Cost-effectiveness analysis comparing continuation of assisted reproductive technology with conversion to intrauterine insemination in patients with low follicle numbers

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Objective: To compare the cost effectiveness of proceeding with oocyte retrieval vs. converting to intrauterine insemination (IUI) in patients with ≤4 mature follicles during assisted reproductive technology (ART) cycles.

Design: Probabilistic decision analysis. The cost effectiveness of completing ART cycles in poor responders was compared to that for converting the cycles to IUI.

Setting: Not applicable.

Patient(s): Not applicable.

Intervention(s): Cost-effectiveness analysis.

Main Outcome Measure(s): Cost effectiveness, which was defined as the average direct medical costs per ongoing pregnancy.

Result(s): In patients with 1–3 mature follicles, completing ART was more cost effective if the cost of a single ART cycle was between $10,000 and $25,000. For patients with 4 mature follicles, if an ART cycle cost <$18,025, it was more cost effective to continue with oocyte retrieval than to convert to IUI.

Conclusion(s): In patients with ≤4 mature follicles following ovarian stimulation in ART cycles, it was on average more cost effective to proceed with oocyte retrieval rather than convert to IUI. However, important factors, such as age, prior ART failures, other fertility factors, and medications used in each individual case need to be considered before this analysis model can be adapted by individual practices. (Fertil Steril © 2014;102:435–9. © 2014 by American Society for Reproductive Medicine.)

Key Words: Poor responders, intrauterine insemination, assisted reproductive technologies, cost effectiveness

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rates and high cancellation rates (8). Moreover, a large percentage of poor responders continue to respond poorly in subsequent ART cycles (9). Management options for poor responders include: cancellation, conversion to intrauterine insemination (IUI), or continuation with the ART cycle by proceeding to oocyte retrieval. This decision process is often difficult for both patients and physicians and involves clinical, financial, logistic, and emotional considerations.

The objective of this study was to identify which procedure is more cost effective in patients with ≤4 mature follicles during ART: conversion to IUI or continuation with oocyte retrieval. This study was conducted based on average outcome data in the literature and the average direct medical costs in clinics across the United States. However, the model used may be individualized to assist both patients and physicians in deciding whether to proceed with oocyte retrieval or convert to IUI in these patients.

MATERIALS AND METHODS

Since all probabilities and costs for the decision analysis were obtained from existing publications and publicly available information, this study was exempt from review by institutional review board. A decision-tree model (Fig. 1) was created to compare the societal costs of achieving an ongoing pregnancy with ART cycles that were converted to an IUI vs. with ART cycles that continued through oocyte retrieval in patients with 1–4 mature follicles. Patients with this number of mature follicles were assumed to have ART cycles that were either continued or converted to IUI; in addition, some of the ART cycles that proceeded through oocyte retrieval were assumed to have ended without an embryo for transfer. The cost and probability of each scenario contributed to the final cost analysis. One-way sensitivity analysis was conducted by varying either the ongoing pregnancy rates or the individual procedural costs.

A computerized literature search in the MEDLINE, EMBASE, and randomized controlled trial registries, covering the period up to December 2013, on ART or IUI in poor responders or patients with low follicle numbers, was conducted. No language limitations were applied. The outcome data used in the decision-tree model originated from the published peer-reviewed articles identified in this literature review (8, 10–21). Costs were estimated by averaging the charges that were published on 21 fertility-center websites throughout the United States in various geographic regions. These 21 fertility centers were randomly chosen from the largest IVF clinics with estimated charges available online.

The charges included costs for: physician visits, ultrasounds, lab tests, and medications for both groups; and oocyte retrieval; embryo transfer (ET); and embryology lab in ART group, or IUI in IUI conversion group. Costs for gonadotropins and human chorionic gonadotropin (hCG) were estimated using the listed pricing of the Freedom Fertility Pharmacy. Clinic charges in 2010 US dollars were used as surrogates for direct costs and then converted to 2013 US dollars by adjusting for inflation using the US Department of Labor, Bureau of Labor Statistics consumer price index inflation calculator (www.bls.gov/data/inflation_calculator.htm). The ranges used in the sensitivity analyses were based on data from the same public sources.

