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## Armitage P. Randomisation and alternation: a note on Diehl *et al*

**Commentary on:** Diehl HS, Baker AB, Cowan DW (1938). Cold vaccines: an evaluation based on a controlled study. *Journal of American Medical Association* 111:1168-73.

**Cite as:** Armitage P (2002). Randomisation and alternation: a note on Diehl *et al*. The James Lind Library ([www.jameslindlibrary.org](http://www.jameslindlibrary.org)). Accessed Monday 11 July 2005.

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The series of trials of cold vaccines, reported in 1938 by Diehl *et al.*, is often quoted as an example of the early use of randomisation as opposed to alternation; see elsewhere in this website. The authors stated that the subjects (university students) 'were assigned at random and without selection to a control or to an experimental group'. However, the phrase 'at random' was at that time often used loosely, to imply some form of non-selective assignment, without the connotation of strict randomization. The situation has been clarified by L A Waller (1997).

The Bio-Medical Library of the University of Minnesota contains an unpublished manuscript by Diehl summarising an address he gave in 1941. In describing the 1938 results, he states: 'At the beginning of the study, students who volunteered to take these treatments were assigned *alternately* and without selection to control groups and experimental groups'. Waller notes that, in earlier trials of treatments for the common cold, published in 1933 and 1935, Diehl had assigned students to different treatments by alternation.

There is one other puzzling feature of the 1938 paper. Table 1 shows the results of a trial of a bacterial vaccine administered subcutaneously, compared with a placebo injection. The trial took place in two successive years, 1935-36 and 1936-37. The numbers of subjects completing the study in the two years are given as:

Vaccinated: 156 and 116, respectively;

Control: 107 and 169, respectively.

The totals in the two groups are similar (272 and 276), but the imbalance in each separate year is surprising and quite inconsistent with the stated allocation system. Without the clarification provided by Diehl's later account one might have surmised that treatments were assigned with inadequate control in the first year, the numbers in the second year being adjusted to make the totals balance. However, another explanation may be that the columns in Table 1 have been transposed, so that the numbers on the two treatments should be (116, 107) in one year, and (156, 169) in the other year. The slight differences between the numbers in each year could have arisen from unequal numbers failing to complete the course. Support for this view comes from the fact that Table 5, giving results for a trial of an oral vaccine, shows no similar anomaly.

### References

Waller LA (1997). A note on Harold S Diehl, randomization, and clinical trials. *Controlled Clinical Trials* 18: 180-183.

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