Preimplantation genetic testing for aneuploidy is cost-effective, shortens treatment time, and reduces the risk of failed embryo transfer and clinical miscarriage

Shelby A. Neal, M.D.,[a,b] Scott J. Morin, M.D., T.S.,[a,b] Jason M. Franasiak, M.D., T.S.,[a,b] Linnea R. Goodman, M.D.,[a] Caroline R. Juneau, M.D.,[a,b] Eric J. Forman, M.D., H.C.L.D.,[a] Marie D. Werner, M.D., H.C.L.D.,[a,b] and Richard T. Scott Jr., M.D., H.C.L.D.[a,b]

[a] IVI/RMA New Jersey, Basking Ridge, New Jersey; and [b] Sidney Kimmel College of Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania

Objective: To determine if preimplantation genetic testing for aneuploidy (PGT-A) is cost-effective for patients undergoing in vitro fertilization (IVF).
Design: Decision analytic model comparing costs and clinical outcomes of two strategies: IVF with and without PGT-A.
Setting: Genetics laboratory.
Patients: Women ≤ 42 years of age undergoing IVF.
Intervention(s): Decision analytic model applied to the above patient population utilizing a combination of actual clinical data and assumptions from the literature regarding the outcomes of IVF with and without PGT-A.
Main Outcome Measure(s): The primary outcome was cumulative IVF-related costs to achieve a live birth or exhaust the embryo cohort from a single oocyte retrieval. The secondary outcomes were time from retrieval to the embryo transfer resulting in live birth or completion of treatment, cumulative live birth rate, failed embryo transfers, and clinical losses.
Results: 8,998 patients from 74 IVF centers were included. For patients with greater than one embryo, the cost differential favored the use of PGT-A, ranging from $931–2411 and depending upon number of embryos screened. As expected, the cumulative live birth rate was equivalent for both groups once all embryos were exhausted. However, PGT-A reduced time in treatment by up to four months. In addition, patients undergoing PGT-A experienced fewer failed embryo transfers and clinical miscarriages.
Conclusion: For patients with > 1 embryo, IVF with PGT-A reduces healthcare costs, shortens treatment time, and reduces the risk of failed embryo transfer and clinical miscarriage when compared to IVF alone. (Fertil Steril® 2018;110:896–904. ©2018 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: Cost effectiveness, in vitro fertilization, preimplantation genetic testing for aneuploidy

Preimplantation genetic testing for aneuploidy (PGT-A) is increasingly utilized in embryo selection for patients undergoing in vitro fertilization (IVF) for a wide variety of indications. Utilization of PGT-A has been demonstrated to increase implantation rates and decrease clinical loss rates by selecting for a euploid embryo (1, 2). However, some investigators have expressed concerns that PGT-A adds costs to an already expensive treatment and that, as an embryo diagnostic, it never improves the reproductive potential of any single embryo. They go on to argue that it may be more cost effective to simply transfer all of the embryos (preferably one at a time) and to "let nature sort it out" (3). While it is a given that no diagnostic tool ever improves the reproductive potential of any embryo, the issue of cost is more complex. Although there are significant additional costs associated with PGT-A, it is possible that PGT-A utilization may reduce overall

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Correspondence: Shelby A. Neal, M.D., Reproductive Medicine Associate of New Jersey, 140 Allen Road, Basking Ridge, New Jersey 07920 (E-mail: sneal@ivirma.com).

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¿Cuánto importa el útero? Los resultados perinatales mejoran cuando embriones de ovocitos donados son transferidos a gestantes subrogadas en comparación con las futuras madres receptoras

Objetivo: Evaluar los resultados reproductivos y neonatales de ciclos en los cuales los embriones de ovocitos donados se transfirieron gestantes subrogadas en comparación con las futuras madres receptoras.

Diseño: Estudio de cohorte retrospectivo.

Entorno: No aplica.

Paciente (s): Futuras madres receptoras y gestantes subrogadas que reciben embriones de ovocitos donados en 2014 en los Estados Unidos.

Intervención (s): Ninguna.

Principales medidas de resultado: Embarazo clínico, Tasa de nacidos vivos, aborto, multiplicidad, prematuridad, y peso al nacer de los embarazos concebidos tras la transferencia de embriones de ovocitos donados tanto en madres subrogadas como en las futuras madres receptoras.

