

Abstract

Objective: Sperm capacitation is a necessary precursor to fertilization. The Cap-Score™ was developed to assess the capacitation status of men. This enables personalized management of infertility for some couples by selecting among timed intra-uterine insemination (IUI), versus moving immediately to in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) in those with a low Cap-Score™. The objective of this study was to estimate the differences in clinical pregnancy rates and medical costs comparing the use of the Cap-Score™ with timed IUI (CS-TI) and the current standard of care (SOC), namely 3 IUI cycles followed by 3 IVF-ICSI cycles.

Design: Decision-analytic modeling

Materials and Methods: We developed and parameterized a decision-analytic model of management of unexplained infertility for a hypothetical woman 35 to 37 years of age, using her own eggs, based on data from published and unpublished sources. We calculated the clinical pregnancy rates and medical costs comparing CS-TI and SOC. The test has not yet been launched, and no price has been established, so the medical costs include only other costs.

Results: Compared to SOC, CS-TI is projected to increase the cumulative pregnancy rate by 2.18% (91.15% vs. 88.97%). Compared to SOC, CS-TI is projected to reduce mean medical costs by \$4,818 (\$23,048 vs. \$27,866). CS-TI is projected to reduce mean IUI costs by \$638 (\$6,019 vs. \$6,783) and mean IVF-ICSI costs by \$4,180 (\$17,029 vs. \$21,210) compared to SOC.

Conclusions: Use of the Cap-Score™ to personalize management of couples with unexplained infertility is projected to result in higher clinical pregnancy rates and reduced medical costs in couples with women 35 to 37 years of age.

Introduction

- Approximately one million women in the US have infertility, defined as inability to get pregnant after at least twelve months of unprotected sex. An even larger number—7.5 million—have diminished fecundity, the impaired ability to get pregnant or carry a baby to term.
- Among couples who are unable to conceive, a male factor is present in 20 – 50% and 50% of the causes of male infertility are undetectable by traditional semen analysis. Additionally, up to 30% of infertile couples have unexplained infertility—infertility for which the underlying cause is unknown.
- At the intersection between infertility with a male factor and unexplained infertility lies a potential sperm-related cause of infertility: failure of sperm capacitation.
- Sperm capacitation consists of the functional maturation of sperm membranes triggered by stimuli in the female genital tract. Capacitation results in increased sperm motility or hyperactivity. It precedes and is a precondition for the acrosome reaction and a precursor to fertilization.
- Capacitation timing can be utilized to personalize natural conception as well as assisted reproductive technologies (ART) by optimization of times for IUI relative to ovulation and timing of co-incubation of sperm and oocytes for in-vitro fertilization (IVF).
- The Cap-Score™ measures localization of ganglioside GM1 and was developed to reflect changes in the capacitation status of men as a functional assessment to complement traditional semen analysis. The Cap-Score™ identifies subpopulations of sperm capable of capacitating; a low Cap-Score™ is defined as a score that is one standard deviation below the mean.
- The objective of this study was to assess the potential clinical and economic impact of the Cap-Score™.

Methods

- We developed and parameterized a decision analytic model (figure 1) comparing the use of the Cap-Score™ with timed IUI (CS-TI) and the current standard of care (SOC), namely 3 IUI cycles followed by 3 IVF-ICSI cycles.
- The outcomes of the model were clinical pregnancy, total medical costs, IUI costs, and IVF costs.
- Data were obtained from published and unpublished sources (table 1).
- As a measure of the precision of estimates, we calculated 95% credibility intervals (CIs) by defining probability distributions for each parameter estimate and using 10,000 runs of Monte Carlo simulation.
- We also assessed parameter uncertainty by performing univariate sensitivity analyses.

