

LETTER

Trials: The worst possible design (except for all the rest)

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To the Editor

Penston [1,2] has done well to draw attention to the serious problems that occur with randomized trials as they are currently conducted in practice. Logically, it is certainly true that one cannot attribute an observed difference between treatment groups to the difference in treatments (the intended inference) if there are other plausible explanations, such as selection bias [3] or some other bias. But the parallel argument seems to have been missed. If trials are not getting the job done, then can we attribute this failure to the involvement of statisticians, without even considering other possible explanations?

It is true that much statistical work, perhaps even a majority (however we might choose to measure this quantity), is grossly incompetent. Is the answer, then, to dismiss with statistical involvement altogether? Or should we instead be calling for better statistical work? If a statistician cannot be bothered, for example, to use an exact analysis because the approximation is easier [4], or if a statistician uses permuted blocks (which, despite the suggestion [2] to the contrary, actually serve to practically ensure selection bias), then do we conclude that things would be better if only there were no statisticians? The reality, as noted, is that in some cases (the word “infrequent” intentionally omitted), statisticians do cause more problems than they solve and do contribute to the scandal of medical research [5]. This does not justify condemning all statisticians with a broad brush, nor does it justify condemning all statistics-based research.

But beyond that, even if it were the case that all statisticians were grossly incompetent, this still would not mean that statistics as a discipline should not have a profound influence in medical research. At its best, statistical input is an asset, not a hindrance and this

remains true regardless of how competent statisticians, as a group, happen to be in the ephemeral here and now. As another parallel, trials also remain an asset, not a hindrance, in that they remove so many other biases inherent in other study designs. So while Penston [1,2] is quite correct that the vulnerability of trials to multiple biases is both real and underappreciated, the solution is not to dispense with trials any more than we want to throw out the baby with the bath water. The message should be instead that we need to be very cautious in accepting the results of any study, but the design that gives the best fighting chance is the randomized clinical trial, which is the worst of all possible designs, other than the rest.

One other point merits attention. It was suggested that the consumer would be disappointed when he or she got home to open the poke and find the cat instead of the pig. But let us not lose sight of the fact that there are two distinct sets of consumers, those making decisions and those suffering the consequences of those decisions. Trials tend to offer certainty, even when this certainty is misleading and just plain wrong. In practice, the poke is never inspected after the sale, because there is no incentive for doing so. After all, those who read the trial reports will, with few exceptions, not be the ones taking the drugs studied by these trials. If the trials “prove” that the drug works, but in actuality it doesn’t, this is not a serious problem for those who prescribe the drug to others, or to those who might publish the report (and, in a sense, “buy” the poke that is the trial). What we have here is moral hazard, or one party acting on behalf of another, but not suffering the consequences of the decisions so rendered. So in addition to needing better trials, more careful consideration of what can go wrong in trials, better reporting of trial results and better statistical input, we also need a more educated and involved general public.

References

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