Resultado (s): La edad media de las futuras madres receptoras (N=18 317) y madres subrogadas (N= 1927) fue de 41.6 y 31.6 años, respectivamente. Comparado con una futura madre receptora, los pacientes que optan por una gestante subrogada tienen mayor probabilidad de conseguir un embarazo clínico (65.2% vs. 56.3%, proporción de probabilidades ajustadas de 1.33, 95% intervalo de confianza (IC) 1.17–1.51) y tasa de nacidos vivos (57.1% vs. 46.4%, aOR 1.37, 95% CI 1.21–1.55) usando embriones frescos o congelados de ovocitos donados. De los nacidos en embarazos únicos (n=716 usando una gestante subrogada y n=5632 en las futuras madres receptoras), la incidencia de prematuridad fue significativamente más baja en las gestantes subrogadas que en las futuras madres receptoras (17.5% vs. 25.4%, aOR 0.78, 95% CI 0.61–0.99). La incidencia de bajo peso en el nacimiento entre los nacidos en embarazos únicos se redujo significativamente en los ciclos con gestantes subrogadas (6.4% vs. 12.1%, aOR 0.62, 95% CI 0.44–0.89).

Conclusión (s): Las futuras madres receptoras tuvieron tasas de embarazo más bajas y los resultados neonatales más pobres en comparación con los obtenidos en una gestante subrogada. Esto sugiere que una historia de infertilidad afecta negativamente al ambiente uterino, independientemente del ovocito.

TABLE 1

Assumptions of the model including clinical parameters and cost data for IVF, PGT-A, and related clinical procedures.

Assumption	%	Cost[b]	US$
Probability of:		PGT-A	
Live birth of euploid embryo (8)	60	Embryo biopsy	1,000
Loss of euploid embryo (2)	6	PGT-A – per embryo	150
Live birth of aneuploid embryo	0		
Loss of unscreened embryo[a]	20		
Ectopic pregnancy	0		
Dropout rate with remaining frozen embryos	0	Fresh embryo transfer	1,050
Percentage of frozen embryo transfers for initial transfer:		Vitrification	1,000
PGT-A	100		
No PGT-A	70		
Percentage of patients returning for a second baby	0	Frozen embryo transfer cycle	3,812
D&C for management of clinical pregnancy loss	100	D&C for management of clinical loss (5)	1,304

Note: D&C = dilation & curettage; IVF = in vitro fertilization; PGT-A = preimplantation genetic testing for aneuploidy.
[a] Reproductive Medicine Associates of New Jersey IVF patients, 2010-2016.
[b] Data accrued from the finance department of the study institution.

Neal. Preimplantation genetic testing cost. Fertil Steril 2018.

Building the Model

Having assigned the values for the variables, it was possible to assemble the models for outcomes with and without the use of PGT-A. In every case, patients would continue in care until one of two endpoints were attained: either they had a live birth or they completely exhausted their supply of embryos.

This model is not completely realistic for two major reasons, with both favoring the no-PGT-A group. First, it assumes a dropout rate of zero which is certainly not the case. The high dropout rate after any treatment cycle and higher risk of futile cycles in the no-PGT-A group means that this group would be more likely to be impacted by patients abandoning care prior to transferring all available embryos, which would reduce their cumulative delivery rate. This consideration violates one of the assumptions of the study, which is that because diagnostics do not change the reproductive potential of individual embryos, the cumulative live birth rate is the same for both strategies. This assumption is not true if patients abandon care, and the lower live birth rates per cycle would likely result in a greater penalty for the no PGT-A group. There is no evidence-based way to estimate the dropout rate in this population and thus we did not include this factor in the model.

The second consideration is the potential impact of patients seeking a second baby utilizing the same cohort of embryos. In this case, patients who previously utilized PGT-A receive the benefits of PGT-A the second time with zero incremental costs. Obviously, this dramatically favors PGT-A utilization and its omission heavily and unrealistically favors the no PGT-A group. Ultimately, as it is not possible to know how many patients will return for a second baby in these groups (it might not be the same), the potential for second babies was not included. This model represents a very conservative and rigorous assessment of the cost effectiveness of PGT-A.

Figure 1 summarizes the decision tree for the two treatment strategies. Only patients who did not undergo PGT-A were eligible for a fresh embryo transfer. Fresh embryo transfers were performed at a rate of 30%, with the remainder of patients undergoing embryo cryopreservation due to risk of ovarian hyperstimulation or dysynchrony based on premature progesterone elevations which may induce endometrial advancement or slow embryo development to the blastocyst stage. The remainder of embryo transfers were performed in a subsequent frozen cycle. For patients who underwent PGT-A, all embryos were cryopreserved and euploid embryos were selected for transfer in an ensuing frozen embryo transfer cycle.

