to others who have not. Therefore, patients may possess a distinct recollection of previous occurrences compared to controls.
- **Telescopic bias:** This phenomenon happens when a question pertains to the recent past, typically within the last month, but it is also possible for occurrences that happened even further back to be mentioned.
- **Interviewers bias or exposure suspicion bias:** It happens when the interviewer is aware of the identities of the individuals involved in the cases. Having this prior information may prompt him to scrutinize the cases more rigorously than the controls when it comes to a positive history of a suspected causal factor [8].

Interviewer's bias is due to

- Lack of equal probing for exposure history between cases and controls (exposure suspicion bias)
- Lack of equal measurement of health outcome status between exposed and un-exposed (diagnostic suspicion bias).

Observer bias

This phenomenon arises when researchers manipulate the results of a study, encompassing exceedingly nuanced modifications in both the researchers' interactions with study participants and the selective observations made by observers. Observer expectation bias can be influenced by the understanding of the hypothesis, disease status, or exposure status, including the intervention received, which might impact data collection. Possible sources of mistake in a questionnaire might arise from the actions of interviewers, such as conducting the interview or providing assistance to respondents, even through non-verbal cues, as well as placing emphasis on certain items [5].

Reporting bias

In this study, participants have the opportunity to "collaborate" with researchers by providing answers based on their perceived areas of interest (obsequiousness bias) or when the presence of a particular scenario prompts them to share family-related information.

For example

Measures or sensitive questions that embarrass or hurt can be refused [5].

Hawthorne effect

The phenomenon was documented during the 1920s at the Hawthorne plant of the Western Electric Company, located in Chicago, IL. Participant awareness of being observed is a factor that leads to an increase in productivity or other measured outcomes. As an illustration, laboratory physicians experience an elevated level of consensus once they become aware of their involvement in a study on the dependability of diagnostic tests [5].

Lead time bias

It occurs when the duration of illness is extended due to the detection of a problem during its dormant phase. This bias is significant for assessing the effectiveness of screening. It occurs when the cases identified in the screened group had a longer duration of disease compared to those diagnosed in the non-screened group [5].

Protopathic bias

It happens when an exposure is affected by the initial (subclinical) phases of a disease. It is also generated when a pharmaceutical substance is prescribed for a first indication of a condition that has not yet been diagnosed. The sick quitter bias refers to the protopathic bias, where individuals with dangerous activities, such as high alcohol use, may stop their habits due to the development of diseases. When studying the present conduct as a risk factor, these individuals may be labelled as non-exposed, leading to an underestimation of the actual link [5].

Work up bias (verification bias)

In the evaluation of the validity of a diagnostic test, a bias is introduced when the administration of the gold standard is affected by the results of the test being assessed. Typically, the reference test is less commonly conducted when the test result is negative. This bias is exacerbated when the clinical aspects of an illness have an impact on the test results [5].

Confounding bias

A confounder is a variable that is linked to both the exposure being studied and the disease, but it is not directly involved in the cause-and-effect relationship between the exposure and the outcome. If the research group fails to take into account this link during the evaluation, possibly due to the absence of recorded confounding variables, it results in a distorted estimation of the examined risk factor. If there is no association between the risk factor and the confounder, the estimation of the effect of the risk factor will be accurate.

Illustration of confounding: Is there a causal relationship between coffee consumption and coronary heart disease? One could infer this, given the observed association. Nevertheless, individuals who consume coffee tend to be smokers more frequently than the general population. In addition to the association between coffee consumption and nicotine intake, there exists a robust causal relationship between smoking and the prevalence of coronary heart disease. Nicotine usage in this scenario acts as a confounding variable for the impact of coffee drinking on the occurrence of heart disease [15].

Confounding arises when a variable is both a risk factor for an outcome among individuals who are not exposed to a certain factor, and is also linked to the factor of interest in the population from which the outcome is derived. This variable is not influenced by the exposure or the disease itself. Confounding is a potential issue that can arise in every epidemiological investigation [5].

Confounding bias is of following types:

Confounding by group

This phenomenon occurs in an ecological analysis, when the occurrence rate of exposure in each community is compared to the disease risk in non-exposed individuals within the same community. It has the potential to generate ecological fallacy.

Consider three communities (A, B, C) with prevalence exposures of 10%, 20%, and 30%, rates of disease in non-exposed individuals of 2%, 3%, and 4%, and rates of disease in exposed individuals of 2%, 3%, and 4%, respectively. There is no correlation between the exposure and the disease, as indicated by the three relative risks being equal to one. However, an ecological analysis, which examines the relationship between the disease rate and the prevalence of exposure, does show a positive association [5].

Confounding by indication

This occurs when an intervention (therapy) is recommended due to a perceived elevated risk, unfavorable prognosis, or the presence of symptoms. In this case, the confounding factor is the indication, which is both associated with the intervention and serves as a risk signal for the condition.

In the investigation of the relationship between cimetidine and stomach cancer, the presence of peptic ulcer is regarded as a possible confounding factor. This type of bias commonly arises in observational studies, particularly those that are retrospective, when analyzing treatments. Protopathic bias is occasionally misinterpreted as confounding by indication [5].

