

A Comparison of the Cost-Effectiveness of In Vitro Fertilization Strategies and Stimulated Intrauterine Insemination in a Canadian Health Economic Model

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Abstract

Background: In vitro fertilization (IVF) with single embryo transfer (SET) has been proposed as a means of reducing multiple pregnancies associated with infertility treatment. All existing cost-effectiveness studies of IVF-SET have compared it with IVF with multiple embryo transfer but not with intrauterine insemination with gonadotropin stimulation (sIUI).

Methods: We conducted a systematic review of studies of cost-effectiveness of IVF-SET versus IVF with double embryo transfer (DET). Further, we developed a health economic model that compared three strategies: (1) IVF-SET, (2) IVF-DET, and (3) sIUI. The decision analysis considered three cycles for each treatment option. IVF treatment was assumed to be a combination of cycles with transfer of fresh and frozen-thawed embryos. Probabilities used to populate the model were taken from published randomized clinical trials and observational studies. Cost estimates were based on average costs of associated procedures in Canada.

Results: The results of published studies on the cost-effectiveness of IVF-SET versus IVF-DET were not consistent. In our analysis, IVF-DET proved to be the most cost-effective strategy at \$35 144/live birth, followed by sIUI at \$66 960/live birth, and IVF-SET at \$109 358/live birth. The results were insensitive both to the cost of IVF cycles and to the probability of live birth.

Conclusion: This economic analysis showed that IVF-DET was the most cost-effective strategy of the options, and IVF-SET was the least cost-effective. The results in this model were insensitive to various probability inputs and to the costs associated with sIUI and IVF procedures.

Résumé

Contexte : La fécondation *in vitro* (FIV) s'accompagnant du transfert d'un seul embryon (TSE) a été proposée comme moyen de diminuer le nombre de grossesses multiples associées à la prise en charge de l'infertilité. Toutes les études de rentabilité existantes portant sur la FIV-TSE l'ont comparé à la FIV s'accompagnant du transfert de multiples embryons, mais non à l'insémination intra-utérine s'accompagnant d'une stimulation aux gonadotrophines (IIUs).

Méthodes : Nous avons mené une analyse systématique des études de rentabilité comparant la FIV-TSE à la FIV s'accompagnant du transfert de deux embryons (TDE). Qui plus est, nous avons développé un modèle d'économie sanitaire comparant trois stratégies : (1) FIV-TSE, (2) FIV-TDE et (3) IIUs. L'analyse décisionnelle a pris en considération trois cycles pour chacune des options de traitement. Il a été présumé que le traitement de FIV était une combinaison de cycles de transfert d'embryons frais et d'embryons congelés-décongelés. Les probabilités utilisées pour peupler le modèle ont été tirées d'études observationnelles et d'essais cliniques randomisés publiés. Les estimations des coûts ont été fondées sur les coûts moyens d'interventions connexes au Canada.

Résultats : Les résultats des études publiées comparant la rentabilité de la FIV-TSE à celle de la FIV-TDE n'étaient pas uniformes. Dans le cadre de notre analyse, la FIV-TDE s'est avérée la stratégie la plus rentable à 35 144 \$/naissance vivante, suivie de l'IIUs à 66 960 \$/naissance vivante et de la FIV-TSE à 109 358 \$/naissance vivante. Les résultats étaient sensibles tant au coût des cycles de FIV qu'à la probabilité d'une naissance vivante.

Conclusion : Cette analyse économique a indiqué que la FIV-TDE était l'option la plus rentable et que la FIV-TSE était l'option la moins rentable. Dans le cadre de ce modèle, les résultats n'étaient pas sensibles à divers intrants de probabilité ni aux coûts associés aux interventions d'IIUs et de FIV.

