Models of cost-effectiveness of recombinant FSH versus urinary FSH

Dear Sir,

We read with great interest the two articles comparing the cost-effectiveness of recombinant (r)FSH versus urinary (u)FSH (Daya et al., 2001; Sykes et al., 2001). We appreciate the efforts
Letters to the Editor

Comparison-01 pregnancy rate / started cycle
Outcome: 01 pregnancy rate / started cycle

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daya &amp; Gunby (2000)</td>
<td>540 / 1831</td>
<td>418 / 1592</td>
<td></td>
<td>62.4</td>
<td>1.17 [1.01,1.37]</td>
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<tr>
<td>Diedrich (2000)</td>
<td>71 / 354</td>
<td>85 / 373</td>
<td></td>
<td>13.1</td>
<td>0.85 [0.60,1.21]</td>
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<tr>
<td>Gordon et al. (2000)</td>
<td>11 / 39</td>
<td>23 / 89</td>
<td></td>
<td>2.0</td>
<td>1.13 [0.48,2.62]</td>
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<tr>
<td>Ng et al. (2001)</td>
<td>4 / 20</td>
<td>5 / 20</td>
<td></td>
<td>0.8</td>
<td>0.75 [0.17,3.33]</td>
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<tr>
<td>Strehler et al. (2001)</td>
<td>78 / 296</td>
<td>80 / 282</td>
<td></td>
<td>11.9</td>
<td>0.90 [0.63,1.30]</td>
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<td>Westergaard et al. (2001)</td>
<td>65 / 190</td>
<td>75 / 189</td>
<td></td>
<td>9.8</td>
<td>0.79 [0.52,1.20]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>769 / 2730</td>
<td>686 / 2545</td>
<td></td>
<td>100.0</td>
<td>1.06 [0.94,1.19]</td>
</tr>
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Test for heterogeneity chi-square = 6.14 df = 5 P = 0.29
Test for overall effect z = 0.91 P = 0.4

Figure 1. Update comparison between recombinant versus urinary FSH.

undertaken by the authors of both papers to build up cost-effectiveness models in IVF/ICSI programmes. In both articles, the cornerstone of building up the model was the assumption that rFSH is associated with a better pregnancy rates per started cycle than uFSH. This assumption is based on evidence provided by a meta-analysis (Daya and Gunby, 1999).

The National Institute of Clinical Excellence (NICE) has recently announced that it will be analysing the cost effectiveness of treatment for fertility in UK (Barlow, 2001). It is expected that this analysis will be based on the best available evidence. We do not think these two articles (Daya et al., 2001; Sykes et al., 2001) will be considered to help the decision-makers for the reasons discussed below.

The Cochrane Library is the best single source for evidence-based medicine and its systematic reviews are well designed and well conducted. However, when registering a review with the Cochrane Collaboration, reviewers agree to keep it up to date. This entails repeating, at periodic intervals, the steps involved in the original review. The most logistically demanding aspect of keeping a review up to date is the identification of new studies (Cochrane Library Handbook, 2001). Unfortunately, this was not the case on this topic. Although this systematic review was updated in 2000 (Daya and Gunby, 2000), no further update has been undertaken since then, thus there is a possibility of missing some important studies that may affect the results.

On conducting a Medline search and searching the abstract of the ESHRE and ASRM meetings for 2001, we identified five additional randomized controlled trials testing the exact question upon which cost-effectiveness was based (Gordon et al., 2001; Ng et al., 2001; Strehler et al., 2001; Westergaard et al., 2001; Diedrich et al., 2002).

Based on the updated-meta-analysis of Daya and Gunby (Daya and Gunby, 2000) we added the five trials and there was no significant difference between rFSH and uFSH in pregnancy rate/started cycle (Figure 1). Estimated odds ratio (OR) is 1.06 [95% confidence interval (CI) 0.94–1.19]. If we exclude the Gordon et al. trial because it used varying doses of LH (Gordon et al., 2001), OR is 1.06 (0.93–1.19). If we compare trials between rFSH versus HMG alone, OR is 0.9 (0.7–1.09). If we compare rFSH versus uFSH–HP (highly purified) alone, OR is 1.12 (0.93–1.35). If we compare rFSH versus purified uFSH, the OR is 1.2 (0.9–1.5). Thus there was no significant difference in the subgroup analysis. In our data analysis we used only studies that performed down-regulation using long protocol.

Given the cost of medications presented in both articles, it does not need modelling to assume with confidence that uFSH is more cost-effective than the costly rFSH. There is no reason to suggest that the cost-effectiveness modelling presented by the authors is restricted to the UK. Extracting data from selected studies (sponsored by the same pharmaceutical company) as done in the Sykes et al. article and ignoring all other studies because they were done in UK does not seem to be appropriate.

As far as we know there is no national variation in response to either rFSH or uFSH. Publishing these two articles in a journal like Human Reproduction will definitely have great impact of wider application in other countries. Implementing the principles of evidence-based medicine, whether in the UK, the Netherlands, Egypt, etc. (even if they are different health care systems) will ultimately result in providing our patients with the best care in a cost-effective way.

In conclusion, the assumption on which both papers built their own models is now outdated and the conclusions reached by the authors in both articles are therefore not valid.

References
Diedrich, K. (2002) Results of multicountry multi-center, randomized clinical trial comparing the efficacy and safety of highly purified menotrophin and
In conclusion, the results from valid randomized trials confirm the clinical superiority of rFSH in treatment with assisted reproductive techniques and its greater cost-effectiveness confers benefit that will be appreciated by policy makers, health care providers, insurance companies and consumers.

References