Introduction
- Advancements in in vitro fertilization (IVF) have had positive effects in combating infertility, a global issue affecting 70 million reproductive-aged women.1
- The introduction of controlled ovarian stimulation (COS) for the induction of multi-follicular development, as well as treatment with gonadotropins releasing hormone agonists down-regulation protocols, are techniques that have contributed greatly to the success rate of IVF.2
- While a multitude of downstream factors in the IVF protocol of ovarian stimulation can affect live birth outcome, gonadotropins are used in IVF treatment to facilitate the follicles for oocyte retrieval. Hence, when measuring the cost-effectiveness of gonadotropin preparations, the number of oocytes retrieved is a meaningful endpoint because oocyte production is the first step in the IVF pathway that is most directly influenced by ovarian stimulation with these agents.
- Along these lines, it has been shown that the retrieval of 15 oocytes from one COS cycle correlates with an optimal chance per live birth.3
- The number of embryos generated is also an important endpoint when considering gonadotropin cost-effectiveness, as the number of embryos available for fresh or frozen/thawed transfers per COS, which directly affects the cumulative pregnancy and live birth rate.4,5

Objective
- The purpose of this analysis was to quantify the cost-effectiveness of recombinant follicle-stimulating hormone (r-hFSH) and highly purified human menopausal gonadotropin (HP-hMG) in the IVF process using Swedish cost inputs.
- The cost-effectiveness metrics analyzed were cost per oocyte retrieved, cost per embryo generated and the cost per optimal chance of live birth.

Methods
Model structure
- An Excel-based model was developed to calculate the cost-effectiveness of COS with r-hFSH vs. HP-hMG utilization in Sweden as measured by the cost per oocyte retrieved, cost per embryo generated and cost per optimal chances of live birth for r-hFSH and HP-hMG.
- Costs per oocyte retrieved and embryos generated were calculated by multiplying the prices (ex-factory prices) of r-hFSH and HP-hMG in Sweden by the average dose of gonadotropin utilized per COS cycle, divided by the average number of oocytes retrieved or embryos produced from the clinical trial.
- The cost per optimal chance of live birth was calculated by denoting the cost of drug necessary to produce 15 oocytes, which has been shown in the literature to correlate with the greatest probability of obtaining a live birth.6
- The model takes a payer and IVF center perspective and does not necessarily focus on the drug cost per vial.

Clinical data inputs
- A literature search was conducted in PubMed to identify prospective, randomized, head-to-head clinical trials comparing r-hFSH to HP-hMG on the endpoints of oocytes retrieved and embryos generated.
- Only studies that exclusively utilized GONAL-f as the HMG in the published literature satisfied this requirement, from which the inputs for oocytes retrieved, embryos generated.
- Clinical inputs for the model were inputted as the average values for those found in the published literature (Table 1).7

Cost of gonadotropin inputs in the model
- Only gonadotropin drug costs were included in the model, as medical costs of IVF were assumed to be equal for both r-hFSH and HP-hMG and would therefore not affect the comparison.
- Costs for r-hFSH and HP-hMG were 75 IU-vial equivalent prices sourced from the published ex-factory prices in Sweden.7

Results
- The cost per oocyte retrieved for r-hFSH (806 kr) was 17% less than for HP-hMG (981 kr) in Sweden (Table 2; Figures 1 and 2).
- The cost per embryo generated for r-hFSH (2447 kr) was 17% less than for HP-hMG (2947 kr) in Sweden (Table 2; Figure 1).
- The cost per optimal chance of live birth for r-hFSH (4294 kr) was 17% less than for HP-hMG (5194 kr) in Sweden (Table 2; Figure 2).
- Accordingly, in determining the cost-effectiveness of gonadotropin agents used in IVF, it is important to consider outcomes resulting from treatment, and not merely focus on the drug cost per vial.

Conclusions
- Findings indicate that when measuring cost-effectiveness using cost per oocyte retrieved, cost per embryo generated and the cost per optimal chance of live birth, COS with r-hFSH is more cost-effective than COS with HP-hMG.
- Limitations of the analysis include the following:
  - The model outputs are cohort agnostic and did not take into consideration age, previous birth status, adverse events experienced, or other differentiating factors.
  - The model does not take into consideration the impact of different down-regulation protocol procedures.
  - The model assumes that there is a linear relationship between IUs of gonadotropin used and oocytes retrieved, as well as embryos generated.
- The model assumes that all patients treated with a given number of IUs achieved the same outcome in terms of oocytes retrieved and embryos generated (mean point estimate of respective dataset).
- The model clinical inputs do not distinguish between IVF and IVF + intra-cytoplasmic sperm injection techniques.

References
5. TLV website. Extrapolated margin to calculate ex-factory prices for competitors (approx. 2%); September 27, 2013.

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Disclosures
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Table 1. Model inputs.

Table 2. Model outputs.

Figure 1. Cost per oocyte retrieved.

Figure 2. Cost per embryo generated.

Figure 3. Cost per optimal chance of live birth.