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Bias, Overview

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Abstract: This article provides an overview on bias. Bias is defined as the deviation of results or inferences from the truth, or processes leading to such deviation. The article also provides a catalogue of 109 biases at the following stages of research: literature review 4, study design 31, study execution 3, data collection 46, analysis 15, interpretation of results 7, and publication 3.

Bias is defined as the "deviation of results or inferences from the truth, or processes leading to such deviation" [12]. In other words, it is the extent to which the expected value of an estimator differs from a population parameter. Bias refers to **systematic errors** that decrease the validity of estimates, and does not refer to **random errors** that decrease the precision of estimates. Unlike random error, bias cannot be eliminated or reduced by an increase in sample size.

Bias can occur as a result of flaws in the following stages of research [17]:

1. literature review,
2. study design,
3. study execution,
4. data collection,
5. analysis,
6. interpretation of results, and
7. publication.

1 Literature Review Bias

Literature review bias (syn. reading-up bias) refers to errors in reading-up on the field [17]. Examples include:

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Foreign language exclusion bias: literature reviews and **meta-analyses** that ignore publications in foreign languages [5].

Literature search bias: caused by lack of a computerized literature search, incomplete search due to poor choice of keywords and search strategies, or failure to include unpublished reports or hard-to-reach journals through interlibrary loans.

One-sided reference bias: investigators may restrict their references to only those studies that support their position [17].

Rhetoric bias: authors may use the art of writing to convince the reader without appealing to scientific fact or reason [17].

2 Design Bias

Design bias refers to errors occurring as a result of faulty design of a study [12]. This can arise from faulty selection of subjects, noncomparable groups chosen for comparison, or inappropriate sample size.

2.1 Selection Bias

Selection bias is a distortion in the estimate of effect resulting from the manner in which subjects are selected for the study population. Bias in selection can arise: (i) if the **sampling frame** is defective, (ii) if the sampling process is nonrandom, or (iii) if some sections of the target population are excluded (noncoverage bias) [14].

2.1.1 Sampling Frame Bias

This type of bias arises when the sampling frame that serves as the basis for selection does not cover the population adequately, completely, or accurately [14]. Examples include:

***Ascertainment** bias*: arising from the kind of patients (e.g. slightly ill, moderately ill, acutely ill) that the individual observer is seeing, or from the diagnostic process which may be determined by the culture, customs, or individual disposition of the health care provider [12]. (See also diagnostic access bias.)

Berkson bias (*see* **Berkson's Fallacy**) (syn. admission rate bias, hospital admission bias): caused by selective factors that lead hospital cases and controls in a case–control study (*See* **Case-control study, hospital-based**) to be systematically different from one another [1, 6].

Centripetal bias: the reputations of certain clinicians and institutions cause individuals with specific disorders or exposures to gravitate toward them [17].

Diagnostic access bias: patients may not be identified because they have no access to diagnostic process due to culture or other reasons. (See also ascertainment bias, hospital access bias.)

Diagnostic purity bias: when "pure" diagnostic groups exclude **comorbidity**, they may become nonrepresentative [17].

Hospital access bias: patients may not be identified because they are not sick enough to require hospital care, or because they are excluded from hospitals as a result of distance or cost considerations. (See also ascertainment bias, diagnostic access bias, referral filter bias.)

Migrator bias: migrants may differ systematically from those who stay home [17].

Neyman bias (syn. attrition bias, prevalence–incidence bias, selective survival bias; *see* **Bias from Survival in Prevalent Case-Control Studies**): caused by excluding those who die before the study starts because the exposure increases mortality risk [4, 6].

Telephone sampling bias: if **telephone sampling** is used to select a sample of individuals, then persons living in households without telephones would be systematically excluded from the study population, although they would be included in the target population.

2.1.2 Nonrandom Sampling Bias

This type of bias arises if the sampling is done by a nonrandom method, so that the selection is consciously or unconsciously influenced by human choice [14]. Examples include:

Autopsy series bias: resulting from the fact that autopsies represent a nonrandom sample of all deaths [12].