Following each embryo transfer, there were two initial potential outcomes: pregnant or not pregnant. Of those who became pregnant, the possible outcomes considered were a live birth or a clinical loss. Biochemical losses were included in failure to achieve a pregnancy as the cost of this outcome was similar. The rare possibility of ectopic pregnancy was not accounted for in this model.

Following an unsuccessful embryo transfer (one that resulted in either no pregnancy or a clinical loss) patients were characterized as either having exhausted their supply of available embryos and thus completed the treatment cycle, or as having additional embryos available for transfer. If additional embryos were available, the model specifies that they would undergo an additional frozen embryo transfer cycle with the same range of outcomes as were possible in the first frozen embryo transfer cycle.

Overall IVF-related costs were calculated for each patient in the database. Costs were accrued until the embryo transfer resulting in a live birth or exhaustion of the embryo cohort obtained from a single oocyte retrieval. The total costs were then recalculated for the same patients, utilizing their proportion of euploid embryos to project clinical outcomes while if they did not undergo PGT-A. Of note, the costs of stimulation, retrieval and embryology services up until the point of embryo biopsy were assumed to be equivalent in the two models and were therefore omitted from the model.

Average time from retrieval to the embryo transfer resulting in live birth or resumption of treatment following exhaustion of the embryo cohort was also calculated for both

expenditures by eliminating futile transfers of chromosomally abnormal embryos that either fail to produce a viable gestation or, worse yet, result in an ongoing chromosomally abnormal pregnancy. The question of the cost effectiveness of PGT-A is important and should impact clinical decision making and be incorporated into patient counseling.

To date, few published models have systematically examined the cost effectiveness of IVF/PGT-A. In its early stages, PGT-A was performed using blastomere biopsy and fluorescence in situ hybridization to test a limited number of chromosomes for aneuploidy. One cost analysis model determined that for women ages 38–40, IVF alone was less costly than IVF/PGT-A per healthy infant (4). However, given the known safety issues associated with blastomere biopsy (5) and the diagnostic limitations of fluorescence in situ hybridization, these techniques are neither recommended nor practiced routinely and thus this model is virtually unrelated to contemporary assisted reproductive technology (ART) practice.

Techniques have evolved over the years and best practices now utilize trophectoderm biopsy and next generation sequencing-based methods for evaluating embryo ploidy. There are no analyses based on large clinical data sets which evaluate the cost effectiveness using PGT-A with contemporary analytical techniques and modern approaches to ART care. A recent trial looked at the cost effectiveness of IVF/PGT-A for recurrent pregnancy loss, but those conclusions cannot be extrapolated to the broader population of patients who have already elected to undergo IVF and are faced with the decision of whether or not to pursue PGT-A in conjunction with this treatment (3, 6).

The decision analytic model presented in this paper seeks to clarify the overall costs of IVF/PGT-A compared to IVF alone, utilizing an actual patient database, as well as assumptions based upon the literature, and taking into consideration the cost of all treatment rendered from the cycle in which PGT-A was undertaken until the embryo transfer resulting in live birth or exhaustion of the embryo cohort.

MATERIALS AND METHODS

Assigning Values for Clinical Outcomes and Costs

A cost analysis was performed comparing two treatment strategies: euploid single embryo transfer (SET) versus unscreened SET. To conduct this analysis, a model was built using a combination of actual clinical data and assumptions from the literature. The clinical data was obtained from a database of all PGT-A cases referred to a single genetics laboratory between January 2011 and March 2016. Given that these cases were derived from 74 different IVF centers, limited clinical information, such as infertility diagnoses and pregnancy outcomes, was available for review. Therefore, this database includes patients undergoing IVF for a wide variety of indications including, but not limited to, infertility, recurrent pregnancy loss, and fertility preservation as there was insufficient information available to tailor inclusion criteria to specific patients. Cases in which embryos were derived from donor gametes or with the intention of transferring to a gestational carrier were also included. The oocyte age was known for each case. The embryo cohort size and number of euploid embryos per case was obtained from the genetics laboratory. Patients $\leq$ 42 years of age were included. For patients who appeared in the database more than once (i.e. patients who cycled multiple times), only their first cohort of embryos was considered. Those with embryo cohort size $>$ 95th percentile were excluded from analysis as to not skew the data.

