



# Cap-Score™ accurately predicts probability of generating pregnancy across maternal age stratifications



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## Abstract

**Study question:** Do predicted probabilities of generating pregnancy based on the Cap-Score™ male fertility assay differ from observed outcomes even when stratified by maternal age?

**Summary answer:** In women eligible for intrauterine insemination (IUI), Cap-Score remains predictive across maternal age stratifications, with predicted and observed clinical pregnancy outcomes matching closely.

**What is known already:** Sperm must capacitate to fertilize. Cap-Score, which quantifies capacitation status to functionally assess male fertility, was prospectively shown to predict pregnancy. Based on clinical pregnancy outcomes from IUI patients at five fertility clinics and across a wide age range, the relationship between Cap-Score and the probability of generating pregnancy (PGP) was previously defined. However, maternal age is well known to be linked with reduced fertility. The ability of Cap-Score to predict PGP across stratified maternal ages is unknown and tested here. IUI was chosen as an experimental model since the number and timing of inseminations relative to ovulation could be documented and controlled.

**Study design, size, duration:** Data were collected (11/2016-09/2018) from 231 couples who generated a pregnancy within, or completed, 3 rounds of IUI, and 23 couples who became pregnant through natural conception (NC). Relationships between maternal age and PGP were tested using analysis of variance (ANOVA). Differences between predicted and observed pregnancy rates, and age and outcome, were examined using Chi-Square analysis. The potential relationship between Cap-Score and delivery or miscarriage was also evaluated on a preliminary basis (t-test).

**Participants/materials, setting, methods:** Semen was collected as part of a standard fertility evaluation at 5 different centers. Samples having fewer than 10x10<sup>6</sup> motile sperm were excluded. Fixed specimens were shipped overnight to Androvia, where the Cap-Score assay was performed. Only female fertility that would preclude attempts at IUI led to exclusion, resulting in a representative test population of patients pursuing IUI across age ranges.

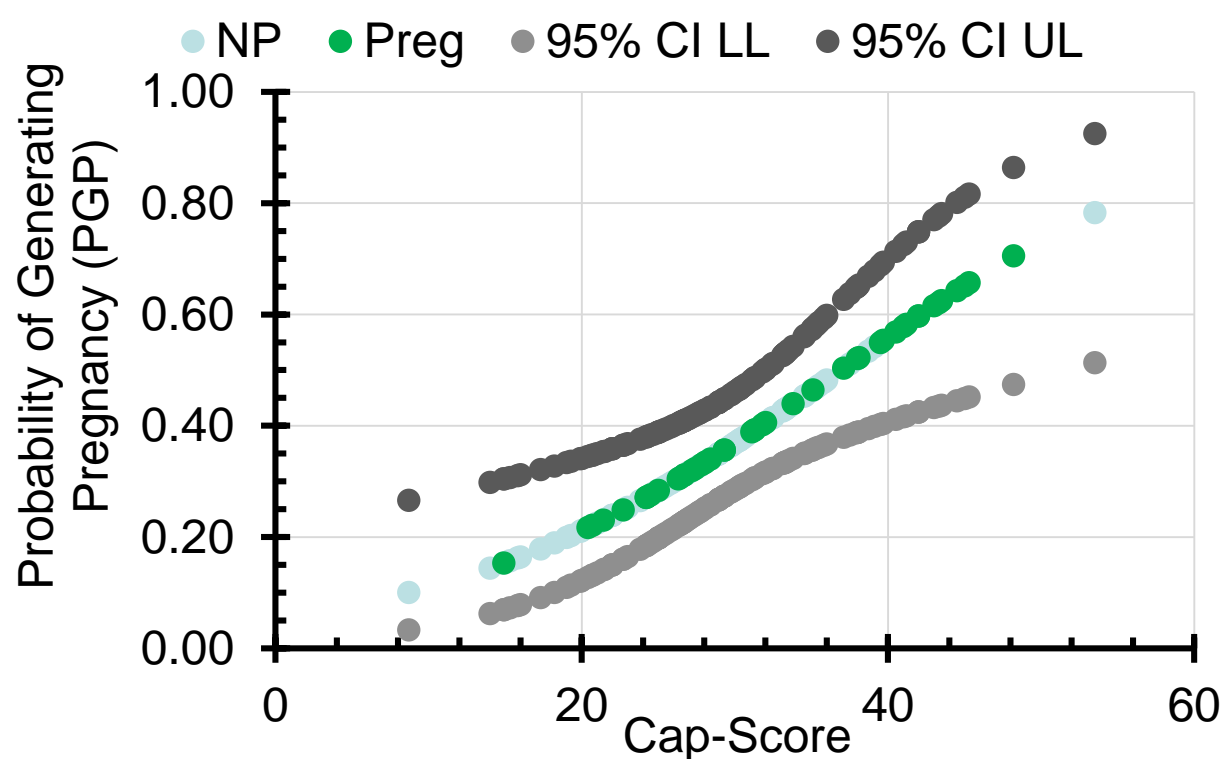
**Main results and the role of chance:** Observations were separated into the following age groups: ≤29, 30-34, 35-39, and ≥40. There was no relationship between outcome and age group (p=0.661). The average PGP derived from the Cap-Scores (predicted, PRED) and the observed pregnancies (OP) in each group were, respectively: ≤29 (35% PRED, 35% OP, n=34); 30-34 (37% PRED, 40% OP, n=115); 35-39 (34% PRED, 33% OP, n=66); and ≥40 (33% PRED, 25% OP, n=16). There were no differences between observed and predicted pregnancy rates in any maternal age group (p=0.943, 0.446, 1.000, and 0.678, respectively). Cap-Scores and resultant PGPs reflect male fertility and did not differ across maternal age stratifications (ANOVA p=0.398). Preliminary data from one center from 38 couples pregnant by IUI (66% live births; 34% miscarried) and 23 by NC (65% live births; 35% miscarried) were also evaluated to determine if live births were similar between high and low Cap-Scores. There was no difference in Cap-Score between miscarriages and live births in either the IUI (p=0.198) or NC groups (p=0.458). The role of chance is increased when evaluating data from a single center versus multicentric studies, and when evaluating smaller versus larger datasets.