Detection bias (syn. selective surveillance bias, verification bias): caused by errors in methods of ascertainment, diagnosis, or verification of cases in an epidemiologic investigation, for example verification of diagnosis by laboratory tests in hospital cases, but not in cases outside the hospital [6,12]. (See also diagnostic work-up bias, unmasking bias.)

Diagnostic work-up bias (syn. sequential-ordering bias): arises if the results of a diagnostic or screening test affect the decision to order the "**gold standard**" procedure that provides the most definitive result about the disease [16], for example those who have a negative screening test are systematically excluded from the gold standard procedure [3]. (See also detection bias, unmasking bias.)

Door-to-door solicitation bias: subjects obtained by door knocking are more likely to be the elderly, unemployed, and less active individuals who tend to stay at home.

Previous opinion bias: the tactics and results of a previous diagnostic process on a patient, if known, may affect the tactics and results of a subsequent diagnostic process on the same patient [17]. (See also diagnostic work-up bias.)

Referral filter bias: as a group of patients are referred from primary to secondary to tertiary care, the concentration of rare causes, multiple diagnoses, and severe cases may increase [17]. (See also hospital access bias.)

Sampling bias: caused by the use of nonprobability sampling methods that do not ensure that all members of the population have a known chance of selection in the sample [12] (*see* **Quota, Representative, and OtherMethods of Purposive Sampling**).

Self-selection bias (syn. self-referral bias): subjects contact the investigators on their own initiative in response to publicity about the investigation.

Unmasking bias (syn. signal detection bias): an innocent exposure may become suspect if, rather than causing a disease, it causes a sign or symptom which leads to a search for the disease [17] (*see* **Bias From Diagnostic Suspicion in Case-Control Studies**). (See also detection bias, diagnostic work-up bias.)

2.1.3 Noncoverage Bias

This type of bias arises if some sections of the population are impossible to find or refuse to cooperate [14]. Examples include:

Early-comer bias (syn. latecomer bias): "early-comers" from a specified sample may exhibit exposures or outcomes which differ from those of "latecomers" [6], for example early-comers in a study tend to be healthier, and less likely to smoke [17]. (See also response bias.)

Illegal immigrant bias: when census data are used to calculate death rates, bias is caused by illegal immigrants who appear in the numerator (based on death records) but not in the denominator (based on census data).

Loss to follow-up bias: caused by differences in characteristics between those subjects who remain in a cohort study and those who are lost to follow-up [6] (*see* **Bias from Loss to Follow-up**).

Response bias (syn. nonrespondent bias, volunteer bias): caused by differences in characteristics between those who choose or volunteer to participate in a study and those who do not [7,12] (*see* **Bias from Nonresponse**). An example is the forecast of the US presidential election in a 1936 survey of 10 million individuals that went wrong because the response rate was only 20%, and the respondents presumably came from a higher social class than the general electorate [14]. (See also early-comer bias.)

Withdrawal bias: caused by differences in the characteristics of those subjects who choose to withdraw and those who choose to remain [6,12].

2.2 Noncomparability Bias

Noncomparability bias occurs if the groups chosen for comparison are not comparable. Examples include:

Ecological bias (syn. **ecologic fallacy**): the associations observed between variables at the group level on the basis of ecological data may not be the same as the associations that exist at the individual level.

Healthy Worker Effect (HWE): an observed decrease in mortality in workers when compared with the general population [4] (*see* **Occupational Epidemiology**). This is a type of membership bias [6].

Lead-time bias (syn. zero time shift bias): occurs when follow-up of two groups does not begin at strictly comparable times, for example when one group has been diagnosed earlier in the natural history of the disease than the other group owing to the use of a screening procedure [12] (*see* **Screening Benefit, Evaluation of**).

Length bias : caused by the selection of a disproportionate number of long-duration cases (cases who survive longest) in one group and not in the other. An example is when prevalent cases (*See* **Prevalence**), rather than incident cases (*See* **Incidence**), are included in a **case–control study** [12].

Membership bias: membership in a group (e.g. workers, joggers) may imply a degree of health which differs systematically from that of the general population because the general population is composed of both healthy and ill individuals [6,17].

Mimicry bias: an innocent exposure may become suspect if, rather than causing a disease, it causes a benign disorder which resembles the disease [17].