Based on websites from clinics across the United States, the median cost of ART cycles up to and including the hCG trigger was estimated to be $9,000 in poor responders, with a range from $5,500 to $10,500. The median charges for remaining cycles were estimated to be $5,000 for completion of ART cycles, with a range from $3,500 to $10,000; and $500 for converted IUI cycles, with a range from $275 to $700. Therefore, the median cost for the continuation of the ART group was $14,000, which included the cost for ovarian stimulation ($9,000) plus oocyte retrieval and the rest of the ART cycle ($5,000); for the IUI conversion group, the median cost was $9,500, which included the cost for ovarian stimulation ($9,000) plus completion of the cycle with IUI ($500).

The cost analysis was conducted using the overall average cost to achieve one ongoing pregnancy, which is different from the healthcare cost for an individual patient. Using average pregnancy rates from published studies on poor responders, a calculation was made of the average total cost per ongoing pregnancy for ART patients that were converted to IUI vs. ART patients that proceeded with oocyte retrieval, grouped by the number of mature follicles at the time of the hCG trigger. One-way sensitivity analyses were completed for each follicle group to determine the average cost per

![FIGURE 1](https://example.com/figure1.png)

**Decision-tree model. Empty circle denotes chance node. Filled square denotes decision node.**

ongoing pregnancy, keeping constant the average pregnancy rates and median procedure costs for completed ART cycles, and varying the ongoing pregnancy rates for converted IUI cycles. In addition, sensitivity analyses were completed to determine whether decreasing ART costs would make IUI conversion more cost effective, keeping constant the average cost per ongoing pregnancy for converted IUI for each follicle group, and varying the cost of a single completed ART cycle across a range of costs for each follicle group from $10,000 to $20,000. Similar sensitivity analyses were done, with varying cost of converted IUI cycles.

RESULTS

For each patient group, continuation with ART resulted in higher ongoing pregnancy rates on average, and lower average total cost per ongoing pregnancy when compared with conversion to IUI (Table 1). For example, patients with 4 mature follicles had an average ongoing pregnancy rate of 12% if the cycles are converted to IUI, compared with 22% if the ART cycles are completed. This resulted in the difference in average cost per ongoing pregnancy: $79,167 vs. $63,636, respectively, for conversion vs. completion (Table 1).

Sensitivity analyses in which the average pregnancy rates and costs for completed ART cycles were kept constant, whereas the ongoing pregnancy rates for converted IUI cycles were varied, showed that for conversion to be more cost effective than completion, IUI needs to achieve ongoing pregnancy rates of 3%, 5%, 13.5%, and 15%, in patients with 1, 2, 3, or 4 mature follicles, respectively. These rates are much higher than the published average in each follicle group (Table 2).

When the cost per ongoing pregnancy for converted IUI is kept constant, and the cost of a single completed ART cycle is varied, in the 1–3 follicle groups, completing ART was more cost effective if the cost of a single ART cycle is $10,000–$25,000. In the 4-follicle group, if an ART cycle costs < $18,025, it is more cost effective to proceed with oocyte retrieval than to convert to an IUI. At amounts > $18,025, converting to IUI was more cost effective (Fig. 2).

Similar sensitivity analyses were done to determine the effect of varying the cost of converted IUI cycles. In the 1- and 3-follicle group, when the median total cost for the ART cycle is kept at $14,000 for each follicle group, then conversion to IUI is more cost effective than continuation with ART only when the cost for the converted IUI cycle is <$5,000. In the group with 4 mature follicles, if a converted IUI cycle costs <$7,650, it is more cost effective than continuation with ART.

DISCUSSION

Based on the available public data, the current decision-tree model results suggest that continuation with ART is more cost effective than conversion to IUI in poor responders with ≤ 4 mature follicles. The current model was based on published information and involved a probabilistic decision analysis that does not factor in individual patient data such as age, prior poor response, hormonal status, or medication usage. The results of the decision-tree model could be adapted by individual practices to help with decision making for poor responders, based on the number of mature follicles and individual patient demographics. Individual practices could use their own pregnancy rates to identify the most cost-effective procedure specific to their own patient population.

The ability to predict pregnancy outcomes after ART is difficult for any patient, and especially for those with poor response to gonadotropin stimulation. ART is expensive, both financially and emotionally, and the decisions associated with ART become more difficult as follicle counts decrease. Very little guidance is available to assist clinicians and patients with making these difficult decisions during ART. The current literature is limited to retrospective cohort studies or case series. To answer the question of which treatment strategy is best in poor responders, a randomized controlled trial that considers various factors such as age, follicle numbers, infertility history, and prior treatments would be ideal. However, enrollment of patients into such a clinical trial could be difficult, owing to significant financial involvement and complex considerations in the decision-making process. A cost-effectiveness analysis is a major step toward providing physicians and patients with guidance when facing these difficult and individualized decisions.

