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Master´s in Pharmacological Research

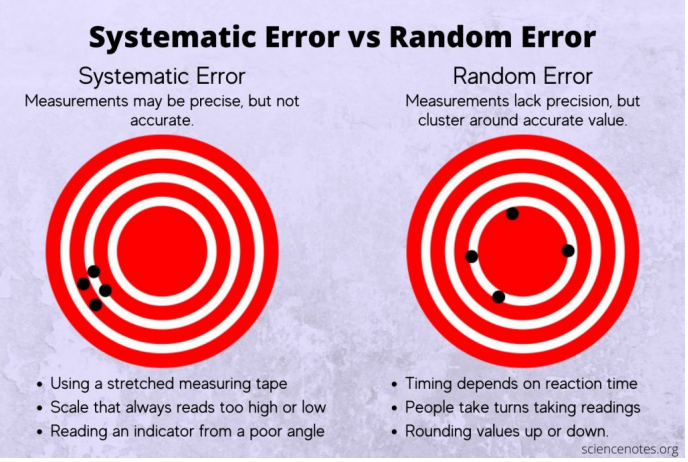
Systematic errors

Multiple systematic flaws that can affect the way a study is conducted during clinical trials and result in results that are less favorable than anticipated can be found.

First, let's clarify what an error is. The most frequent definition for an error is the discrepancy between a measurement's true value and recorded value. There are two types of errors: random and systematic.

To understand this, it is necessary to know what, in the context of a clinical experiment, a systematic error and a random error entail:

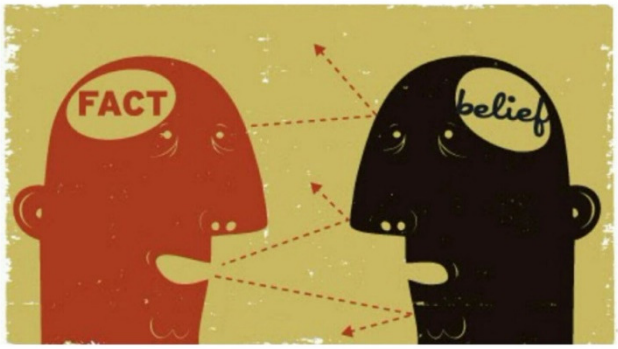
Variability, another name for a random error, can be brought on by variables that differ from measurement to measurement. Placing the same weight on an electronic scale multiple times and getting random readings that differ from one reading to the next is an example of random error. The discrepancies between these readings and the real weight are due to the scale's random measuring inaccuracy.



What is a systematic error?

Systematic error, also known as systematic bias, is a predictable error linked to malfunctioning hardware or poor experiment design. This refers to deviations that aren't only the result of random chance. One of the most straightforward instances involves a measuring gadget that has been incorrectly calibrated.

Once we are aware of the distinctions between these two types of errors, we can identify a variety of systemic errors in clinical trials, including some of the following:



- Non-response bias: happens when survey respondents are unable or unwilling to answer any or all the questions in the survey, this also means that people taking the survey are only people willing to do it. For instance, if you only get half as many survey responses as you anticipated. Because respondents either forgot to complete the survey or did not wish to do so, you are left with a sample that no longer accurately reflects the study's population. This is known as a non-response bias.
- Selection bias: A mistake in an association or outcome results from selection bias, which happens when individuals or groups in a study entirely diverge from the population of interest. For instance, if you only recruit participants from clinics, you will not include any patients who do not visit those clinics or seek therapy during the study.
- Performance bias: If there are variations between the study groups because of consistent performance differences outside of the study therapy received, performance bias may be present. Due to participant and staff masking (or blinding) techniques, there is a possibility of performance

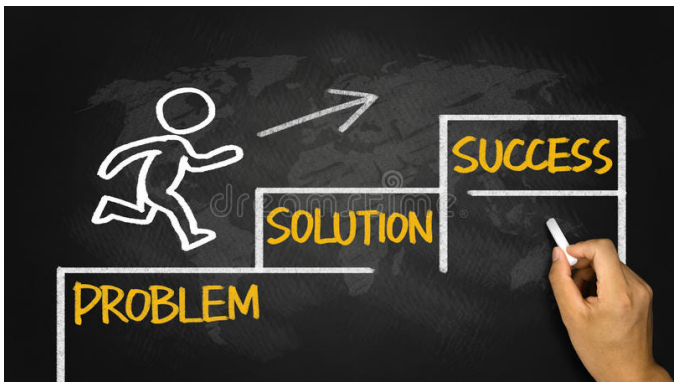
bias. Participants in a weight loss study may increase their protein intake, for instance, if the study is looking at whether a high-protein diet helps people lose weight.

