Problems with Attrition Bias

Definition	Attrition bias – A bias occurring as a result of subjects lost to follow-up through withdrawals or other study attrition. ▪ We also are concerned with missing data points when we consider attrition bias. This would include discontinuations, for example. Reports of follow-up data for patients who have discontinued their treatment could skew results if they were no longer receiving treatment of any kind or if they were being treated via another intervention.
Important Considerations	▪ Randomization creates a treatment group and control group with similar observable and unobservable characteristics that are representative of the larger population from which the sample was drawn. ▪ Attrition occurs when an outcome is not measured for all randomized subjects. ▪ Attrition can result in distortion of results due to potential resulting differences between those from whom we have data and those we do not. In other words, the groups may now be different in terms of prognostic variables from immediately post-randomization. This can create differences between study groups or between those who remain in a study and those who are lost to follow-up as examples. ▪ Differences in outcomes can no longer assumed to be due to the intervention because attrition may have left groups with differences in prognostic variables and those differences may be the explanation for the difference in results. ▪ Overall and differential attrition may bias the reported differences between the groups. ▪ Even if loss between the groups is equal bias may exist if the relationship between the attrition and the bias differs between the treatment and control groups. ▪ Attrition is a threat to internal validity. External validity is also threatened because the groups may no longer be representative of the larger population.
The Evidence	▪ Some researchers suggest a simple five-and-20 rule of thumb, with fewer than 5% loss probably leading to little bias, greater than 20% loss potentially posing serious threats to validity, and in-between levels leading to intermediate levels of problems.[1] ▪ Loss of patient data, i.e., when data is excluded from the analysis may result in type I or type II errors: With loss of 20% risk of type I error* is 10%. With loss of 40% risk of type I is 50%.[2] o *Type 1 - or alpha error - A difference is reported, but there is no difference. This can be due to bias, confounding or chance. ▪ Kaplan-Meir estimates use models to account for attrition and may result in a relative distortion of results of approximately 50%.[2] ▪ Other references supporting above.[3] ▪ Quantifying the amount of distortion and predicting the direction of distortion with post-randomization loss of subjects remain problematic. Our position is that loss of 5% or more of subjects with differential loss between groups, or 10% or more without differential loss may create significant changes in results.
Conclusion	▪ Quantifying the amount of distortion and predicting the direction of distortion with post-randomization loss of subjects remain problematic. Our position is that loss of 5% or more of subjects with differential loss between groups, or 10% or more without differential loss may create significant changes in results.

Delfini Primer: Problems with Attrition Bias

References

[1] Sackett DL, Richardson WS, Rosenberg W, Haynes RB. Evidence based medicine: how to practice and teach EBM. New York: Churchill Livingstone, 1997.

[2] Lachin JL. Statistical considerations in the intent-to-treat principle. Control Clin Trials. 2000 Oct;21(5):526. PMID 11018568

[3] Tierney JF, Stewart LA. Investigating patient exclusion bias in meta-analysis. Int J Epidemiol. 2005 Feb;34(1):79-87. Epub 2004 Nov 23. PMID: 15561753

Examples

Example 1: Effect of ITT Analysis in A Comparison of Surgical and Nonsurgical Treatment of Displaced Midshaft Clavicular Fractures

Analysis	Original Analysis			ITT Analysis with LOCF		
Results	Surgery (N=62) 7.5% loss	Nonsurgical (N=49) 24.6% loss	P Value	Surgery (N=67)	Nonsurgical (N=65)	P Value
Non-union	2/62	7/49	0.042	2/67	7/65	0.09

- Canadian Orthopaedic Trauma Society. Nonoperative treatment compared with plate fixation of displaced midshaft clavicular fractures. A multicenter, randomized clinical trial. *J Bone Joint Surg Am.* 2007;89:1-10.

Example 2: Mortality in Trial of Anturane Vs Placebo — Change in P-value with Attrition

	Anturane (%)	Placebo (%)	P-value
Randomized	74/813 (9.1)	89/816 (10.9)	0.20
"Eligible"	64/775(8.3)	85/783 (10.9)	0.07
Attrition (%)	1.2%	0.5%	

- The Anturane Reinfarction Trial Research Group. Sulfinpyrazone in the prevention of cardiac death after myocardial infarction. *N Engl J Med* 1978; 298: 289–95.