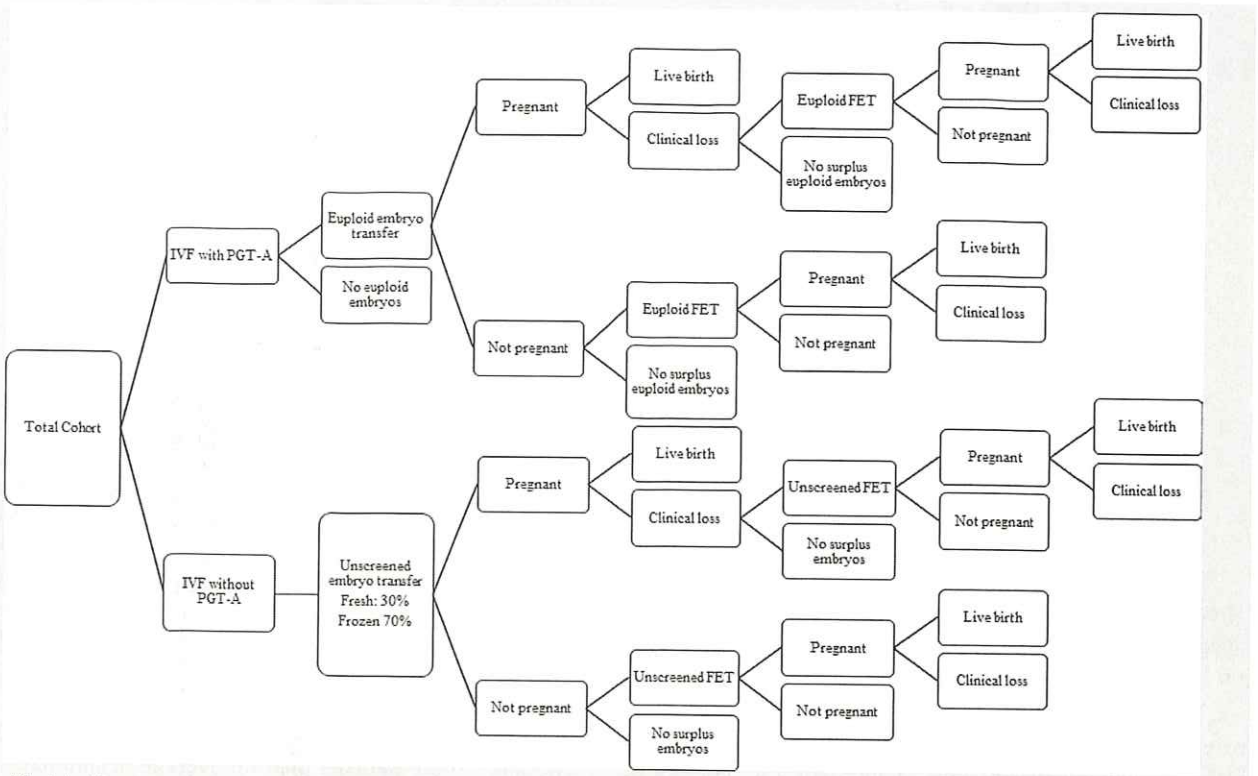
In creating the model, it was essential to select evidence-based values for the critical clinical endpoints such as the proportion of embryos which are designated as euploid or aneuploid, the sustained implantation rates with and without the use of PGT-A, and the clinical loss rates in pregnancies following the transfer of screened or unscreened embryos. It was also important to assign costs to the various procedures included in the model. Costs for trophectoderm biopsy were based on those used in our program which we believe are typical of those used in the industry. Costs for the actual PGT-A was based on a contemporary blended average cost for two large reference laboratories providing clinical PGT-A (Good Start Genetics and Igenomix). Costs for other procedures were assigned based on representative cost estimates provided by the American Society for Reproductive Medicine (ASRM) (Table 1). Probability of live birth and clinical loss for the PGT-A arm was established based on the literature, as rates have been found to be relatively stable across age groups (7). It was assumed that known aneuploid embryos were not transferred.

For the control arm of unscreened embryos, the age of the female partner is a major confounding factor. In an ideal setting, actual clinical data for each age would be consolidated and the cumulative outcomes in terms of delivery rate, loss rate, and number of transfer cycles would be available. Regrettably, that is not possible, as patients commonly drop out of care and proceed to another retrieval after a few failed transfers without exhausting a cohort of embryos before cycling again or abandoning care. For this model, the outcomes for each patient were based on the known proportion of euploid and aneuploid embryos for each year of maternal age and then the outcomes calculated based on that distribution.