- Detection bias: The potential for variations between the comparison groups in terms of how the results are measured or judged. For instance, a recent systematic analysis revealed that non-blinded outcome assessors overstated odds ratios in randomized trials by 36% on average.
- Attrition bias: The systematic reasons for patient withdrawals in a study that disproportionately affect a particular subset of patients might lead to attrition bias. The withdrawal imbalance may affect the findings and inferences taken from the study if a cause for withdrawal is present—or more prevalent—in the comparator groups. The imbalance would obviously affect the outcomes if a particular patient population in one of the comparator groups were to withdraw from the study at a higher rate. For instance, those with more severe depression might have a harder time sticking to the diet plan and hence be more likely to drop out of the research in an intervention study on diet in adults with depression.
- Reporting bias: When there are questions about the outcomes stated in a study's results, reporting bias may happen. The main issue with this type of bias is selective outcome reporting, which refers to the publication of some measured outcomes within a study's findings but not others. This frequently takes the form of a study reporting on significant outcome findings while leaving out less significant outcome findings. For instance, because it was never your intention to investigate how vegetables affect health outcomes, you may have been the victim of outcome reporting bias if you discovered that people who ate more vegetables were healthier than those who didn't and then concluded that this meant eating vegetables improves health.
- Channeling bias: When the study cohort that patients are assigned to is determined by the severity of their illness or patient prognostic characteristics, this is known as channeling bias. When patients are randomly assigned to groups in nonrandomized trials, this bias is more likely to occur. For instance, when medications with comparable therapeutic purposes are given to patient groups with diverse prognoses. A new medicine's alleged benefits could steer patients with specific pre-existing morbidity toward it, leading to illness states that might be mistakenly linked to drug use.
- Interviewer bias: Describes a consistent bias in how data is gathered, documented, or evaluated. When the interviewer is aware of the patient's disease status, interviewer bias is more prevalent. A patient with Buerger illness participating in case-control research that aims to uncover risk factors in the past might serve as an illustration of this. If the interviewer is aware that the patient has Buerger disease, they may delve more into questions about risk factors like smoking.
- Chronological bias: When historical controls are employed as a reference group for patients receiving an intervention, chronology bias emerges. Medical practices such as disease diagnosis, treatment delivery, and desired outcome measurement could all be impacted by secular changes. For instance, TIA was once solely a clinical diagnosis until MRI requirements were added to the diagnostic in 2009. As a result, the sickest TIA patients were reclassified and now were suffering from a stroke.
- Recall bias: s a phenomenon where participants' memories of things that happened before or during treatment may be influenced by treatment outcomes, whether positive or negative. For instance, the thought to link the measles, mumps, and rubella vaccine to autism. Children receive this vaccination at a crucial time in their social and linguistic development. As a result, a causal association may be inferred from the fact that parents of children with autism are more likely to remember vaccine delivery during this developmental regression.
- Transfer bias: When study cohorts experience unequal losses to follow-up, transfer bias may develop. For instance, think of a study comparing the results of vertical scar versus inferior pedicle Wise pattern breast reductions. Patients with the Wise pattern may be less likely to require long-term follow-up since they frequently experience less contour issues right after surgery.
- Exposure misclassification: The use of proxies or poorly defined exposure can lead to incorrect classification of exposure. This could happen, for instance, in a study comparing the effectiveness of becaplermin and saline dressings for treatment of diabetes-related foot ulcers. If patients who

were administered becaplermin instead of those who were directly seen using the medicine were included in the study, the outcomes may have been significantly different.

- Outcome misclassification: If nonobjective metrics are utilized, the outcome classification may be incorrect. Clinical symptoms and indications, for instance, are infamously inaccurate predictors of venous thromboembolism. Less than 50% of the time, a patient's physical examination results in an appropriate diagnosis.
- Citation bias: Is the unwillingness of researchers and trial sponsors to publish negative results because they think that doing so may reflect poorly on their own abilities or the effectiveness of their own products.
- Publicity bias: arises when patients contact the researcher directly out of interest in the condition or treatment being researched. A novel cancer treatment is being developed, for instance, and because the advertisement lacked boldness, people began approaching the investigator personally to share their instances.
- Media bias: Implies a chronic or widespread bias in violation of the journalistic standards, as opposed to the viewpoint of a specific journalist or piece.
- Healthy worker bias: The term "healthy worker bias" refers to a particular kind of selection bias that is typically observed in observational studies of occupational exposures with an incorrect reference group. For instance, a person who is ill is unlikely to work as a manual laborer. As a result, studies of manual laborers are not studies of people who would perform manual labor if they were healthy, but rather studies of persons who are now healthy enough to do so.
- Over coverage: this happens when the study includes data from outside the population and the target population and sampling frame used to create the sample do not match up exactly. For instance, a researcher might want to contact addresses listed in a phone book to explore the opinions of registered voters. If some voters have more than one listed phone number, there may be over coverage.
- Under coverage: occurs when your survey sample does not fully reflect segments of your research population. For instance, gathering information at a town meeting or mall may appear like a simple way to receive the information you require. However, you run the danger of underrepresenting several communities if you solely poll mall visitors about their thoughts. For instance: who only make local purchases.
- Measurement errors: can be attributed to the respondent, the interviewer, the questionnaire, the data collecting method, or the respondent's record-keeping system. They happen when the response given deviates from the real value. For instance, when a patient answers a question even though he or she does not fully understand the question, an error may still occur.
- Processing error: An error in survey data that occurs from improperly carrying out properly prepared implementation strategies. All post-collection activities and questionnaire printing are considered processing faults. For instance, if you were to acquire study data and a value was missing, not registered, but later identified during analysis, that would indicate a processing mistake because not all data was appropriately captured.
- Information/Classification bias: a distortion in the measure of association brought on by insufficient precise measurements of significant study variables. For instance, believing that the more information that can be gathered to decide, the better, even if that additional information is unimportant.
- Confounding: A systematic distortion in the measure of connection between exposure and health outcome brought on by combining the effect of the primary exposure under consideration with unrelated risk factors The impact of one variable interacts with the impact of another. For instance, if age is independently more likely to be associated with a good result and by chance, more older persons are assigned to an active intervention than to a placebo, the intervention may appear to be beneficial when it is not.

