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PII S0015-0282(02)03260-0

Reply of the Author:

Dr. Mahutte and colleagues have posed numerous questions about the methodology and conclusions of our paper on cost-effectiveness modeling of recombinant FSH versus urinary FSH in assisted reproduction (1). We appreciate the opportunity to respond.

To address the first query, the clinical superiority of recombinant FSH over urinary FSH was not based on assumptions; rather, it was clearly established in meta-analyses of randomized clinical trials (2, 3). Although the differences in pregnancy outcome in all of the trials were not statistically significant because of insufficient power, this lack of significance should not be confused with equivalence, as intimated by Dr. Mahutte et al. In addition, publication bias generally favors positive studies, not those with no significant difference, as was observed in all the trials in question. Furthermore, the funnel plot analysis included in the Cochrane analysis demonstrated no publication bias regarding the randomized clinical trials included in the meta-analysis (3).

The second query pertained to the methodology. The retail price per ampule was established from a survey of 60 U.S. pharmacies that specialize in the infertility market. Procedural and other associated costs of ART were averaged across 100 ART centers in the United States. The variability around the probability estimates was provided by expert opinion. From these estimates of range, SDs were calculated (not estimated) by using a standard formula as described in our paper. A probability expressed in percentage automatically uses two decimal places, and when expressing a percentage, it is common to use decimal format (e.g., 32.5% = 0.325). In addition, the model we used is sufficiently robust to not observe significant differences in results when the number of decimal places is reduced.

Dr. Mahutte and colleagues do not appear to be familiar with the use of modeling in cost-effectiveness analysis. Effectiveness and cost values calculated by the model are strictly proportional to the number of virtual patients. We chose 100,000 patients for our model to avoid dealing with fractions of patients in sections of the decision tree in which there were several branches. The results of the cost-effectiveness analysis would have remained the same whether there were 100, 1000, or 100,000 patients in the Markov cohort.

The speculation that the cost analysis would have changed if we utilized a worst-case scenario for recombinant FSH versus a best-case scenario for urinary FSH ignores the fact that cost-effectiveness and not cost analysis is the focus of our study. Furthermore, used of a "minimum-maximum" scenario to approximate a "real-world" event is superceded in our model by simulating all possibilities of parameter combinations with a multivariate sensitivity analysis using the Monte Carlo technique. This type of sensibility analysis represents the state of the art, whereby robust methods are used to construct valid confidence intervals so that statistical tests can be performed to examine whether recombinant FSH is more cost-effective than urinary FSH.

Finally, we are not aware of any published prospective randomized clinical trials comparing recombinant FSH and hMG that are of sufficient statistical power to demonstrate a difference in clinical pregnancy rates. By our calculations, to demonstrate equivalence, such a study would require thousands of patients. Until such a study is undertaken, it is not possible to draw conclusions on any potential equivalence between the two products.

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PII S0015-0282(02)03261-2

Laterality associations?

To the Editor:

Dr. Donnez provides important information with his series of patients with ureteral and rectovaginal endometriosis (1). The predilection of parous endometriosis for the left uterosacral ligament was sustained in the four parous patients (3 of 4 cases were left sided), and he also provides a thoughtful discussion of laterality of the disease. It is difficult not to look for an association between left-sided (posterior pelvis) endometriosis and the right-sided (anterior