Figure 1: Decision Analytic Model

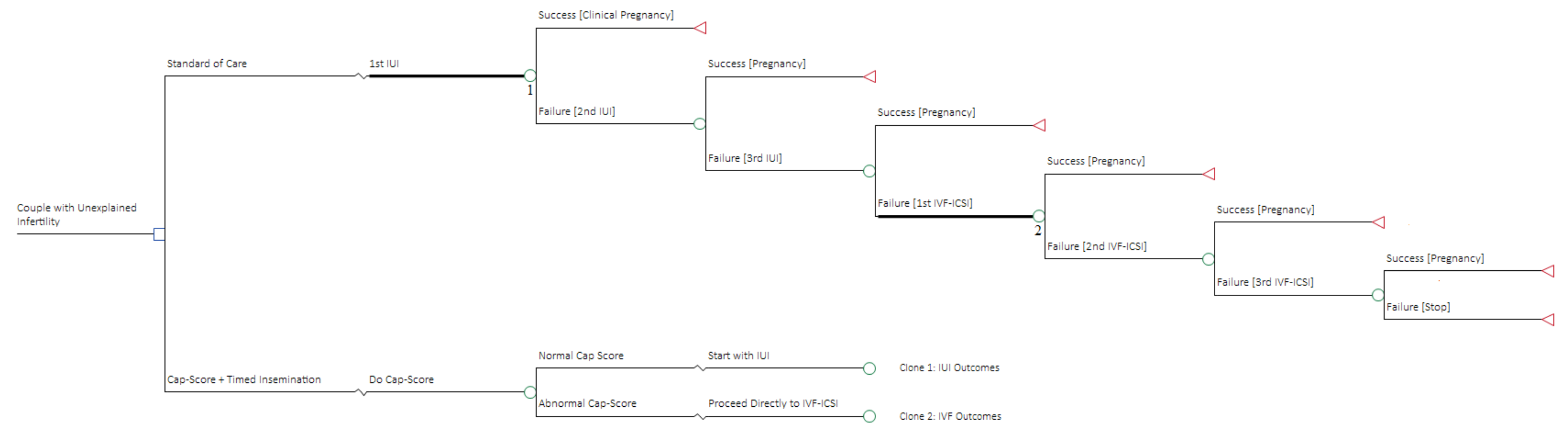


Table 1: Parameter estimates used in the model

Parameter	Baseline	Sensitivity Range	Reference
Costs			
IUI	\$2,550	\$1,275 – \$3,825	Expert opinion
IVF-ICSI	\$17,651	\$8,825 – \$26,476	Chambers et al.
Probabilities			
Low Cap-Score Test	0.385	0.308 – 0.462	Travis et al.
Clinical pregnancy (per cycle)			
With IUI in SOC	0.118	0.059 – 0.177	Stone et al.
With IUI after Cap-Score Test	0.400	0.320 – 0.480	Expert opinion
With IVF-ICSI	0.445	0.356 – 0.534	SART
Live birth (per cycle)			
With IUI	0.495	0.248 – 0.743	Stone et al.
With IVF-ICSI	0.829	0.793 – 0.865	SART

Table 2: Baseline Results, Mean (95% Credibility Interval)

Outcome	SOC	CS-TI	Δ
Clinical Pregnancy Rate	88.97%	91.15%	2.18%
	(81.94% – 93.81%)	(85.78% – 94.91%)	
IUI Costs	\$6,657	\$6,019	-\$638
	(\$3,337 – \$10,095)	(\$3,020 – \$9,102)	
IVF Costs	\$21,210	\$17,029	-\$4,180
	(\$10,087 – \$34,391)	(\$8,233 – \$26,791)	
Total Costs	\$27,866	\$23,048	-\$4,818
	(\$15,887 – \$41,803)	(\$13,671 – 41,803)	

Results Summary

- Compared to SOC, CS-TI is projected to increase the cumulative pregnancy rate by **2.18%** (91.15% vs. 88.97%).
- CS-TI is projected to reduce mean IUI costs by **\$638** (\$6,019 vs. \$6,783) and mean IVF-ICSI costs by **\$4,180** (\$17,029 vs. \$21,210) compared to SOC.
- Compared to SOC, CS-TI is projected to reduce mean total medical costs by **\$4,818** (\$23,048 vs. \$27,866).
- Results were generally robust to univariate sensitivity analysis.
 - The differences in all four outcomes were most sensitive to the probability of clinical pregnancy with IUI in the absence of the Cap-Score™.

Conclusion

- Use of the Cap-Score™ to personalize management of couples with unexplained infertility is projected to result in higher clinical pregnancy rates and reduced medical costs in couples with women 35 to 37 years of age.
- The Cap-Score™ is a potentially valuable clinical tool for management of unexplained infertility because it improves outcomes and saves money, and is therefore likely to increase access to treatment for infertility.