For example, a 35-year-old patient with 4 total embryos resulting in 2 euploid embryos has a 50% chance (2 of 4) of picking a euploid embryo at first transfer, which then has a 60% chance of live birth based on the literature, leading to a probability of live birth of 30% at first single embryo transfer ($0.5 \times 0.6 = 0.3$). It was assumed that transfer of aneuploid embryos would lead to a zero percent change of pregnancy and unscreened embryos have a 20% chance of implanting and resulting in a clinical loss (8). Furthermore, it was assumed that the likelihood of selecting a euploid embryo for transfer was not influenced by morphology.

Cycles without PGT-A were assumed to have a 30% fresh transfer rate based on contemporary practice with vitrification assumed for the other cycles due to hyperstimulation risk or issues related to endometrial embryonic dysynchrony. All subsequent transfers were performed in a frozen embryo transfer cycle. Sensitivity analysis was conducted to ascertain the impact on the model when varying the fresh transfer rate.

FIGURE 1



Simplified decision tree. Two treatment strategies were assessed: in vitro fertilization (IVF) with preimplantation genetic testing for aneuploidy (PGT-A) and IVF without PGT-A.

Neal. Preimplantation genetic testing cost. Fertil Steril 2018.

strategies. These calculations utilized internal data based upon treatment delays for patients who experienced a failed embryo transfer or a clinical loss between 2009 and 2015 and had additional embryos available for transfer. From this database, it was determined that the average patient spends 56 days away from treatment after a failed embryo transfer and 134 days away from treatment after a clinical loss. These numbers were used to compute cumulative time in treatment for both groups.

Analysis

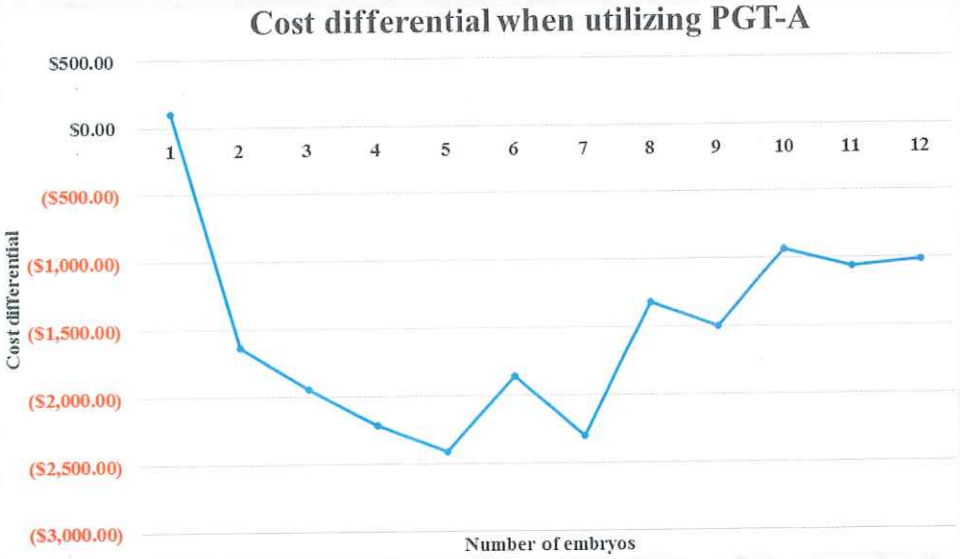
The study is descriptive in nature by design. The primary outcome of the study was the cost to achieve a live birth or exhaustion of an embryo cohort obtained from a single oocyte retrieval. Costs were calculated for each individual patient and then aggregated for the entire population based on the number of available blastocysts at the time PGT-A would be done. In addition, cost data was stratified by Society for Assisted Reproductive Technology (SART) age group. The secondary outcomes included time from retrieval to embryo transfer resulting in live birth or exhaustion of the embryo cohort, cumulative live birth rate, number of failed embryo transfers and number of clinical losses. All retrospective data analysis was performed under IRB approved protocols.

RESULTS

The study population includes 8,998 patients from 74 IVF centers undergoing PGT-A at the same genetics laboratory. The mean age of patients at retrieval was 36.0 ± 4.3 years. The median number of embryos submitted for evaluation was four (range 1–40). The availability of other demographic and clinical data was limited as many patients were referred from outside IVF centers. Number of embryos, distribution of patients, age, mean number of euploid embryos and mean euploidy rate are specified in Supplemental Table 1 and by SART age group in Supplemental Table 2.