Nonsimultaneous comparison bias (syn. noncontemporaneous control bias): secular changes in definitions, exposures, diagnoses, diseases, and treatments may render noncontemporaneous controls noncomparable [17], for example use of historical controls [12] (*see* **Bias from Historical Controls**).

2.3 Sample Size Bias

Samples that are too small may not show effects even when they are present; samples that are too large may show tiny effects of little or no practical significance [17]. Another name for sample size bias is wrong sample size bias.

3 Study Execution Bias

Study execution bias refers to errors in executing the experimental maneuver (or exposure) [17]. Examples include:

Bogus control bias: when patients who are allocated to an experimental maneuver die or sicken before or during its administration and are omitted or reallocated to the control group, the experimental maneuver will appear spuriously superior [17].

Contamination bias: when members of the control group in an experiment inadvertently receive the experimental maneuver, the differences in outcomes between experimental and control patients may be systematically reduced [17] (*see* **Bias Toward the Null**).

Compliance bias: in experiments requiring patient adherence to therapy, issues of efficacy become confounded with those of compliance, for example when high-risk coronary patients quit exercise programs [17] (*see* **Noncompliance, Adjustment for**).

4 Data Collection Bias

Data collection bias (syn. information bias, **measurement error**, **misclassification** bias, observational bias) refers to a flaw in measuring exposure or outcome that results in differential quality or accuracy of information between compared groups [12] (*see* **Bias, Nondifferential**). Bias in data collection can arise from (i) defective measuring instruments, (ii) wrong data source, (iii) errors of the observer, (iv) errors of the subjects, and (v) errors during data handling.

4.1 Instrument Bias

Instrument bias (syn: instrument error) refers to defects in the measuring instruments [17]. This may be due to faulty calibration, inaccurate measuring instruments, contaminated reagents, incorrect dilution or mixing of reagents, etc. [12]. Examples include:

Case definition bias: definition of cases, for example based on different versions of **International Classification of Diseases (ICD)** codes, or first-ever cases vs. recurrent cases, may change over time or across regions, resulting in inaccurate trends and geographic comparisons [13]. (See also diagnostic vogue bias.)

Diagnostic vogue bias: the same illness may receive different diagnostic labels at different points in space or time, for example the British term “bronchitis” vs. North American “emphysema”) [17]. (See also case definition bias.)

Forced choice bias: questions that provide inadequate choices, for example only “yes” and “no”, and without other choices like “do not know” or “yes but do not know type”, may force respondents to choose from the limited choices. (See also scale format bias.)

Framing bias: preference depends on the manner in which the choices are presented, for example telling a prospective candidate for surgery that an operation has a 5% mortality, vs. 95% survival rate.

Insensitive measure bias: when **outcome measures** are incapable of detecting clinically significant changes or differences, type II errors occur [17].

Juxtaposed scale bias (syn. questionnaire format bias): juxtaposed scales, a type of self-report response scale which asks respondents to give multiple responses to one item, may elicit different responses than when separate scales are used [10].

Laboratory data bias: data based on laboratory test results are subject to errors of the laboratory test including faulty calibration of the instruments, contaminated or incorrect amounts of reagents, etc.

Questionnaire bias: leading questions or other flaws in the questionnaire may result in a differential quality of information between compared groups [6] (*see* **Questionnaire Design**).

Scale format bias: even vs. odd number of categories in the scale for the respondents to choose from can produce different results, for example (Agree) 1–2–3 (Disagree) tends to obtain neutral answers, i.e. 2, while (Agree) 1–2–3–4 (Disagree) tends to force respondents to take sides. (See also forced choice bias.)

Sensitive question bias: sensitive questions such as personal or household incomes, sexual orientation, or marital status, may induce inaccurate answers.

Stage bias: method for determining stage of disease of patients may vary across the groups being compared, across geographic areas, or through time, leading to spurious comparison of stage-adjusted survival rates (*see* **Bias from Stage Migration in Cancer Survival**) [9].

Unacceptability bias: measurements which hurt, embarrass or invade privacy may be systematically refused or evaded [17].

Underlying/contributing cause of death bias: results of data analysis will be different depending on whether the underlying or the contributing cause of death as recorded on the death certificates is used (*see* **Cause of Death, Underlying and Multiple**; **Death Certification**).

