



## Problems with Attrition Bias

<p><b>Definition</b></p>	<p>Attrition bias – Attrition bias is generally thought of as bias that occurs as a result of patients dropping out of or unable to complete a study. We think of attrition bias in a broader sense as having to do with <b>missing data points</b>. The chief problem with attrition bias is that groups contributing data that may have been balanced due to effective randomization may now differ in important prognostic variables—which may affect or explain study results. We also think of attrition bias in a broader sense as having to do with <b>study completion</b>. 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 with another intervention.</p>
<p><b>Important Considerations</b></p>	<p>There are two main concepts that are important in understanding why attrition bias can distort study results: 1) the need for balanced groups to compare the effects of an intervention; and 2) the potential for attrition to be associated with the intervention.</p> <ul style="list-style-type: none"> <li>▪ Randomization—if successful— creates treatment and comparison groups with similar observable and unobservable characteristics that are, ideally, representative of the larger population from which the sample was drawn.</li> <li>▪ When significant attrition occurs, 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.</li> <li>▪ If a subject’s attrition is associated with—and thus possibly caused by— being in the assigned group, the absence of inclusion in the measurement constitutes an attrition bias. The classic example is that of patients who died from some effect of the experimental intervention and then were excluded from the trial analysis, (e.g., defined as early or unrelated deaths). The estimate of effect would be biased in favor of the intervention.</li> <li>▪ Even if loss between the groups is equal, bias may exist if the reasons for discontinuing in the treatment and control groups differ.</li> <li>▪ Attrition is a threat to both internal and external validity. External validity is also threatened because the groups may no longer be representative of the larger population.</li> <li>▪ A review of baseline characteristics of study completers contributing data to the analysis may be helpful, keeping in mind that not all potential confounders will be evaluable.</li> </ul>
<p><b>The Evidence</b></p>	<ul style="list-style-type: none"> <li>▪ Some researchers suggest a simple 5-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]</li> <li>▪ Loss of patient data, i.e., when data is excluded from the analysis may result in type I or type II errors: In one simulation (N=200)with loss of 20%, the risk of type I error* was 10%. With loss of 40% risk of type I error was 50%. [2]             <ul style="list-style-type: none"> <li>○ *Type 1 - or alpha error - A difference is reported, but there is no difference. This can be due to bias, confounding or chance.</li> </ul> </li> <li>▪ Kaplan-Meir estimates use models to account for attrition and has been reported to distort results by a relative 50% or higher.[2]</li> <li>▪ Other references supporting above—[3]</li> <li>▪ Quantifying the amount of distortion and predicting the direction of distortion with post-randomization loss of subjects remain problematic.</li> </ul>
<p><b>Conclusion</b></p>	<ul style="list-style-type: none"> <li>▪ Because there is no good answer for quantifying the amount of attrition that may matter, reviewers will have to come up with their own methods for dealing with this problem.</li> <li>▪ Dr. Steve Simon provides some advice: <a href="http://www.delfini.org/delfiniClick_PrimaryStudies.htm#dropout">http://www.delfini.org/delfiniClick_PrimaryStudies.htm#dropout</a></li> <li>▪ We think his approach is reasonable and also think it is reasonable to be concerned about a rate smaller</li> </ul>

# Delfini Primer: Problems with Attrition Bias

than 10 percent or to accept higher percentages of loss of data on a case-by-case following evaluation of potential reasons for the loss and likelihood of impact on prognostic variables, convincing sensitivity analyses and/or other information, (e.g, similarities of baseline characteristics at randomization and at analysis if the groups remain balanced in terms of prognostic variables).

- For examples and more details, see [http://www.delfini.org/delfiniClick\\_SecondaryStudies.htm#bellsupdate](http://www.delfini.org/delfiniClick_SecondaryStudies.htm#bellsupdate)

## 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		
	Surgery (N=62)	Nonsurgical (N=49)	P Value	Surgery (N=67)	Nonsurgical (N=65)	P Value
Results	7.5% loss	24.6% loss				
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

Category	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.