Figure 2 shows the cost differential when utilizing PGT-A. The data displayed includes all patients who have ≤ 12 embryos, which encompasses >95% of the cohort. For patients who only have one embryo, undergoing PGT-A is costlier than simply transferring the unscreened embryo. For patients with greater than one embryo, the cost differential favors the use of PGT-A with a cost savings ranging from $931–2411, depending upon the number of embryos available for transfer. This pattern of cost savings was noted in all age groups, although the magnitude of cost savings varied by age, with patients >37 years of age saving more and <35 years of age saving less. A subset of patients <35 years of age, those with ≥ 8 embryos available for transfer (30.0% of this age group), did not experience cost savings

FIGURE 2



Cost differential when utilizing preimplantation genetic testing for aneuploidy (PGT-A). PGT-A is not cost-effective for patients who only have one embryo. For patients who have more than one embryo, PGT-A results in cost savings ranging from US$931 to US$2,411.

Neal. Preimplantation genetic testing cost. Fertil Steril 2018.

when utilizing PGT-A and paid on average $358.31 to utilize PGT-A. Comprehensive cost data can be found in Supplemental Tables 3 and 4. Results of the sensitivity analysis incorporating alternative fresh embryo transfer rates of 50% and 70% are displayed in Supplemental Table 5 and demonstrated minimal impact on the model.

IVF with PGT-A was noted to decrease time in treatment, with a shorter average time from retrieval to embryo transfer resulting in live birth or completion of treatment due to exhaustion of the embryo cohort (Fig. 3). While the difference in time in treatment was apparent even in those patients who only had one embryo available for transfer, it was most pronounced for patients with greater than two embryos, for whom PGT-A decreased time in treatment by more than three months.

As expected, the cumulative live births per treatment strategy were identical. However, IVF with PGT-A reduced the overall number of embryo transfers, clinical losses and failed embryo transfers (transfers which did not result in pregnancy). Patients who did not utilize PGT-A required nearly twice as many embryo transfers to achieve the specified endpoint.

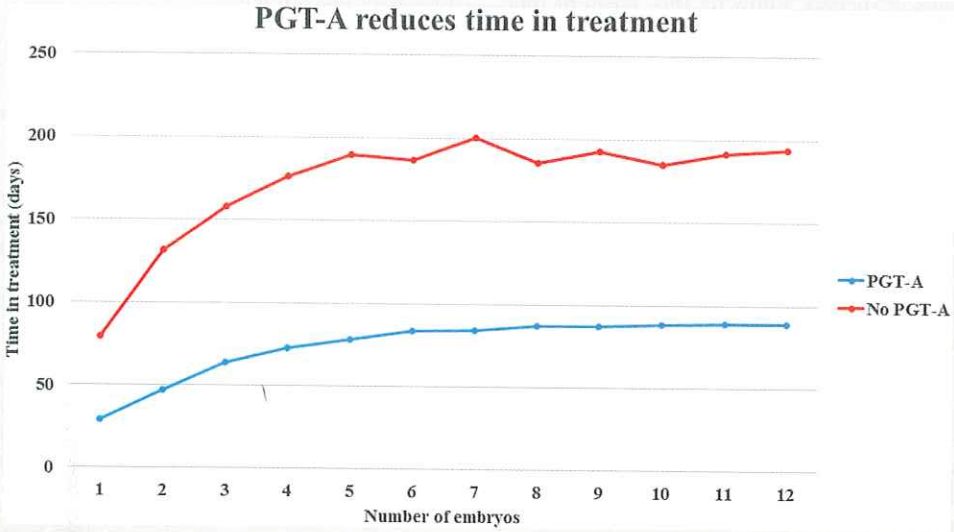
DISCUSSION

PGT-A is increasingly utilized to improve clinical outcomes but there is little data available regarding the net impact on cost. Our cost analysis demonstrates an overall cost savings for patients with more than one embryo who choose to undergo IVF/PGT-A as opposed to IVF alone. This cost savings persists across all age groups, although did not apply to a small subset of patients <35 years of age with ≥ 8 embryos available. These patients paid on average a nominal fee of $358.31 to utilize PGT-A and therefore did not save money by utilizing PGT-A. Cost should be considered when counseling a patient about whether to pursue PGT-A as many patients omit PGT-A due to financial concerns. The results of this analysis demonstrate that all but a select group of patients experience cost savings when utilizing PGT-A.