Voluntary reporting bias: voluntary reporting system vs. mandatory reporting system can generate differences in the quality and completeness of routine data.

4.2 Data Source Bias

Data source bias refers to wrong, inadequate, or impossible source or type of data. Examples include:

Competing death bias: some causes of death (e.g. cancers) are associated with older age, while others (e.g. infectious diseases) are associated with younger age. Therefore in places where infectious diseases are prevalent, the cancer rates will be underestimated owing to competing causes of death from infectious diseases (*see* **Competing Risks**).

Family history bias: positive family history is not an accurate indicator of familial aggregation of a disease and the influence of genetic factors, because it is a function of the number of relatives and the age distribution of relatives [11].

Hospital discharge bias: hospital discharge data do not reflect hospital admission data since they are affected by length of hospital stay, and therefore do not provide accurate information for disease incidence.

Spatial bias: many environmental data used for health applications, for example geographic information systems (GIS), derive from point measurements at monitoring or survey stations. Unfortunately, many environmental monitoring networks are too sparse spatially and biased towards high pollution sites, generating an inaccurate pollution surface [2].

4.3 Observer Bias

Observer bias is due to differences among observers (interobserver variation) or to variations in readings by the same observer on separate occasions (intraobserver variation) [12] (*see* **Observer Reliability and Agreement**). Examples include:

Diagnostic suspicion bias (syn. diagnostic bias): a knowledge of the subject's prior exposure to a putative cause (e.g. ethnicity, drug use, cigarette smoking) may influence both the intensity and the outcome of the diagnostic process [6,17] (*see* **Bias From Diagnostic Suspicion in Case-Control Studies**).

Exposure suspicion bias: a knowledge of the subject's disease status may influence both the intensity and outcome of a search for exposure to the putative cause [6,17] (*see* **Bias from Exposure Suspicion in Case-Control Studies**).

Expectation bias: observers may systematically err in measuring and recording observations so that they concur with prior expectations, for example house officers tend to report "normal" fetal heart rates [17].

Interviewer bias : caused by interviewers' subconscious or even conscious gathering of selective data [12], for example questions about specific exposures may be asked several times of cases but only once of controls [17]. Can result from interinterviewer or intrainterviewer errors [6].

Therapeutic personality bias: when treatment is not blind, the therapist's convictions about efficacy may systematically influence both outcomes and their measurement (e.g. desire for positive results) [17] (*see* **Blinding or Masking**).

4.4 Subject Bias

Subject bias (syn. "observee" bias) refers to the inaccuracy of the data provided by the subjects (respondents, "observees") at the time of data collection. Examples include:

Apprehension bias: certain measures (e.g. pulse, blood pressure) may alter systematically from their usual levels when the subject is apprehensive (e.g. blood pressure may change during medical interviews) [17].

Attention bias (syn. **Hawthorne effect**): study subjects may systematically alter their behavior when they know they are being observed [17].

Culture bias: subjects' responses may differ because of culture differences, for example some **ethnic groups**, because of their cultural background, do not want to share publicly their pain or problems such as unemployment, marital troubles, youth crime, and parental difficulties.

End aversion bias: subjects usually avoid end of scales in their answers, try to be conservative, and wish to be in the middle.

Faking bad bias (syn. hello–goodbye effect): subjects try to appear sick in order to qualify for support. Also, subjects try to seem sick before, and very well after, the treatment.

Faking good bias (syn. social desirability bias): socially undesirable answers tend to be underreported. (See also unacceptable disease bias, unacceptable exposure bias.)

Family information bias: the family history and other historical information may vary markedly depending upon whether the individual in the family providing the information is a case or a control, for example different family histories of arthritis may be obtained from affected and unaffected siblings [17].

Interview setting bias: whether interviews are conducted at home, in a hospital, the respondent's workplace, or the researcher's office may affect subjects' responses.

Obsequiousness bias: subjects may systematically alter questionnaire responses in the direction they perceive desired by the investigator [17].

Positive satisfaction bias (syn. positive skew bias): subjects tend to give positive answers, typically when answering satisfaction questions.