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INTRODUCTION

One of the main adverse effects of assisted reproduction is multifetal pregnancy, which is known to be associated with a wide range of maternal and neonatal complications.¹⁻³ IVF is the only infertility treatment that permits

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quantification and control of the risk associated with multiple pregnancies. In IVF, this risk is defined by the number of embryos transferred in a given cycle. Advances in IVF techniques in the last decade have made it possible to transfer only a single embryo with an acceptable probability of pregnancy, a strategy known as an elective SET. This possibility has led to the promotion of IVF-SET as a solution to the problem of multiple pregnancies associated with assisted reproduction.¹⁻³ As a result, several European countries in which IVF treatment is subsidized by the government (Finland, Sweden, Belgium, and the Netherlands) have started promoting the policy of routine SET in IVF cycles.^{1,4,5}

In contrast, in North America, IVF is mainly accessible only in the private sector, without government subsidy. In the United States, the availability and extent of IVF insurance coverage varies across states.⁶ In Canada, IVF treatment is partially funded in only two provinces (Ontario and Prince Edward Island),⁷ and Quebec provides partial reimbursement through a tax credit. In the absence of comprehensive coverage, the majority of patients pay for an IVF procedure. Therefore, both patients and providers often prefer to transfer multiple embryos in IVF cycles in order to maximize the chance of success per cycle. Not surprisingly, the average rate of multiple pregnancies after IVF in North America is higher than that in Europe: in Europe the rate is about 24%,⁸ but in Canada it is 30%,⁹ and in the United States it is 34%.¹⁰

Published economic studies have drawn inconsistent conclusions regarding the cost-effectiveness associated with IVF-SET and IVF-DET. A decision analysis by De Sutter et al. in 2002 did not demonstrate any substantial difference between IVF-SET and IVF-DET in cost per child born.¹¹ Two later prospective studies,^{12,13} however, showed that although more IVF-SET cycles were needed to achieve birth rates similar to those achieved with IVF-DET, the avoidance of multiple pregnancies with use of IVF-SET (and the associated high costs of neonatal care) render it more cost-effective than IVF-DET. The Danish health technology assessment report was undertaken to assess the potential effect on the national health care system of

making IVF-SET a mandatory policy in Denmark.¹⁴ The report demonstrated that promoting IVF-SET would lead to an increase in the number of IVF cycles and associated procedures (such as hormonal stimulation and embryo freezing and thawing), which in turn would necessitate the employment and education of additional staff. As a result, the public health system might incur an additional financial burden.^{15,16}

The lack of consistency in the findings of economic studies to date could be explained by differences in the types of costs considered and the perspective used (i.e., patient, care provider, payer, or other). The objective of this study was to evaluate the cost-effectiveness of IVF-SET in the Canadian context from the perspective of public payers. Unlike previous studies, this study compares the cost-effectiveness of IVF-SET not only with IVF-DET but also with intrauterine insemination with gonadotropin stimulation. The reason for inclusion of sIUI in our comparison is that it is the closest alternative reproductive technology to IVF and is more widely insured than IVF in Canada.

METHODS

A Markov decision model was developed, using TreeAge Pro 2006 software (TreeAge Software Inc., Williamstown, MA). The model considered three treatment options: (1) sIUI, (2) IVF-SET, and (3) IVF-DET. One of the assumptions made in the model was that all patients were women under the age of 36 years, with no previous sIUI or IVF treatment and a good fertility prognosis. Only short-term costs were considered (i.e., long-term costs of the complications associated with multiple births were excluded). In addition, the costs of drugs for ovarian stimulation as well as those used in conjunction with IVF treatment were included in the analysis. The total cost of drugs per cycle was estimated to range from \$500 to \$1500 for sIUI and from \$2500 to \$4500 for IVF. These cost estimates were obtained from expert consultations and from the websites of infertility clinics (the Appendix shows a list of these websites with estimated cost of drugs for sIUI and IVF patients). We used the mid-point of these ranges for our base case analysis, while the extremes were employed during sensitivity analyses. The perspective of the public payer was employed in this study. The decision nodes for intrauterine insemination are illustrated in Figure 1 and those of IVF-SET and IVF-DET are illustrated in Figure 2.

Base Case Model

For the base case model, IVF treatment was assumed to be a combination of fresh and cryopreserved embryo transfers with a maximum of three treatment cycles. The probabilities of pregnancy and live births used as inputs into the model for cryopreserved cycles were lower than those used

ABBREVIATIONS

DET	double embryo transfer
HOM	higher-order multiple
IVF	in vitro fertilization
NICU	neonatal intensive care unit
RCT	randomized controlled trial
SET	single embryo transfer
sIUI	stimulated intrauterine insemination

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