The literature regarding costs associated with PGT-A in a patient population already undergoing IVF using contemporary techniques is relatively sparse. One model designed to assess the cost-effectiveness of IVF/PGT-A for women >37 years of age by considering the cost and clinical outcomes of fresh embryo transfers following an autologous IVF cycle found that IVF/PGT-A is a cost-effective strategy as measured by an incremental cost effectiveness ratio (ICER), a metric that accounts for the difference in treatment effect (9). Of note, this model only examined the cost and outcome of a single fresh embryo transfer for each patient and did not consider the cost of sequential frozen embryo transfers for those who failed to conceive in the fresh cycle. As most patients who fail their first transfer will go on to transfer additional embryos, the cumulative cost and clinical outcomes must be considered. A more recently published model accounted for the cost of sequential embryo transfers and concluded that IVF/PGT-A is unlikely to be cost-effective unless testing can be made less expensive (10). However, this model utilized a hypothetical population and pregnancy rates were not reflective of current practices.

This study is unique in that it provides information to assist clinicians and patients with clinical decision-making

FIGURE 3



Average time from retrieval to final outcome, either embryo transfer resulting in live birth or completion of treatment due to exhaustion of embryo cohort in vitro fertilization (IVF)/preimplantation genetic testing for aneuploidy (PGT-A) reduces time in treatment when compared to IVF alone. For patients with greater than two embryos, PGT-A reduces time in treatment by more than 3 months.

Neal. Preimplantation genetic testing cost. Fertil Steril 2018.

regarding the option to pursue PGT-A as they attempt to limit the financial and emotional burdens that can accompany infertility care. It is important to consider the many potential hidden costs of unscreened transfers not accounted for in this model. Transferring unscreened embryos that are in fact aneuploid may result in a negative pregnancy test, a clinical loss or, worse yet, an affected baby. Such transfers take an emotional toll on patients, result in increased time off from work to pursue treatment, and delay the time to a healthy live birth. Therefore, even when costs are equivalent, PGT-A adds substantial benefit through its ability to decrease miscarriage and more quickly achieve a live birth.

In addition to reducing cost, our model also demonstrates that IVF/PGT-A reduces the overall time spent in treatment when compared to IVF alone. The decrease in time spent in treatment was most pronounced for patients with greater than two embryos and exceeded three months, primarily owing to a reduction in unsuccessful transfers following PGT-A. This finding is important as multiple studies have demonstrated that patient dropout increases with number of failed IVF cycles (11–13). Although our model did not take patient dropout into consideration, this factor can be expected to affect those who do not utilize PGT-A to a greater extent, as they require more embryo transfer cycles to reach a given endpoint. While reducing overall treatment costs for this group, dropout also reduces the odds of achieving a live birth.

To combat the lower per-cycle pregnancy rates associated with transferring unscreened embryos, some patients will opt to transfer two unscreened embryos. However, this treatment strategy is associated with a significantly increased risk of multiple gestation. Forman et al. (2) conducted a randomized controlled trial comparing euploid SET to unscreened double embryo transfer (DET) and found that the two groups had similar ongoing pregnancy rates; however, multiple gestations accounted for almost half of the pregnancies achieved following DET (7). As multiple gestations confer an increased risk of maternal and neonatal morbidity, this treatment strategy is not ideal. Furthermore, although the IVF-related costs associated with unscreened DET may be less when compared to PGT-A/SET (as the cost of PGT-A is avoided) and unscreened SET (as the number of transfers needed to achieve a pregnancy is fewer), this cost savings is far outweighed by the obstetric and neonatal costs associated with multiple gestation (14). In an effort to promote singleton gestation and reduce the number of multiple pregnancies, the ASRM recently published a committee opinion advocating SET for patients with a euploid embryo or an otherwise favorable prognosis, defined as "availability of vitrified day-5 or day-6 blastocysts, euploid embryos, 1st FET cycle, or previous live birth after an IVF cycle" (15). For many patients, then, the main question is no longer how many embryos to transfer, but whether to pursue PGT-A prior to SET.

Many patients undergo IVF with hopes of having more than one child. Although this model does not illustrate the costs associated with pursuing a second live birth from the same embryo cohort, it would stand to reason that IVF/PGT-A would be an even more cost-effective strategy in this situation, as these patients already have screened embryos and would not need to pay for PGT-A again. In addition, cost savings could be applied if all the remaining

embryos in a cohort proved to be aneuploid, forgoing expensive storage fees and the false security of expected future frozen embryo transfer success. Knowing this ahead of time would also allow the option to bank embryos for future pregnancies at a younger age with a higher chance of success.