Proxy respondent bias (syn. surrogate data bias): for deceased cases or surviving cases (e.g. brain tumors) whose ability to recall details is defective, soliciting information from proxies (e.g. spouse or family members) may result in differential data accuracy.

Recall bias : caused by differences in accuracy or completeness of recall to memory of prior events or experiences [6], for example mothers whose children have had leukemia are more likely than mothers of healthy children to remember details of diagnostic X-ray examinations to which these children were exposed *in utero* [12].

Reporting bias (syn. self-report response bias): selective suppression or revealing of information such as past history of sexually transmitted disease [12]. (See also unacceptable disease bias, unacceptable exposure bias, sensitive question bias.)

Response fatigue bias: questionnaires that are too long can induce fatigue among respondents and result in uniform and inaccurate answers.

Unacceptable disease bias: socially unacceptable disorders (e.g. sexually transmitted diseases, suicide, mental illness) tend to be underreported [12]. (See also reporting bias, faking good bias.)

Unacceptable exposure bias: socially unacceptable exposures (e.g. smoking, drug abuse) tend to be underreported. (See also reporting bias, faking good bias.)

Underlying cause bias (syn. rumination bias): cases may ruminate about possible causes for their illness and thus exhibit different recall or prior exposures than controls [17]. (See also recall bias.)

Yes-saying bias: some subjects tend to say "yes" to all questions.

4.5 Data Handling Bias

Data handling bias refers to the manner in which data are handled. Examples include:

Data capture error: errors in the acquisition of the data in digital form, normally by manual encoding (coding error), digitizing (data entry error), scanning, or electronic transfer from pre-existing data bases [2]. (See also data entry bias.)

Data entry bias: difference in data entry practices may cause unreal observed differences in geographic variations in incidence rates [18]. (See also data capture error.)

Data merging error: incorrect merging of data from different databases, for example erroneous merging and failure to merge as a result of illegible handwriting on the routine forms, different dates of service recorded in different databases, etc. (See also record linkage bias.)

Digit preference bias (syn. end-digit preference bias): in converting analog to digital data, observers may record some terminal digits with an unusual frequency [17], for example rounding off may be to the nearest whole number, even number, multiple of 5 or 10, or, when time units like a week are involved, [8, 15], etc. [12].

Record linkage bias: computerized **record linkage** is based on a probabilistic process based on identifiers (*see* **Matching, Probabilistic**). Some identifiers, e.g. some surnames, may have a poor record linkage weight, causing linkage problems, and therefore tend to exclude subjects having those identifiers.

5 Analysis Bias

Analysis bias results from errors in analyzing the data. It can arise from (i) lack of adequate control of confounding factors, (ii) inappropriate analysis strategies, and (iii) *post hoc* analysis of the data set.

5.1 Confounding Bias

Confounding bias occurs when the estimate of the effect of the exposure of interest is distorted because it is mixed with the effect of a **confounding** (extraneous) factor. A confounding factor must be a risk factor for the disease, be associated with the exposure under study, and not be an intermediate step in the causal path between the exposure and the disease [6]. Examples include:

Latency bias: failure to adjust for the **latent period** in the analysis of cancer or other chronic disease data.

Multiple exposure bias: failure to adjust for multiple exposures.

Nonrandom sampling bias: when a study sample is selected by **nonrandom** (nonprobability) sampling, failure to account for variable sampling fractions in the analysis may introduce a bias, for example weighting by the strata population sizes is needed for a disproportionate stratified sample (*see* **Stratified Sampling**).

Standard population bias: choice of standard population will affect estimation of standardized rates (a weighted average of the category-specific rates) [7] (*see* **Standardization Methods**).

Spectrum bias (syn. case mix bias): heterogeneous groups of patients with different proportions of mild and severe cases can lead to different estimates of **screening** performance indicators [16].

5.2 Analysis Strategy Bias

Analysis strategy bias (syn. analysis method bias) refers to problems in the analysis strategies. Examples include:

Distribution assumption bias: wrong assumption of sampling distribution in the analysis, for example time variables follow **lognormal distribution** rather than **normal distribution**, and therefore **geometric mean** time rather than mean time should be used [8].