### TABLE 2

<table>
<thead>
<tr>
<th>Mature follicle no.</th>
<th>Convert to IUI (published average)</th>
<th>Continue ART (published average)</th>
<th>Ongoing pregnancy rate (%)</th>
<th>Threshold rate at which IUI becomes more cost effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.6</td>
<td>4.5</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.7</td>
<td>7.6</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>7.0</td>
<td>20.0</td>
<td>13.5</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>12.0</td>
<td>22.0</td>
<td>15.0</td>
<td></td>
</tr>
</tbody>
</table>

Note: The ongoing pregnancy rates for both the IUI and ART groups were based on estimates from the literature and were used to inform the decision-tree model cost estimates.


### TABLE 1

<table>
<thead>
<tr>
<th>Mature follicle no.</th>
<th>Convert to IUI</th>
<th>Continue ART</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average ongoing pregnancy rate (%)</td>
<td>Cost per ongoing pregnancy ($)</td>
</tr>
<tr>
<td>1</td>
<td>1.6</td>
<td>614,488</td>
</tr>
<tr>
<td>2</td>
<td>1.7</td>
<td>578,341</td>
</tr>
<tr>
<td>3</td>
<td>7.0</td>
<td>140,454</td>
</tr>
<tr>
<td>4</td>
<td>12.0</td>
<td>81,932</td>
</tr>
</tbody>
</table>

Note: The ongoing pregnancy rates were based on estimates from the literature and were used to inform the decision-tree model cost estimates.

In addition to age, there are biomarkers of ovarian reserve that may be useful in predicting outcomes in patients who are poor responders. Multiple publications have suggested that basal follicle-stimulating hormone plays a role in predicting pregnancy outcomes after IVF (3, 22). Since these early studies, there have been investigations of other biomarkers, such as antral follicle count (AFC), anti-müllerian hormone (AMH), and inhibin B. Unfortunately, the ability of any of these biomarkers alone to predict pregnancy outcomes has been variable (23). In a more recent study, investigators were able to significantly increase the accuracy of predicting ovarian response by combining age, AFC, and AMH (24). The ability of the markers to predict pregnancy outcome, however, was poor even when age, FSH, AMH, and AFC were considered. The authors concluded that the clinical usefulness of ovarian reserve testing prior to IVF is limited to the prediction of ovarian response (24, 25).

The three articles that divided patients into two age groups did not investigate outcomes based on individual follicle numbers (14, 20, 26). One recent study did show that in patients age ≤ 40 years with ≤ 3 follicles, ART resulted in a statistically significantly improved live-birth rate compared with IUI conversion. The live-birth rates were comparable between the two groups if the patients were older than 40 years (21). Because this was the only study that analyzed pregnancy outcomes in poor responders grouped by both age and number of follicles, age was not included in the current decision-tree model. However, the sensitivity analyses cover a range of possible pregnancy rates to help overcome this limitation.

Sensitivity analysis: varying the cost of ART while maintaining the cost of IUI conversion for the: (A) 1-follicle group; (B) 2-follicle group; (C) 3-follicle group; and (D) 4-follicle group. Blue diamonds represent the IUI group; red squares represent the ART group. In 1- to 3-follicle groups, completing ART was more cost effective if the cost of a single ART cycle was within the range $10,000–$25,000. In the 4-follicle group, if an ART cycle costs < $18,025, it was more cost effective than conversion to IUI. Above this cost level, converting to IUI was more cost effective.
In conclusion, both patients and clinicians often have difficulty making the decision on whether to proceed with oocyte retrieval with only 1–4 mature follicles after ovarian stimulation during ART. The current cost-effectiveness analyses using average direct costs showed that it was more cost effective to proceed to oocyte retrieval than convert to IUI. Because this decision-tree model was based on published information, it did not factor in individual-level data, such as age, prior ART failures, other fertility factors, and medications used in each individual case. However, this model could be adapted by individual practices using their own patient demographic data and medical costs to help with decision making in their specific patient populations.

REFERENCES