Bias in specific trials

Bias in intervention allocation

This occurs when the distribution of interventions is not consistent across the entire population. Non-randomized trials are more common. It is recommended to hide the allocation sequence of intervention in randomised experiments. Empirical evidence indicates that trials lacking clear or sufficient concealment tend to report inflated treatment effects when compared to trials with proper concealment [16].

Compliance bias

The trials require strict adherence to the intervention, and the degree of compliance directly affects the assessment of the intervention's success.

For example, when patients with a high-risk profile cease their exercise regimens.

Contamination bias

It occurs when intervention actions inadvertently affect the control group. It skews the estimation of the intervention impact towards the null hypothesis. The higher incidence of this phenom-

enon is observed in community intervention trials due to the interconnectedness between people of diverse communities and the influence exerted by mass media, health professionals, and other factors [17].

Absence of intention to treat analysis

In randomized studies, the analysis should be conducted while maintaining participants in the group to which they were originally allocated. The primary objectives of randomization are to mitigate the effects of confounding variables and selection bias. Excluding individuals who do not follow the rules or receive an incorrect treatment from the analysis can lead to a lack of comparability between the different groups in a randomized trial. Exceptions exist to the principle of intention to treat analysis [5].

Conceptual Bias

The proposed research suffers from a lack of conceptual clarity. This provides scientists with the option to employ subjective interpretation, which may differ among individuals. Occasionally, the reasoning employed may be flawed, and at times, the very foundation of the reasoning can be erroneous [14].

Design bias

This bias arises when there is inadequate matching between the case group and control group, and when the confounding factors are not appropriately included throughout the study [14].

Instruction bias

In situations when instructions are unclear or nonexistent, investigators rely on their own judgement, which might differ among individuals and change over time [14].

Instrument bias refers to the situation where the measuring instrument is not accurately calibrated. A scale can exhibit bias by either overestimating or underestimating the true value. Another potential factor is the insufficiency of an instrument to offer a comprehensive depiction [14].

Recurring testing prejudice

In a pretest-posttest scenario, participants often retain memory of earlier questions, leading them to correct previous errors during the posttest. As a result, they may do better without the influence of the intervention. An observer can develop expertise through repeated exposure in order to elicit the correct response [14].

Mid-course bias

Occasionally, participants may need to be eliminated from the study if they experience an unrelated ailment, such as an injury, or if their condition becomes so severe that it is no longer in their best interest to continue participating in the trial. The reaction of the observed population may be modified if a new facility, such as a health center, is established or shut down during the study period. If two separate trials are being conducted concurrently within the same population, there is a possibility of one study influencing or interfering with the other. An unforeseen occurrence, such as an outbreak, can modify the reaction of individuals who are not impacted [14].

Attrition bias

Attrition bias pertains to systematic disparities between groups in the removal of participants from a research. Participants dropping out of the study result in incomplete outcome data. The nonresponse pattern can vary between different groups, with one group experiencing a higher dropout rate of severe cases, while another group mostly sees moderate cases dropping out [14].

Recording bias

There are two sorts of errors that might occur while recording, one resulting from the failure to accurately interpret the writing on case sheets. Physicians have a reputation for having handwriting that is difficult to read. This phenomenon is most likely to occur with visually similar numerals, such as 1 and 7, and 3 and 5. Hence, the data entry could potentially contain inaccuracies. The second reason is attributed to the investigator's negligence [14].

Bias resulting from insufficient statistical power

The ability of these statistical tests to identify differences or associations is heavily influenced by the number of individuals included in the sample size of the study. When the study is performed on a limited sample size, it becomes difficult to identify even a substantial difference, resulting in an incorrect negative conclusion. The conclusion can be altered when the study is conducted on a sufficient number of participants.

Data gathering bias

The population comprises all individuals who possess a specific feature of interest. Given the constraints of time and resources, it is often impractical to investigate a whole population. Therefore, we typically focus our research on a representative sample to examine a specific phenomenon of interest. Through this approach, our aim is to extrapolate the knowledge gained from a representative subset to the full population. In order to accomplish this, it is necessary for a sample to accurately reflect the characteristics of the entire population. If this condition is not met, the findings will not be applicable to a broader population, meaning that the study will lack external validity. Sampling is an essential and pivotal phase in any research [18].

During the process of data collection for research, researchers have many means via which they can inadvertently introduce bias into the study. If, for instance, certain patients have a higher or lower likelihood of participating in the study during patient recruitment, the resulting sample would not accurately represent the population under investigation. Consequently, individuals who are

less inclined to participate in the study will be inadequately represented, while those who are more inclined to participate will be disproportionately represented compared to the general population, to which the study's findings are intended to be applicable. This phenomenon is commonly referred to as selection bias. In order to guarantee that a sample accurately reflects a population, it is necessary to employ random sampling, wherein each subject has an equal chance of being selected for the study. Sampling bias can occur when the sample size is insufficient to accurately represent the target population [19].

