

## In vitro fertilization in France: economic aspects and influence of the gonadotrophin choice (urinary vs. recombinant) on cost

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**Introduction.** Since a few years, recombinant FSH (r-FSH) has been progressively replacing urinary products (u-FSH) that were withdrawn from the market in many countries by the pharmaceutical companies. This policy resulted in a dramatic increase in ovarian stimulation cost, multiplied by 3 to 4. On the other hand, if the reasons to promote r-FSH are related to efficacy and safety, these advantages remain controversial and no specific safety risk was ever demonstrated for urinary versus recombinant products in the literature. Since few years, a new highly purified u-FSH became available on the market, and it may be useful to analyze the influence of these two categories of products on the IVF cost.

**Patients and methods.** Costs were calculated in a Public Health setting, by studying 2 phases: the stimulation cycle (including down-regulation) and the pregnancy (including the neonatal period). The calculation included the side effects and the frozen embryos transfers. Economic data came from various sources: the French nomenclature on medical treatments (NGAP), the French drugs dictionary (Vidal) and the French Information system medical plan (PMSI). FSH costs were computed according the currently marketed products, i.e., Fostimon® (IBSA, Switzerland) for urinary FSH, and Gonal-F® (Serono, Switzerland) and Puregon® (Organon, The Netherlands) for r-FSH. Two efficacy differences between u-FSH and r-FSH were considered for the calculations, those reported in the Daya's meta-analysis (3.7% in favor of r-FSH for the clinical pregnancy rate per initiated cycle) and in the only double blind study (Frydman et al., no difference).

The overall ART cost included the frozen embryos transfer cycles and, also, the pregnancy costs because of the specificity of ART pregnancies (high preterm birth and small for gestational age rates), mostly related to the multiple pregnancy rates. In the absence of literature data, no difference was considered between the 2 FSH preparations.

**Results.** Even though r-FSH was associated with a lower mean number of administered units per cycle (2369 vs. 2602), the stimulation with u-FSH resulted in a mean lower cost of 500 Euros per oocyte pick-up (OPU) cycle (1121 vs. 1658 Euros for FSH administration only, and 2422 Euros Vs. 2959 Euros for a whole OPU cycle, respectively for u-FSH and for r-FSH). After including the cancellation rate (12 %), the unsuccessful OPU (1.8%), the failed fertilization cycles (13.9% of OPU), the cost was calculated per initiated cycle, at 2247 Euros for u-FSH and 2784 Euros for r-FSH.

For the complete year 1999, in France, where 45,455 cycles were initiated, the potential over-cost of recombinant products reaches 24 millions Euros when considering only the cycles (128,4 Vs. 104,0 millions Euros for r-FSH and u-FSH, respectively). The per baby IVF cost can be estimated at 12,337 Euros for r-FSH and at 11,681 Euros (in case of a difference of 3.7% pregnancy rate per oocyte recovery) to 9,991 Euros (in case of equivalence between the 2 drugs) for u-FSH. We made the hypotheses of 10,000 couples entering in an IVF process, offered a full course of up to 4 IVF cycles, with a decreasing pregnancy rate and a withdrawal rate of respectively 1% and 20% at each consecutive cycle. When only taking into account the cost of an IVF cycle, there was a lower cost for urinary products of 3075 Euros per delivery if there was no difference between the two categories in term of pregnancy rates. This difference was decreased to 2430, 1722, 1006 and 358 Euros if the differences in term of pregnancy rate were respectively of 1%, 2%, 3% and 4%.

In total, the annual cost of ART reaches approximately 130 millions Euros in France, for the cycles only, and 170 millions Euros when including the pregnancy costs.

**Conclusion.** This gives a Public Health lighting to the gonadotrophins choices in the matter of ovulation stimulation. It shows the economic impact according to the FSH selection, which can be of huge importance in the developing world, from a public health point of view. More generally, it shows the impact that any medical choice can have at the level of a population, even though single doctors do not consider elevated individual over-costs.