Cost-effectiveness analysis of preimplantation genetic screening and in vitro fertilization versus expectant management in patients with unexplained recurrent pregnancy loss

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Objective: To determine whether in vitro fertilization with preimplantation genetic screening (IVF/PGS) is cost effective compared with expectant management in achieving live birth for patients with unexplained recurrent pregnancy loss (RPL).
Design: Decision analytic model comparing costs and clinical outcomes.
Setting: Academic recurrent pregnancy loss programs.
Patient(s): Women with unexplained RPL.
Intervention(s): IVF/PGS with 24-chromosome screening and expectant management.
Main Outcomes Measure(s): Cost per live birth.
Result(s): The IVF/PGS strategy had a live-birth rate of 53% and a clinical miscarriage rate of 7%. Expectant management had a live-birth rate of 67% and clinical miscarriage rate of 24%. The IVF/PGS strategy was 100-fold more expensive, costing $45,300 per live birth compared with $418 per live birth with expectant management.
Conclusion(s): In this model, IVF/PGS was not a cost-effective strategy for increasing live birth. Furthermore, the live-birth rate with IVF/PGS needs to be 91% to be cost effective compared with expectant management. (Fertil Steril® 2015;103:1215–20. ©2015 by American Society for Reproductive Medicine.)
Key Words: Cost effectiveness, in vitro fertilization, preimplantation genetic screening, recurrent pregnancy loss

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Recurrent pregnancy loss (RPL) is a multifactorial disorder defined by two or more clinical miscarriages (1). Although the overall incidence of RPL is low and estimated at less than 5% of women (2), it presents a significant diagnostic and treatment challenge for both patients and clinicians. Guidelines for the evaluation of patients with RPL include evaluation of the uterine cavity and blood work to determine parental karyotypes and presence of antiphospholipid antibodies (1). An etiology for RPL, however, is not identified in at least 50% of cases, and a treatment plan is thus not clearly defined (3). The role of chromosomal abnormalities in miscarriage has been widely reported, with 50% to 70% of first trimester miscarriages attributed to aneuploidy (4, 5). Furthermore, for patients greater than 35 years of age with RPL, fetal aneuploidy is responsible for up to 80% of first trimester losses (6). Due to the prevalence of aneuploidy in first trimester losses and the increased prevalence of aneuploidy in the RPL population, preimplantation genetic screening (PGS) has been proposed as a method for reducing miscarriage by

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selecting euploid embryos for transfer. The current standard of care for patients with unexplained RPL espoused by the American Society for Reproductive Medicine is expectant management (1, 7). However, the emotional trauma that can accompany clinical miscarriages and a perceived urgency to conceive felt by many RPL patients lead them toward alternative treatment options, including assisted reproductive technology, and specifically to in vitro fertilization (IVF) and PGS (8).

The clinical outcomes and cost effectiveness of PGS and IVF in the treatment of RPL patients is uncertain. Neither longitudinal prospective studies nor randomized clinical trials comparing IVF and PGS with expectant management, the current standard of care, have been performed to date for the treatment of RPL patients. Furthermore, IVF and PGS are technically challenging, resource-intensive procedures that are expensive and not widely available (9). We used the current literature to evaluate the cost effectiveness of IVF and PGS compared with expectant management in patients with unexplained RPL.

MATERIALS AND METHODS

A decision analytic model was created using TreeAge Pro 2014 (2014 version; TreeAge Software) to compare the cost effectiveness of IVF–PGS versus expectant management for patients with unexplained RPL (Fig. 1). As no human participants were involved in creating this theoretical model, this study was exempt from institutional review board approval. Two treatment strategies were compared: IVF–PGS versus expectant management.