Not all IVF centers and genetics laboratories assign the same cost to embryo biopsy and PGT-A. It is important to acknowledge that altering the cost of these components may impact the model and the conclusions that may be drawn from it. Over the past decade, however, there have been substantial advancements in technology and we have seen costs associated with PGT-A decline as new platforms have been introduced and become more efficient. This model uses a conservative estimate for the cost of PGT-A calculated from an average of commercially available options for PGT-A. This cost is likely to decrease in the future, as advancements in technology emerge.

The strengths of this study include the large database of patients from which we obtained actual data regarding the proportion of euploid embryos per number of embryos tested. The broad inclusion of all cases referred for aneuploidy screening was in part due to the unavailability of clinical diagnoses for patients as they were referred from 74 different IVF centers, but also due to a desire to maximize the external validity of our study. The same patients were used for both arms of the model, thereby eliminating differences regarding demographics and clinical characteristics. In addition, the model uses clinical outcome probabilities and costs reflective of contemporary practice. It accounts for the outcome and cost of not only the first embryo transfer, but all subsequent embryo transfers until the transfer resulting in live birth or exhaustion of the embryo cohort.

Our study does have several limitations. It was assumed that all losses were treated with dilation and curettage when, in fact, some patients may elect to resolve their losses spontaneously or medically at a lesser expense (16). Our study does not account for the rare event of ectopic pregnancy, although the incidence of ectopic pregnancy would likely be similar amongst the two groups (17). In addition, we did not account for the cost of prenatal diagnostic testing. One may surmise that this cost would be greater for patients who underwent transfer of an unscreened embryo as these patients may be more likely to pursue invasive diagnostic testing at a greater expense due to the lack of a preimplantation assessment. We also did not account for costs associated with the rare but expensive possibility of a viable aneuploid delivery in the group that did not utilize PGT-A.

In our study, it was assumed that an embryo designated as abnormal would result in live birth 0% of the time, based upon a non-selection studying utilizing a contemporary method of PGT-A (18). Certainly the possibility of a false positive result exists and studies using more dated platforms suggest that this occurs up to 4% of the time (19, 20). Overall, the risk of a false positive is low and therefore this scenario was not incorporated into our model.

Given the current information available, it appears that IVF/PGT-A is more cost-effective than IVF alone for patients who have greater than one embryo. Patients with only one embryo may still elect to pursue PGT-A for the associated clinical benefits but will, in general, not experience a cost savings with this strategy.

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La fecundación in vitro (FIV) con test genético preimplantacional para aneuploidías es coste-efectivo, acorta el tiempo de tratamiento y reduce el riesgo de transferencia embrionaria fallida y aborto clínico en pacientes seleccionadas comparado con FIV solo

Objetivo: Determinar si el test genético preimplantacional para aneuploidías (TGP-A) es coste-efectivo para pacientes que se someten a fecundación in vitro (FIV).

Diseño: Modelo analítico de decisión comparando costes y resultados clínicos de dos estrategias: FIV con y sin TGP-A.

Ámbito: Laboratorio de genética.

Pacientes: Mujeres $\leq$ 42 años de edad que se someten a FIV.

Intervención(es): Modelo analítico de decisión aplicado a la población de pacientes antedicha utilizando una combinación de datos clínicos reales y suposiciones de la literatura con respecto a los resultados de FIV con y sin TGP-A.

Variable(s) de resultado principal(es): El resultado primario fue el coste acumulado relacionado con FIV para lograr un nacido vivo o agotar la cohorte embrionaria de una única captación ovocitaria. Los resultados secundarios fueron tiempo desde la captación ovocitaria hasta la transferencia embrionaria que resultara en un nacido vivo o terminación del tratamiento, tasa acumulada de nacido vivo, transferencias embrionarias fallidas y pérdidas clínicas.

Resultados: 8998 pacientes de 74 centros de FIV fueron incluídas. Para pacientes con más de un embrión, el diferencial de costes favoreció el uso de TGP-A, desde $931-2411 y dependiendo del número de embriones estudiados. Como se esperaba, la tasa acumulada de nacido vivo fue equivalente en ambos grupos una vez que todos los embriones fueron agotados. Sin embargo, el TGP-A redujo el tiempo en tratamiento hasta cuatro meses. Además, las pacientes sometidas a TGP-A experimentaron menos transferencias embrionarias fallidas y abortos clínicos.

Conclusión: Para pacientes con más de un embrión, FIV con TGP-A reduce los costes sanitarios, acorta el tiempo de tratamiento y reduce el riesgo de transferencia embrionaria fallida y aborto clínico comparado con FIV solo.