Bias

Bias is like some furtive creature that slinks about under the cover of night. Usually it is impossible to know if the creature is around. That being the case, trialists tend to function under the "better safe than sorry" mode of operation. That means they assume the creature is present and, hence, take precautions against it even when its presence is unlikely.

There are two strains of the creature – the absolute and the relative strain. The absolute strain is the more destructive of the two strains. It thrives in settings where randomization and masking is precluded or not practiced. It roams freely in non-comparative settings where the researcher is, in effect, in pursuit of absolute truth (eg, in observational studies aimed at identifying risk factors for a given disease).

The domain of the relative strain is in settings where the search is for relative truth (eg, as in randomized trials where the aim is to find if one treatment is better than another). The absolute species of the strain is basically of no consequence even if present in such settings. For example, there is no doubt that there are biases in the selection of people enrolled into a trial, but that bias is of no consequence in comparison of treatment groups so long as the selection bias is the same across treatment group. The ability to compare by differencing (ie, by subtracting to produce a treatment difference based on effects observed in one treatment group versus another) serves to remove the effect of the absolute strain from the comparison.

The bias feared most by trialists is treatment-related bias. Randomization is done to protect against that bias in the assignment process.

Shielding investigators from interim results is done to keep knowledge of treatment differences from influencing the behavior of clinic personnel in the treatment or data collection procedures. Its purpose is to protect against treatment-related feedback bias.

Double-masked administration of treatment is done to keep knowledge of the treatment assignment from influencing the way in which persons are managed or observed. When treatment cannot be masked, trialists may attempt to protect against treatment-related bias by "separation" – arrangements in which management of treatment and observation of persons are vested in different people with attempts to keep observers from knowing treatment assignment.

Treatment effects monitoring committees (aka data and safety monitoring committee) are sometimes masked to treatment group. The masking is imposed in an attempt to force an added level of objectivity in the monitoring process. The effect of the masking is to leave the monitoring body uncertain as to whether a treatment difference observed is for or against the study treatment and, hence, to force the monitoring body to focus on the difference observed without regard to the sign of the difference.

The trouble with the "better safe than sorry" mode of operation in regard to masking is that it has liabilities (to say nothing about the logistics of masking) to the extent it has the potential of carrying risks of harm for persons studied. A key element in the ethical tenets underlying research on human beings is that persons under study must receive proper care rendered by qualified competent personnel. That means that one cannot impose procedures to increase objectivity at the expense of competency. In regard to masking it means that masking can be imposed only so long as competency is not compromised.

Similarly, a monitoring body should not be masked if the masking serves to reduce its ability to

understand, interpret, or react to observed treatment differences. The trouble with masked monitoring comes when a treatment difference emerges. Monitoring bodies are disposed to recommend continuing longer in the face of a beneficial effect than in the face of a negative effect. Yet the masking requires the monitoring body to be indifferent to sign and requires them to make recommendations independent of sign.

bias *n* - [fr OF *bias*, oblique, fr OProv, perhaps from Gk, *epikarsios*, oblique] 1. An inclination of temperament, state of mind, or action based on perception, opinion, or impression serving to reduce rational thought or action, or the making of impartial judgments; a specified instance of such an inclination; **prejudice**. 2. A tendency toward certain **measurements**, **outcomes**, or conclusions over others as a result of a conscious or subconscious mind set, temperament, or the like; a specific expression of such a tendency. 3. Any behavior or performance that is differential across groups in a **comparative study**; **treatment-related bias**. 4. **Deviation** of the **expected value** of an **estimate** of a **statistic** from its true value. 5. Last[?]: *Deviation of results or inference from the truth, or processes leading to such deviation.* 6. Last: *Any trend in the collection, analysis, interpretation, publication, or review of data that can lead to conclusions that are systematically different from the truth.* See *bias* for list. ***Usage note***: Distinguish between uses in which **bias** (defns 1 or 2) is being proposed in a speculative sense as opposed to an actual instance of bias. Usages in the latter sense should be supported with evidence or arguments to substantiate the claim. Usages in the former sense should be preceded or followed by appropriate modifiers or statements to make clear that the user is speculating. Similarly, since most undifferentiated uses (in the sense of defns 1 or 2) are in the speculative sense, prudent readers will treat all uses of the term as being in that sense, unless accompanied by data, evidence, or arguments to establish bias as a fact. Not to be confused with **systematic error**. Systematic error, if discovered, can be removed from finished data; bias is more elusive and not easily quantified. See **prejudice** for additional comments.

publication bias *n* - 1. An inclination or tendency toward **publication** of results that support conclusions favoring a particular **hypothesis** or position. 2. Any influence or factor that results in a differential inclination or tendency toward publication, regardless of whether related to the nature or direction of **results** (eg, influences or factors such as gender of the investigator, source of funding for the study, or specific design and operating features of the study). ***Usage note***: Most usages are in the sense of defn 1 and are offered in a speculative or cautionary sense (as opposed to a declarative sense) in that demonstration of the **bias** is often difficult or impossible. The **bias** (defn 1) operates when the decision of investigators to prepare a paper for publication is influenced by the nature or strength of the conclusion that can be drawn from the results, or when referees and editors of the journals base their decisions for acceptance or rejection on the statistical importance of the results or on the nature of the conclusions stated or implied by the results. The supposition for **trials** is that the bias is more likely to operate in trials not showing any difference (**nil result**) than for those showing a difference, and among those showing a difference the bias is assumed to be more likely for trials producing **negative results** (defn 2) than for those producing **positive results**. The bias, if operating, has serious implications for **meta-analysis**. Usages in the sense of defn 2 are quite different from those for defn 1 and should be noted as departing from the conventional definition of the bias. In the sense of defn 2, the reference is to any factor influencing publication, whether or not related to the nature or direction of results, including those fixed before or when the study is started, such as the age, gender, or rank of the investigator, or type or source of funding.