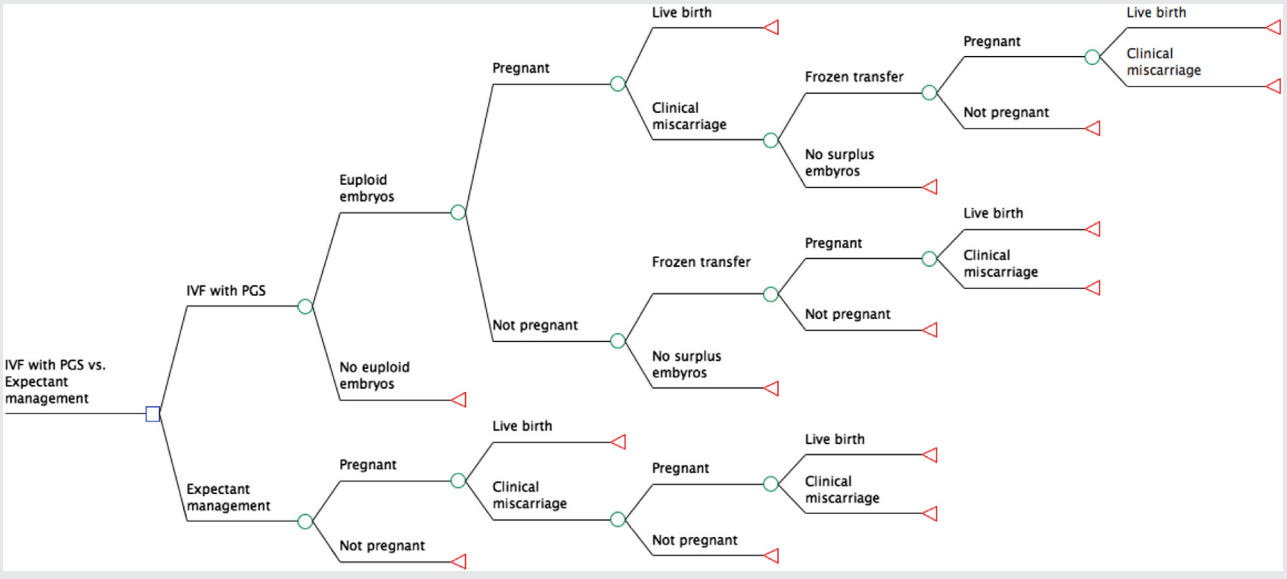
In the IVF–PGS strategy, patients underwent one IVF cycle followed by PGS and fresh embryo transfer if a euploid embryo was produced. After embryo transfer, the possible outcomes included pregnancy followed by live birth, or clinical miscarriage, or no pregnancy. Patients who had a clinical miscarriage or did not become pregnant after the first embryo transfer were allowed to attempt a frozen embryo transfer if they had surplus embryos. In the expectant management strategy, patients attempted spontaneous conception. Possible outcomes included pregnancy followed by live birth, or clinical miscarriage, or no pregnancy. Patients who had a clinical miscarriage after their first attempt were allowed a second attempt at conceiving spontaneously. Patients were randomly assigned to the two treatment strategies, and the baseline clinical outcomes for each strategy were obtained from published data.

We assumed that no patients dropped out between their first and second attempts at either strategy, and we also assumed that baseline clinical outcomes were unchanged between the first and second attempts at either strategy. In the IVF–PGS strategy, we assumed that transfers were only performed if at least one euploid embryo was produced, and that a second attempt at IVF–PGS with a frozen transfer was only performed if at least one surplus euploid embryo was present upon completion of the fresh transfer.

No ectopic or cervical pregnancies were present in either patient cohort, so all pregnancies ended in either live birth or clinical miscarriage. Clinical pregnancy and live-birth rates calculated from the analytic model are expressed per strategy, and clinical miscarriage rates are expressed per pregnancy.

Probabilities for clinical outcomes with IVF and PGS in RPL patients were obtained from a 2012 study by Hodes-Wertz et al. (10). This is the single largest study to date of outcomes using 24-chromosome screening by array comparative genomic hybridization in a well-defined RPL population.

FIGURE 1



Simplified decision tree. Patients with unexplained recurrent pregnancy loss were assigned to one of two treatment strategies: expectant management or in vitro fertilization (IVF) with preimplantation genetic screening (PGS).

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