**Limitations, reasons for caution:** Caution is needed when evaluating smaller datasets and those from a single center. Women over 40 had the smallest sample size and thus the greatest risk of stochastic impact. Preliminary data suggest no relationship between Cap-Score and miscarriage. More data from multiple clinics are needed to address this issue definitively.

**Wider implications of the findings:** Female age and fertility are indisputably linked; however, if eligible for IUI, then PGP based on Cap-Score accurately predicted outcomes even when stratified by maternal age. This likely reflects that PGPs were originally quantified based on actual clinical pregnancy outcomes collected across a representative age range for female partners.

## Introduction

Cap-Score™ functionally assesses sperm capacitation/male fertility and prospectively predicts pregnancy. Based on clinical pregnancy outcomes from IUI, the relationship between Cap-Score and the probability of generating pregnancy (PGP) was previously defined using data from 5 clinics (Figure 1). The ability of Cap-Score to predict PGP across stratified maternal ages is unknown and tested here.



**Figure 1. Cap-Score™ and its association with pregnancy.** Logistic regression generated an equation explaining the relationship between Cap-Score™ and PGP. All individuals in this analysis completed at least three rounds of IUI or generated pregnancy. Data were obtained from 5 clinics and across a wide age range (n=124; PGP range: 10-78%). Published data, *Schinfeld et al., 2018*

## Experimental design

Relationships between maternal age and PGP were tested using analysis of variance (ANOVA). Differences between predicted and observed pregnancy rates, and age and outcome, were examined using Chi-Square analysis. The potential relationship between Cap-Score and delivery or miscarriage was also evaluated on a preliminary basis (t-test), to address the question of whether pregnancies from IUI from men with low Cap-Scores would have a higher miscarriage rate.

## Results

Observations (n= 231) were separated into the following age groups: ≤29, 30-34, 35-39, and ≥40. **Table 1** shows average PGP derived from the Cap-Scores and the observed pregnancies in each group. There were no differences between observed and predicted pregnancy rates in any maternal age group (p=0.943, 0.446, 1.000, and 0.678). Cap-Scores and resultant PGPs reflect male fertility and did not differ across maternal age stratifications (ANOVA p=0.398). There was no relationship between outcome (pregnancy) and age group (p=0.661). Preliminary data from one center from 38 couples pregnant by IUI and 23 by Natural Conception (NC), were also evaluated to compare Cap-Scores between couples that miscarried or delivered. There was no difference in Cap-Score between miscarriages and live births in either the IUI (p=0.198) or NC groups (p=0.458), **Table 2**.

Table 2	Live Birth	Miscarriage	Average Cap-Score™	Live Birth vs Miscarriage (p value)
IUI (n=38)	66%	34%	Live birth: 30%	0.198
			Miscarriage: 33%	
NC (n=23)	65%	35%	Live birth: 26%	0.458
			Miscarriage: 28%	

## Conclusions

- Female age and fertility are indisputably linked; however, if eligible for IUI, then Cap-Score accurately predicted pregnancy outcomes even when stratified by maternal age.
- Preliminary data suggest no difference in live births between IUI and natural conception.
- Pregnancies from IUI involving men with low Cap-Scores were no more likely to suffer miscarriage than if they have conceived naturally.
- The strong association between Cap-Score and probability of generating pregnancy underscores the importance of functional assessment of male fertility to inform couples about their pathway to pregnancy and live births.

Table 1 Female Age Ranges	Number of Observations	Average Cap-Score™	Average Predicted PGP	Observed % Pregnant	PGP vs Observed Preg. (p value test of one proportion)
≤ 29	34	28%	35%	35%	0.943
30-34	115	30%	37%	40%	0.446
35-39	66	28%	34%	33%	1.000
≥ 40	16	27%	33%	25%	0.678