

(P value). The goal of this chapter is to serve as a starting point in biostatistics, and to provide a reference point for use in navigating through textbooks on biostatistics.

XII. STATISTICAL ANALYSIS BY SUPERIORITY ANALYSIS VERSUS BY NON-INFERIORITY ANALYSIS

The two arms found in a typical Kaplan–Meier plot can be compared or analyzed by various statistical methods, including superiority analysis and non-inferiority analysis. Where the study drug is compared to a placebo, superiority analysis is used. But where the study drug is compared with an active control drug, or with the standard or traditional treatment, both superiority analysis and non-inferiority analysis are used (84).

While sponsors and investigators prefer that their drug be superior to the control treatment, the difference in efficacy may be insignificant. Where the difference is insignificant, the clinical trial can be rescued, at least in some situations, by non-inferiority analysis.

Following the clinical trial, the statistician analyzes the results to determine if the study drug is superior to the active control drug. The statistician also analyzes the results to determine if the study drug is not significantly inferior to the active control.

With non-inferiority analysis, the goal of the investigator is to prove that the efficacy of the study drug is better than, equivalent to, or only trivially worse than, the active control in terms of efficacy (85). D’Agostino et al. (86) emphasize that, in designing a non-inferiority clinical trial, the comparator drug should be the *best available* comparator drug.

In addition to the superiority trial design, and the non-inferiority trial design, another type of trial design is the equivalence trial. The goal of this type of trial is to demonstrate that the study drug is both insignificantly better than and insignificantly worse than an active control drug. Paggio et al. (87) document the fact that published reports of clinical trials frequently confuse the concepts of non-inferiority and equivalence.

In conducting a clinical trial, the sponsor prefers to show that its study drug is superior to an active control drug in terms of efficacy. However, if superiority in terms of efficacy cannot be shown, and where the investigator is not willing to scrap the results from the clinical trial, the results can be salvaged by using non-inferiority analysis. In practice, statisticians conduct the non-inferiority analysis first, and once this is complete, they conduct the superiority analysis (88). The following situation concerns

⁸⁴ U.S. Dept. of Health and Human Services. Food and Drug Administration. Guidance for Industry. Non-inferiority clinical trials. March 2010; (66 pages).

⁸⁵ Piaggio G, Elbourne DR, Altman DG, Pocock SJ, Evans SJ, CONSORT Group. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT statement. *J Am Med Assoc.* 2006;295:1152–1160.

⁸⁶ D’Agostino Sr RB, Massaro JM, Sullivan LM. Non-inferiority trials: design concepts and issues – the encounters of academic consultants in statistics. *Stat Med.* 2003;22:169–186.

⁸⁷ Piaggio G, Elbourne DR, Altman DG, Pocock SJ, Evans SJ, CONSORT Group. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT statement. *J Am Med Assoc.* 2006;295:1152–1160.

⁸⁸ The author thanks Dr. Jenna Elder for this fact.