Dear Editor,

Tamm and Hilgers [1] are to be congratulated for bringing more attention to a rather important issue in trial design, namely chronological bias. Far too many researchers use permuted blocks without even recognizing that chronological bias is the reason they do it. Only armed with the rationale can we hope to enter an informed discussion regarding the merits, or lack thereof, for using permuted block randomization in actual trials. But chronological bias is only part of the story. If it were the entire story, then we could just use blocks of size two, or even alternate. But we can’t, and the reason we can’t is selection bias. The two are at odds, as the solution to chronological bias is a small block size, and the solution to selection bias is a large block size [2, 3]. At least this would be the case if we were limited to using permuted blocks. Fortunately, we are not.

Fortunately, there are much better randomization procedures, including the maximal procedure [2, 3], which matches permuted blocks for control of chronological bias while beating it for control of selection bias. Given this undisputed fact, coupled with the ease of using the maximal procedure, there really is no reason to continue using the antiquated and obsolete permuted blocks procedure [4], even if the block sizes are varied [5]. Consequently, the conclusion [1] that small blocks are to be preferred is misguided. The permuted blocks procedure has no role to play in serious research, but even if we were to make the mistake of using permuted blocks, the conclusion would still be misguided, since larger blocks are preferable, owing to the fact that selection bias is the more serious concern. Despite the name, or misnomer, chronological bias is not even a bias. One cannot rig it, so far as we know, so as to advantage a preferred treatment group. It is a source of variation, since it is just as likely to favor one treatment group as the other. Selection bias truly is a bias that can favor a preferred treatment group. Finally, the suggestion to use ANOVA is also misguided, since ANOVA is valid only for normally distributed data, which is to say, never.

References