selection bias *n* - 1. A systematic inclination or tendency for elements or units selected for **study** (usually persons in **trials**) to differ from those not selected. See **Berksonian bias** for a special type of selection bias. 2. **treatment-related selection bias** (not a recommended synonym) ***Usage note***:

The **bias** defined by defn 1 is unavoidable in most trials because of selective factors introduced as a result of eligibility requirements for **enrollment** and because of the fact that individuals may decline enrollment (see **consent process**). The existence of the bias does not affect the **validity** of **treatment comparisons** within a trial so long as the bias is the same for all **treatment groups**, eg, as is the case when **treatment assignments** are made by **randomization**.

treatment-related bias *n* - 1. **Bias** related to **treatment**. 2. Bias related to **treatment assignment**. rt: **treatment-related feedback bias**

treatment-related feedback bias *n* - [**trials**] 1. **Bias** in an **observation**, **measurement**, **reporting**, **analysis**, or **administration** process or procedure due to knowledge of **interim treatment results** on the part of the one observing, measuring, reporting, analyzing, or administering. 2. Differential behavior of persons **enrolled** into a trial due to their having knowledge of interim treatment results, eg, a differential **loss to followup** due to differences in the willingness of persons to continue because of their having knowledge of **non-nil** interim treatment results. ***Usage note***: Use with caution as a claim or assertion. The existence of a **feedback bias** is difficult to establish. It does not operate in the absence of knowledge of interim results and is unlikely to operate in the presence of **nil** interim treatment results. Knowledge of an interim treatment result is not sufficient for the bias to operate. One must also be able to argue plausibly that that knowledge can produce the bias. It is difficult to do so in **masked trials**, and especially in **double-masked trials**. Even if a **treater** has access to interim results, that information, to translate into a **treatment-related bias**, must be related to individual patients and must influence how those persons are treated and observed. It is not possible to relate results to individual patients if the treater is effectively masked to **treatment assignment**. Further, even if a treater or data collector is not masked, it is difficult to argue plausibly that a **treatment difference** is due to a treatment-related feedback bias if the process or procedure in question is **robust** to the bias. For example, there is not much of an opportunity for the bias to operate if the measurement in question is not prone to **errors** of interpretation or reporting (eg, as with most event-type **outcomes**, such as death or events indicative of gross morbidity). Nor is there much room for the bias to operate if a process or procedure is well-defined (eg, as in a **treatment protocol** with explicit rules for when and how **treatments** are to be altered in the presence of specified conditions). Generally, the more **objective** the process or procedure, the more difficult it is to plausibly argue that knowledge of interim results can produce a treatment-related feedback bias. See **bias** for additional comments.

treatment-related followup bias *n* - **Followup bias** related to **treatment assignment**.

treatment-related selection bias *n* - Broadly, **bias** related to **treatment assignment** introduced during the selection and **enrollment** of persons or **treatment units** into a **trial**. Often, **selection bias** due to knowing treatment assignments in advance of use and using that information in the selection process. The **risk** of the bias is greatest in **unmasked trials** involving **systematic** assignment schemes (eg, one in which assignments are based on order or day of arrival of **patients** at a **clinic**). It is **nil** in trials involving **simple** (**unrestricted**) **randomization** but can arise in relation to **blocked randomization** if the blocking scheme is known or deduced. For example, one would be able to correctly predict one-half of the assignments before use in an unmasked trial of two **study treatments** arranged in blocks of size two, if the blocking was known or deduced. The chance of the bias operating, even if the blocking scheme is simple, is minimal in **double-masked trials** (because correct guesses are not likely to translate into a treatment-related selection bias when the treatments are masked).

Dictionary entries with bias as a base or modifier term

accidental bias *n*
ascertainment bias *n*
Berksonian bias *n*
bias *n*
bias control *v*
bias free treatment assignment *n*
bias potential *n*
biased *adj*
biased coin randomization *n*
biased coin treatment assignment *n*
biased estimator *n*
citation bias *n*
detection bias *n*
differential bias *n*
digit bias *n*
dilution bias *n*
effort bias *n*
feedback bias *n*
followup bias *n*
gender bias *n*
lead time bias *n*
measurement bias *n*
nonresponse bias *n*
observer bias *n*
potential bias *n*
publication bias *n*
recall bias *n*
reference bias *n*
regression dilution bias *n*
representation bias *n*
response bias *n*
selection bias *n*
treatment assignment bias *n*
treatment-related bias *n*
treatment-related feedback bias *n*
treatment-related followup bias *n*
treatment-related selection bias *n*
unbiased *n*
unbiased estimator *n*
unmasking bias *n*
volunteer bias *n*