

Factorial trials were soon used to good effect to explore two or more independent topics in one experiment as a measure of economy and administrative ease. They were used in further studies of the effects of treatments for hepatitis ([Chalmers et al. 1955](#)), and in trying to sort out the mess of multiple treatment options for patients with gastric ulcers ([Doll and Pygott 1952](#), Doll 1964). Not only could they be used to study alternative therapies, but they were sometimes suitable (size and statistical power permitting) for investigating completely independent clinical problems (see, for example, Physicians Health Study Group 1989; Hennekens et al. 1996). It also became clear that factorial design trials constituted a powerful way of examining combination therapies and synergistic or antagonistic interactions between treatment combinations (ISIS-2 Collaborative Group 1988; MRC Vitamin Study Group 1991)

The complexities that factorial trials can create are not inconsiderable: assessing statistical power, especially if studying interactions; matching separate inclusion/exclusion criteria; dealing with separate side effects, compliance differences and cross-over problems; and coping with trial stopping decisions. However, all these issues were absent in this early example of a factorial trial. It was an affordable, sensible opportunity to examine two 'separate' clinical management issues in one series of patients. How 'simple' medical research once was.....!

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