

Distinctions between Fraud, Bias, Errors, Misunderstanding, and Incompetence

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ABSTRACT: Randomized clinical trials are challenging not only in their design and analysis, but in their conduct as well. Despite the best intentions and efforts, problems often arise in the conduct of trials, including errors, misunderstandings, and bias. In some instances, key players in a trial may discover that they are not able or competent to meet requirements of the study. In a few cases, fraudulent activity occurs. While none of these problems is desirable, randomized clinical trials are usually found sufficiently robust by many key individuals to produce valid results. Other problems are not tolerable. Confusion may arise among scientists, scientific and lay press, and the public about the distinctions between these areas and their implications. We shall try to define these problems and illustrate their impact through a series of examples. *Controlled Clin Trials* 1997;18:637-650 © Elsevier Science Inc. 1997

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Patients who agree to be entered into clinical trials are well-motivated and often somewhat knowledgeable about the disease and the available therapies. In their enthusiasm or commitment to the trial, patients can allow biases to enter into their responses. **An example of this can be seen in a trial conducted at the National Institutes of Health (NIH) [9] on the effectiveness of vitamin C in the treatment of the common cold.** The outcome was duration of cold symptoms. The trial was a randomized, double-blind, placebo-controlled study. Since patients in the study were employees of the NIH, they had either direct or indirect access to laboratories, and were easily able to break the double blind. Overall, there was no discernible difference in the duration of the symptoms between placebo- and vitamin C-treated patients. Patients were asked if they had, in fact, used their own resources in the laboratories to break the blind. For those who had not, vitamin C showed no benefit. For those who had broken the blind, the vitamin C-treated patients reported cold symptoms present for an average of 3.8 fewer days than those who knew they were on the placebo. Since the bias was applied to the primary outcome, it is clear that bias in this case could have created an artificial treatment benefit if all patients had been unblinded.

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