Invited Comment

H.A.F.

Dudley

Surgical Unit, St. Mary's Hospital, London, GB

Prof. Dr. H.A.F. Dudley, Professor of Surgery, St. Mary's Hospital, Surgical Unit, London W2 1PG (GB)

Dr. *Merlo* has addressed a group of problems that surgeons should be constantly aware of and debate. Unfortunately, the practical action-orientated surgeon is often loath to become involved with the intellectual side of trial design and execution, regarding the apparatus of trials as something of a mystery but capable of producing highly reliable results provided he follows a set of rules prescribed by others. Nothing of course could be further from the truth and it is thus important that Dr. *Merlo* should draw our attention to those features of surgical trials which distinguish them from the wider group of drug and non-surgical procedure trials for which trial design was originally developed. I do not think that many physicians would agree that the prescription of drugs is without a placebo effect or a halo of 'art' which may influence the outcome so that in this respect medical and surgical trials are not all that different as Dr. *Merlo* implies. Akin to this is the fact that in relation to surgical procedures after-treatment may also have a considerable effect on results. For example few would doubt that careful advice and counselling of the patient after gastric surgery for duodenal ulcer will influence the patient's adaptation to his new circumstances; yet this factor has never been taken into account in the extensive evaluations of the different procedures which have been done over the past 30 years.

What Dr. *Merlo* refers to as the 'skill' factor requires further discussion. Recently we have drawn attention in relation to large bowel surgery for cancer to the fact that there is a wide distribution of surgical skills [1] which will effectively obliterate real differences that might exist when treatments are compared. Similarly 'noise' is introduced into a trial if the variability between individuals increases faster than the information derived from them – a situation that often pertains in clinical trials where many centres are involved [2]. 'Multicentre' is not a placebo for small numbers, a fact which accounts for the frequent failure of such trials to produce positive as distinct from negative results.

Many other matters both of principle and of detail flow from Dr. *Merlo's* overview.

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Prominent amongst these are the importance, where cost and effort are often so large, are the need to have some clear preconception of the sort of differences which are (a) likely to be encountered, (b) likely to be of interest in terms of altering clinical practice and (c) likely to be detected given the rate of entry into the trial and the duration of study that is practical. Failure to pay attention to these simple factors which can then be used to determine the structure of the trial in terms of numbers has led to many trials 'crashing' without results of any value and to the ingloriousness of the participants.

References

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