Letter to the Editor
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Concealing Block Sizes Is Not Sufficient

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To the Editor:
Kim and Shin[1] correctly noted that blocked randomization has a disadvantage that "the executer can predict the next assignment" and this is clearly incompatible with allocation concealment. So we can agree that permuted blocks with a fixed block size should never be used in randomized trials.[2] But what is the solution to this problem? Kim and Shin[1] indicated that "To solve this problem, the allocator must hide the block size form the executer and use randomly mixed block sizes." This would be an ideal solution if our only objective were to minimize deterministic allocations. But some allocations are predictable even while not being entirely deterministic. For example, if the block size is four, and the identity of the first treatment allocated is known, then the second allocation is not deterministic, but it is still predictable, since it is twice as likely to be the treatment that was not allocated first. These predictable allocations allow investigators betting odds, so even these must be minimized.

The reality is that even with unusual, varied, and concealed block sizes, there will still be some deterministic allocations, and an abundance of predictable allocations. For example, suppose it is known that the block sizes in a given unmasked trial are varied, two and four, and suppose that at a certain point in the trial there are two more patients allocated to the control group than to the active group. Then it can be deduced that the current block size is four, since a block of size two will never allow the imbalance to exceed one. We also know that we are halfway through a CCAA block, so the next two allocations must be to the active group.

But the bigger issue is, as noted, the large number of predictable allocations. Any randomization procedure that is restricted so as to force equal numbers allocated to each treatment group will be vulnerable to the convergent strategy of guessing (without certainty) that the next treatment to be allocated will be the one so far less well represented. This is not particular to permuted blocks with either fixed or varied block sizes. However, varying block sizes will be more susceptible since there are smaller blocks (on average) than there would be with a fixed block size of the largest size used. Hence, the convergent strategy will be more effective with varied block sizes than it will be with fixed block sizes. Table 5.4 of Berger[3] illustrates that fixed block sizes are better than varied block sizes when investigators use the convergent strategy. But of course, as noted, permuted blocks with fixed block sizes should never be used.[2] Clearly, then, neither should permuted blocks with varied block sizes.[4]

Fortunately, there is a better way to randomize. Specifically, the maximal procedure[5] has been amply demonstrated to be uniformly better than the permuted blocks procedure for ensuring allocation concealment and controlling selection bias. It too is vulnerable to the convergent strategy, but not nearly as much as the permuted blocks procedure is, with either fixed or varied blocks, as quantified in Table 5.4 of Berger.[3] Therefore, it is the maximal procedure, and not varied or unusual or concealed block sizes, which is the solution to the problem of prediction.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Jeehyoung Kim and Wonshik Shin, Reply:

Thank you for your valuable and insightful comments. We agree with you that the maximal procedure has some advantages over block randomization with regard to allocation concealment. Still, block randomization is the most popular and most widely accepted method recommended by CONSORT (http://www.consort-statement.org/checklists/view/32-consort/87-randomisation-type). So, we intended to introduce the most common primary methods, such as simple randomization and block randomization, in the article.

Allocation concealment can only be improved, but not perfected, with a larger block size or the combined use of block randomization and simple randomization.[1] In this regard, we hope the maximal procedure, which to our knowledge is not so commonly used among researchers, would be more widely utilized in the future. Also, we hope the excel sheet that can be downloaded for free at http://me2.do/xLOvOXkF would be helpful for readers interested in the maximal procedure. Once again, we appreciate your constructive comments.

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No potential conflict of interest relevant to this article was reported.

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