Bias in data analysis

Bias can be introduced in data analysis when a researcher selectively analyses data in a manner that favours conclusions supporting their study premise. Bias can be created during data analysis through many options, including data fabrication, abuse, or manipulation. Here are a few examples:

- Falsely reporting data from trials that were never conducted (data falsification)
- Excluding data points that do not align with your hypothesis, such as outliers or entire groupings.
- Employing unsuitable statistical tests to analyze your data.
- Conducting numerous tests, such as pair-wise comparisons, testing multiple endpoints, and running secondary or subgroup analyses, that were not initially planned, with the intention of identifying statistically significant differences regardless of the hypothesis.

Data interpretation bias refers to the inclination of certain researchers to favorably interpret results in support of a specific theory, disregarding contradictory evidence. This might occur either deliberately or inadvertently. Fourteen

Presentation bias in results

The selection of a scale for a graph can be manipulated to make a small change appear significant or to make a large change appear insignificant. The second issue is that the researcher may simply present the inconvenient findings that oppose the main conclusion, but fails to emphasize them to the same extent as the favorable discoveries [14].

Minimising/Avoiding bias in epidemiological studies

Steps in minimizing bias [1]:

- Cultivate an impartial scientific mindset by recognizing that you are engaged in the tireless pursuit of truth in your profession.
- Provide a precise and detailed description of the situation.
- Evaluate the legitimacy of the specified target population and the groups to be included in the study, considering the aims and methodology.
- Evaluate the accuracy of the factors leading to a certain result in order to provide accurate responses to your inquiries. Be cautious of epistemic uncertainties that arise due to the limitations of knowing.
- Assess the dependability and accuracy of the measurements needed to evaluate the factors that occur before and result from a situation, as well as the other instruments you intend to use.
- Conduct a preliminary research, test the tools in advance, and modify them as necessary.
- Identify all potential confounding factors and other sources of bias, and devise an appropriate design that can effectively address most, if not all, of these biases.
- Select a representative sample, preferably using a random technique.
- Select an appropriate sample size for each group.
- Acquire the necessary skills and knowledge to effectively evaluate and analyze situations, and ensure that your colleagues also receive proper training in this regard.
- Utilize matching, blinding, masking, and random allocation as necessary.
- Supervise every phase of the research, including regular examination of the data.
- Reduce the occurrence of nonresponse and partial response.
- Verify the accuracy of the data and remove any errors in recording, entries, etc.
- Employ appropriate statistical techniques to analyze the data. Employ standardized or adjusted rates as necessary, do stratified analysis, or utilize mathematical models.
- Exercise utmost caution when composing the report and ensure that comments or opinions are clearly distinguished from the results.

Conclusion

In our review, we have elucidated the several forms of bias that can arise in epidemiological studies and have also outlined strategies to mitigate its impact. Additional research is necessary to elucidate the phenomenon of bias in research. Additional investigation into methods for reducing selection bias and elucidating the process of publication should be provided. There is a scarcity of study or understanding on the various forms of bias in dentistry research. Therefore, it is imperative to prioritize studies that elucidate methods for mitigating bias in dental research.

Bibliography

1. David Chavalarias and John PA Ioannidis. Science mapping analysis characterizes 235 biases in biomedical research". *Journal of Clinical Epidemiology* 63 (2010): 1205-1215.

2. Paolo Vineis. "History of bias". *History of Epidemiology* 47 (2002): 156-161.

3. John Wiley. "Bias overview". Encyclopedia of biostatistics (2005): 1-5.

4. Miguel Delgada Rodriguez, Javier Llorca, Bias glossary 15 (2004): 635-641.

5. Christopher J Panucci and Edwin G Wilkins. "Identifying and avoiding bias in research". National Institute of Health 126.2 (2010): 619-625.

6. Selection bias. Revolvy Quizzes (2016).

7. Biases health knowledge (2009).

8. Soben peter. "Essentials of preventive and community dentistry". 5th edition. Arya Publishers. (2009): 68-70.

9. Sandhya Jain. "Dentistry bias in dental research/dentistry". *Annals of International Medical and Dental Research* 2.5 (2016): 5-9.v

10. More than 30 types of bias. Medical biostatistics.

11. Lorraine K Alexander., *et al*. "Selection bias". Department of epidemiology. 2nd edition.

12. Sources of systematic error or bias: Information bias.

13. www.ump.edu.pl/files/8_483_errors_in_epidemiological_studies.pdf

14. Fernanda de Oliveira Souza, ., *et al*. "Bias in case- control studies: can it be avoided". (2016).

15. Gael P Hammer., *et al*. "Avoiding bias in observational studies". 106.41 (2009): 664-668.

16. G Tripepi., *et al*. "Bias in Clinical Research". A B C of Epidemiology 73 (2008): 148-153.

17. Andrea C Triccoa., *et al*. "Few systematic reviews exist Documenting the extent of bias: a systematic review". *Journal of Clinical Epidemiology* 61 (2008): 422-434.

18. Neil Pearce., *et al*. "Bias in occupational epidemiological Studies". *Occupational Environmental Medicine* 64 (2006): 562-568.

19. Ana Maria Simundic. Bias in Research.

20. F Rivas-Ruiz., *et al*. "Bias in clinical epidemiological study designs". *Allergologia et immunopatholgia* 41.1 (2013): 54-59.