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Testing for Baseline Balance: Can We Finally Get It Right?

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Editor

Austin et al. [1] followed in the footsteps of other authors in condemning hypothesis testing of baseline covariates as inappropriate and illogical. Unfortunately, the pied piper does not always lead us in the right direction; hence we need diligence to determine which advice to follow. Citing 161 references would appear to cover all the bases, but the key publications pointing out the flaw in the logic of the aforementioned argument – including one by M Zwarenstein in this very journal [2] -- were curiously missing. The conclusion that baseline testing is illogical is predicated on the notion that all outcomes of the randomization are equally likely, or, if restrictions are used, then with 1:1 allocation (equal group sizes) any outcome is exactly as likely as its mirror image. This condition, if true, would ensure balance among the population of randomization outcomes, and would render formal baseline testing illogical.

But it is simply not true. Berger [3] documented 30 trials with at least suspected selection bias of the type that would ensure that certain patients end up in certain treatment groups, and for reasons discussed therein, this is likely the tip of the iceberg. When future allocations can be predicted, which is the case when masking is absent or imperfect and restricted randomization is used (i.e., just about always), one can funnel healthier patients to one group and sicker patients to the other group. This is not a hypothetical concern; as stated, it actually occurs in practice. So it may be true that Patient #4, for example, is just as likely to fall into one treatment group as into the other. This does not imply that the *patient* who eventually became Patient #4 shares this same balance property. It may be that the patient in question was destined to receive Treatment A, for example, and became Patient #4 only after it became clear that Patient #4 would be allocated to Treatment Group A. Had this not been the case, the patient in question would have been turned away or deferred until Treatment A was due to be allocated.

This is why a strong case can be made for the logic of formal hypothesis testing of baseline variables [4]. The test is actually a test of selection bias of the type that would render population balance lacking. We cannot know ahead of time that there is no selection bias, which is why testing for it is so crucial [3], and logical. The irony is the flawed logic in continuing to call into question the logic of baseline testing, even after so many publications (there are many more than those cited here) have put the issue to rest. Of course, as a test of selection bias, baseline testing is useful but far from ideal. Far better is the Berger-Exner test [3].

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