

Introduction to Clinical Trials

The evolution of the clinical trial dates from the eighteenth century.^{10,55} Lind, in his classical study on board the *Salisbury*, evaluated six treatments for scurvy in 12 patients. One of the two who were given oranges and lemons recovered quickly and was fit for duty after 6 days. The second was the best recovered of the others and was assigned the role of nurse to the remaining 10 patients. Several other comparative studies were also conducted in the eighteenth and nineteenth centuries. The comparison groups comprised literature controls, other historical controls, and concurrent controls.⁵⁵

The concept of randomization was introduced by Fisher and applied in agricultural research in 1926.⁸ The first clinical trial that used a form of random assignment of subjects to study groups was reported in 1931 by Amberson et al.² After careful matching of 24 patients with pulmonary tuberculosis into comparable groups of 12 each, a flip of a coin determined which group received sanocrysin, a gold compound commonly used at that time. The British Medical Research Council trial of streptomycin in patients with tuberculosis, reported in 1948, was the first to use random numbers in the allocation to experimental and control groups.^{42,58}

The principle of blindness was also introduced in the trial by Amberson et al.² The patients were not aware of whether they received intravenous injections of sanocrysin or distilled water. In a trial of cold vaccines in 1938, Diehl et al.²⁶ referred to the saline solution given to the subjects in the control group as a placebo.

It is only in the past few decades that the clinical trial has emerged as the preferred method in the evaluation of medical interventions. Techniques of implementation and special methods of analysis have been developed during this period. Many of the principles have their origins in work by Hill.^{27,46,47,48}

Because the authors of this book have all spent formative years at the National Institutes of Health (NIH), it is also pertinent to cite a series of papers that reviews the history of clinical trials development at the NIH.*

The purpose of this chapter is to define clinical trials; review the need for them; and discuss timing, phasing, and ethics of clinical trials.

*References 13, 36, 40, 43, 66

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