To avoid this from happening some measures can be taken for each bias or error, so they happen the least possible:



• Non-response bias: keep the survey brief, inform the public of its purpose and potential length, and evaluate timing and distribution procedures. By doing this, you can determine whether you are utilizing the optimal survey distribution and whether it takes a long time to complete. Sometimes, some penalties can be implemented to avoid participants not answering the questions.

• Selection bias: only include study participants who represent your target community; alternatively, you can choose study participants at random if they fit your requirements. You can also conduct a pilot study to spot potential issues and prevent selecting the incorrect group.

- Performance bias: Consider cluster stratification to minimize variability in surgical technique.
- Detection bias: It is crucial to do single-blind outcome assessment at the very least. Single blinding is preferable to no blinding at all, while obviously double-blind studies offer the best protection against bias.
- Attrition bias: You can try to make up for it by using some statistical techniques. Simulated values are substituted for missing data in multiple imputation using likely values. As an alternative, you can compensate for the sample's uneven distribution of members by using sample weighting.
- Reporting bias: In clinical research, registration of trials prior to data collection is used to prevent selective reporting
- Channeling bias: Assign patients to study cohorts using rigorous criteria.
- Interviewer bias: Standardize interviewer's interaction with patient. Blind interviewer to exposure status.
- Chronological bias: Prospective studies can eliminate chronology bias. Avoid using historic controls (confounding by secular trends).
- Recall bias: Use objective data sources whenever possible. When using subjective data sources, corroborate with medical record. Conduct prospective studies because outcome is unknown at the time of patient enrollment.
- Transfer bias: Carefully design plan for patients lost to follow-up before the study.
- Exposure misclassification: Clearly define exposure before the study. Avoid using proxies of exposure.
- Outcome misclassification: Use objective diagnostic studies or validate measures as primary outcome.
- Citation bias: Register trial with an accepted clinical trials registry. Check registries for similar unpublished or in-progress trials before publication.
- Publicity bias: consider the terminology used to promote the clinical study you will be directing to prevent patient confusion.
- Media bias: Reading content from multiple sources, engage in discussions without biased moderation.
- Healthy worker bias: broader exposure group, internal comparisons utilizing various exposure levels, and comparisons between worker groups outside the company.
- Over coverage: Using the mark-and-recapture process, a sample is taken from the population, marked, and then reincorporated. The fraction of previously marked samples is then used to estimate the size of the actual population before another sample is drawn from the population.
- Under coverage: use a straightforward random sample to ensure that the samples include representatives of every segment of your population.

- Measurement error: make sure all measures are accurate, that your questions are valid, that you use a larger sample, and that you control unimportant variables.
- Processing error: double-check data collection, use two or three individuals to collect data to reduce errors, and use data processing software to prevent manually collecting data.
- Information/Classification bias: employing numerous sources of information, collecting data from groups that are compared similarly, and using standard measurement tools.
- Confounding: Randomization eliminates confusion. This involves distributing confounding factors among the study groups, restricting access to individuals having confounding factors, and matching up individuals and groups to achieve an equal distribution of confounding factors.

Learning the many types of bias and its remedies will make it simpler to see them while conducting research, which can help you avoid them when designing studies and get the desired findings.

If you want to dig deeper in bias:

- https://www.nature.com/articles/s41433-021-01759-9#:~:text=There%20are%20five%20main%20forms,)%20%5B1%2C%203%5D
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3094617/
- https://417studies.com/bias-in-clinical-trials/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2917255/

In the following article, bias was found and corrected, this will help you understand how take bias in your hands:

- https://www.nature.com/articles/s41467-020-17041-7?ref=https://giter.site