Enquiry unit bias: choice of unit of enquiry may affect analysis results, for example with the school as the unit of enquiry, half the high schools offered no physics, but when the student becomes the unit of enquiry, only 2% of all high school students attended schools that offered no physics, since the small schools do not teach physics (*see* **Unit of Analysis**).

Estimator bias: the difference between the expected value of an estimator of a parameter and the true value of this parameter [12], for example **odds ratio** always overestimates relative risk).

Missing data handling bias: how **missing data** are handled, for example treated as a missing case vs. interpreted as a "no" answer, will lead to different results.

Outlier handling bias: arising from a failure to discard an unusual value occurring in a small sample, or due to exclusion of unusual values that should be included [12]. The latter is also called tidying-up bias (the exclusion of **outliers** or other untidy results which cannot be justified on statistical grounds) [17].

Overmatching bias: matching on a nonconfounding variable that is associated with the exposure but not the disease can lead to conservative estimates in a matched case–control study [6].

Scale degradation bias: the degradation and collapsing of measurement scales tend to obscure differences between groups under comparison [17].

5.3 Post Hoc *Analysis Bias*

Post hoc analysis bias refers to the misleading results caused by *post hoc* questions, data dredging, and subgroup analysis (*see* **Treatment-covariate Interaction**). Examples include:

Data dredging bias: when data are reviewed for all possible associations without prior hypothesis, the results are suitable for hypothesis-generating activities only [17].

Post hoc *significance bias*: when decision levels or "tails" for type I and type II errors are selected after the data have been examined, conclusions may be biased [17].

Repeated peeks bias: repeated peeks at accumulating data in a randomized trial are not independent, and may lead to inappropriate termination [17] (*see* **Sequential Analysis**).

6 Interpretation Bias

Interpretation bias arises from inference and speculation, for example failure of the investigator to consider every interpretation consistent with the facts and to assess the credentials of each, and mishandling of cases that constitute exceptions to some general conclusion [12]. Examples include:

Assumption bias (syn. conceptual bias): arising from faulty logic or premises or mistaken beliefs on the part of the investigator, for example having correctly deduced the mode of transmission of cholera, John Snow falsely concluded that yellow fever was transmitted by similar means [12].

Cognitive dissonance bias: the belief in a given mechanism may increase rather than decrease in the face of contradictory evidence [17].

Correlation bias: equating correlation with causation leads to errors of both kinds [17].

Generalization bias (syn. lack of external validity): generalizing study results to people outside the study population may produce bias, for example generalizing findings in men to women (*see* **Validity and Generalizability in Epidemiologic Studies**).

Magnitude bias: when interpreting a finding, the selection of a scale of measurement may markedly affect the interpretation, for example $1 000 000 may also be 0.0003% of the national budget [17].

Significance bias: the confusion of statistical significance, on the one hand, with biologic or clinical or health care significance, on the other hand, may lead to fruitless studies and useless conclusions [17] (*see* **Clinical Significance Versus Statistical Significance**).

Underexhaustion bias: the failure to exhaust the hypothesis space may lead to erroneous interpretations [17].

7 Publication Bias

Publication bias refers to an editorial predilection for publishing particular findings, e.g. positive results, which can distort the general belief about what has been demonstrated in a particular situation [12] (*see* **Meta-analysis of Clinical Trials**). Examples include:

All's well literature bias: scientific or professional societies may publish reports or editorials which omit or play down controversies or disparate results [17].

Positive results bias: authors are more likely to submit, and editors accept, positive than null results [17].

Hot topic bias (syn. hot stuff bias): when a topic is hot, investigators and editors are tempted to publish additional results, no matter how preliminary or shaky [17].

8 Related Articles

Bias in Case-Control Studies
Bias in Cohort Studies
Bias in Observational Studies
Selection Bias
Response Bias
Recall bias
Publication Bias
Prevalence-incidence bias
Length bias
Interviewer bias
Inconsistent Bias

Detection bias
Bias, protopathic
Bias, nondifferential
Bias toward the null
Bias from survival in prevalent case-control studies
Bias from stage migration in cancer survival
Bias from nonresponse
Bias from loss to follow-up
Bias from historical controls
Bias from exposure suspicion in case-control studies
Bias from exposure effects on controls
Bias from diagnostic suspicion in case-control studies
Bias
Assessment Bias

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