Matching and the assumptions of standard frequentist statistics

To the Editor:

We read with great interest the recent paper by Tempfer et al. (1) in which they report a significant difference ($P = .04$) in the proportion of live births between treated and untreated women diagnosed with idiopathic recurrent miscarriage. In this matched prospective cohort study the investigators selected a group of 52 of 67 eligible untreated women and matched them, based on the distribution of age and history of miscarriage, to 52 women who received the treatment of interest. They do not explain the reasons for using a matching strategy. Adjustment for potential confounding variables, such as age and history of miscarriage, is an important component of study validity. However, matching is a poor strategy to adjust for confounding under any design, but more specifically under the cohort study design in which simple adjustment procedures address confounding without the loss of eligible but unmatched participants and the inherent costs in identifying matched unexposed (2). Rather, matching is a strategy that may improve study precision by balancing the distribution of matching covariates across exposed and unexposed groups. Matched data violate the independence assumption of standard analytic approaches. Methods that account for the correlation between exposed and unexposed groups introduced as a consequence of the match are required. Conditional on the direction and magnitude of the introduced correlation, matching may reduce or even increase the variance of the difference between two proportions (3) and as such increase or reduce study power. Numerous statistical techniques that account for the correlated observations produced by a matching strategy, such as McNemar’s test, conditional logistic regression, and generalized estimating equations, have been described in the literature (4) and are frequently available in commercial statistics software packages.

doi:10.1016/j.fertnstert.2006.08.075

Reply of the Author:

We thank Drs. Bloom and Whitcomb for their valuable comments regarding our study. We used a matching strategy to strictly balance the study and control groups for the two most important prognostic covariates in women with idiopathic recurrent miscarriage (e.g., age and number of previous miscarriages). We agree that a matching strategy also has disadvantages such as a possible increase of the variance between the two groups regarding other covariates. Following the suggestion by Drs. Bloom and Whitcomb, we have applied McNemar’s test to our data set, which did not change the results.

We want to stress the fact that we did not select a group of 52 of 67 eligible untreated women rather than matching controls consecutively starting with the earliest inclusion date, thus trying to avoid a specific selection bias.

We want to emphasize that we clearly acknowledged the weaknesses of our study design. We have noted in the discussion section that the treatment used in this study “... might be an effective treatment for women with idiopathic recurrent miscarriage ...” and that properly designed “... prospective-randomized trials are encouraged to establish this treatment scheme.”

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August 2, 2006

doi:10.1016/j.fertnstert.2006.08.077