THE FALLACY OF NEGATIVE TRIALS - “ABSENCE OF EVIDENCE IS NOT EVIDENCE OF ABSENCE”

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"Absence of evidence is not evidence of absence" This is quoted from Altman and Bland 1. Many a times researchers cannot find any difference between two treatments and report that there is no difference. The real conclusion should read “there is no evidence to support there is any difference”. They seem alike. But no. They are not.

Many clinical trials are insufficiently powered so that they cannot detect any difference even if a real difference exits. In statistics jargon, the trial is “insufficiently powered”. The power of a trial is the probability that it can detect the difference if the difference really exists.

When we read a positive trial, we would ask ourselves about type I error, which is the p value, or simply, the chance of false positive results. Because the chance of false positive is small, we believe the trial is positive.

When we read a negative trail, we would equivalently ask ourselves about type II error, or simply, the chance of false negative results. Again if the chance of false negative is small, we believe the trial is negative. One minus this chance equals to the power of the trial. Therefore a small chance of false negative is equivalent to a big power. Regrettably, often there is absence of this important figure in negative trials.

Conventionally, the power should be calculated before the trial. A power less than 70% is destined to be inconclusive if it is negative. If it is not done before the trial, we can always calculate it back from the results of the negative trial. It is called retrospective power analysis. If it is below 70%, we cannot make the conclusion that there is no difference.

A lot of negative trials are not published either having been rejected or the authors have abandoned them. This gives rise to serious publication bias in meta-analysis. Insufficiently powered negative trials may show positive results when aggregated statistically together. Some of the important findings can be buried under the unpublished negative trials.

Insufficient powered studies should not be carried out in the first place to avoid putting subjects at unnecessary risk, for an inconclusive finding.

References