multiple regression, in which the candidate variables should include known prognostic variables[13] as well as those which exhibit substantial differences between the groups at baseline. This more general strategy allows for model reduction when some of the prognostic variables are highly correlated. Both the adjusted and unadjusted analyses should be presented and discussed.

In conclusion, different authors have considered separate aspects of the problem of imbalance in randomized trials – size, power, precision and unbiasedness. While all are important, it seems to us that unbiasedness is of most importance.

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A STRATIFIED WILCOXON-TYPE TEST FOR TREND

by David Yu-Wu Pee and L. S. Freedman, *Statistics in Medicine*, **9**, 829–834 (1990)

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Just as the non-parametric Wilcoxon-like trend test proposed by Cuzick[1] had already previously been described,[2] so the stratified extension of it proposed by Pee and Freedman has already been discussed in the literature.[3,4] All three papers rank observations within stratum and compare, within each stratum, the statistic T with its expectation, where

$$T = \sum_{j=1}^{k} d_j R_j.$$

Here j is group ($j = 1, \ldots, k$), and d_j the exposure level and R_j the sum of ranks for group j. The original paper by Shirley[3] gave equal weight to each stratum, but it was clear that because the expectation of an individual rank is proportional to the number of subjects in the stratum, results from subjects in strata with many observations would carry too much weight compared to results in small strata. Pee and Freedman recommended applying weights equal to $1/(n_s + 1)$ where n_s is the number of subjects in the stratum. Although they give a reason why this is statistically optimal, there is a good reason for justifying the weights $2/n_s$ recommended in our letter[4] on Shirley's paper. This is that, if appropriate corrections for ties are made, the rank formula then collapses identically into the well-known Mantel stratified trend test[5] in the situation where response is only at two levels. In practice, of course, either set of weights should lead to very similar conclusions, and provide an extremely useful test of very general applicability.

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AUTHORS' REPLY

We thank Drs. Fry and Lee for pointing out other work on stratified rank tests. We were not aware of the recent paper by Shirley[1] or of their letter to *Applied Statistics*.[2] The proposal in that letter is indeed very close to our suggested test and is asymptotically equivalent. We think that these simple but powerful methods will be helpful in many contexts.

Their remark questioning the novelty of Cuzick's work[3] has been raised before[4,5] and replied to by Cuzick.[6] Cuzick's intention was to bring methodology, developed by others, to the attention of those involved in medical applications. Such is one of the published aims of this journal.

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