


Clinical Trials

# IVF Stimulation - personalized, optimized, and simplified using an advanced decision-support tool: A randomized trial

Urmila Diwekar, Ph.D.<sup>1,2,3</sup><sup>a</sup>, Nayana Patel, M.D.<sup>4</sup>, Niket Patel, M.D.<sup>4</sup>, Harsha Bhandarka, Ph.D.<sup>4</sup>, Molina Patel, M.D.<sup>4</sup>, Paresh Ghoghari, M.D.<sup>4</sup>, Kairavi Vyas, M.Sc.<sup>4</sup>, Sanjay Joag, M.D., Ph.D.<sup>1</sup>

<sup>1</sup> Stochastic Research Technologies LLC, Crystal Lake, Illinois, USA, <sup>2</sup> Vishwamitra Research Institute, <sup>3</sup> University of Illinois at Chicago, <sup>4</sup> Akansha Hospital and Research Institute, Anand, Gujarat, India

Keywords: Clinical decision support tool, Opt-IVF, optimal control, superovulation

---

## Journal of IVF-Worldwide

Vol. 1, Issue 1-3, 2023

---

We assessed the effectiveness of a clinical decision support tool to reduce total cumulative follicle-stimulating hormone dosage used, to eliminate the need for ultrasound exams after day 5 of an individual superovulation cycle, and to improve the number of high-quality embryos obtained. The design we used was a Randomized Control Trial in a private fertility center. This study included 93 women aged 25–45 years undergoing IVF. 48 Test and 45 Control participants included normal and poor responders and patients with polycystic ovarian syndrome. A clinical decision support tool was used to forecast stimulatory hormone dosing for an individual cycle based on follicle size distribution on day 1 and day 5. Cumulative stimulatory hormone doses, oocytes retrieved, number of MII oocytes, total embryos, high-quality embryos obtained during the cycle, and clinical pregnancy rates was the main outcome measures. Test participants required significantly lower cumulative FSH doses during superovulation cycles (average 1883 IU test, 2530 IU control,  $p < 0.01$ ), with significantly higher numbers of total embryos (average 5.4 test, 3.5 control,  $p < 0.01$ ), and high-quality embryos (average 3.1 test, 1.2 control,  $p < 0.01$ ). Test participants had higher MII follicles, although the difference was not statistically significant. The clinical pregnancy rate reported was significantly higher for test participants than control participants (52% test, 26% control,  $p < 0.05$ ). The test group had more poor responders and PCOS patients than the control group. In conclusion, the clinical decision support tool eliminated the need for ultrasound exams after day 5, reduced the doses of stimulatory hormone required, yielded significantly higher numbers of high-quality embryos, and resulted in higher clinical pregnancy rates.

## INTRODUCTION

Infertility affects millions of people of reproductive age worldwide – and impacts their families and communities. Estimates suggest up to 186 million individuals live with infertility globally.<sup>1</sup> In-vitro fertilization (IVF) is the most common technique in assisted reproductive technology. IVF is also effective for infertility in women with polycystic ovarian syndrome (PCOS). Superovulation is a drug-induced method to enable multiple oocytes per menstrual cycle in IVF. The success of IVF depends upon successful superovulation, defined by the number and quality of eggs

retrieved in a cycle. Superovulation is also vital for IUI (Intra-uterine insemination).

The drugs used in this treatment are expensive. A recent article in Forbes suggests that the current cost of IVF in the United States ranges from \$15,000 to \$30,000, and 35% of the cost is related to drugs.<sup>2</sup> Currently, this step is executed using almost daily monitoring of the follicular development using ultrasound and blood tests. The daily dosage of hormones is then chosen for each patient based on the physician's experience. Although there are general guidelines for the dosage, the dose is not optimized for each patient, and overstimulation complications can occur.<sup>3</sup> A recent study of 7399 IVF cycles from Harvard University

---

<sup>a</sup> **Corresponding Author:**

Dr. Urmila Diwekar,  
ORCID iD: 0000-0002-0933-5865  
2714 Crystal Way, Crystal Lake, IL 60012, USA  
Phone: +1 (630) 886-3047  
Email: [urmila@vri-custom.org](mailto:urmila@vri-custom.org)

concluded that Follicle Stimulating hormone (FSH) and Human Menopausal Gonadotropin (HMG) ovarian stimulation drugs are typically applied at saturating or slightly deleterious doses. The dosage of these hormones can be reduced.<sup>4</sup> A recent review<sup>5</sup> on IVF modeling emphasizes that the future of IVF treatment will use optimal treatment based on models. The cost of testing – frequent transvaginal ultrasounds (US), blood tests, and drugs – makes the superovulation stage very expensive. To overcome the shortcomings of this system, we have developed a user-friendly decision support tool (Opt-IVF) that can provide a personalized model of this stage for each patient's superovulation cycle. Customized optimal drug treatment profiles can then be developed for each patient using optimal control methods provided by the software. The model is based on the size distribution of follicles on day 1 and day 5 of a superovulation cycle. This, together with the FSH doses used on days 1 to 4, provides a basis for predicting the FSH doses to be given on day 5 and subsequent days to achieve better outcomes – maximizing the number of mature follicles. The Opt-IVF algorithm can also forecast the best time to begin antagonists and the optimal trigger day to maximize the recovery of mature oocytes. A recent non-randomized clinical trial with retrospective controls<sup>6</sup> has demonstrated the tool's success in clinical practice. Test subjects had higher numbers of mature MII oocytes, required 30% lower cumulative FSH doses, and had higher numbers of high-quality embryos. We report here on a randomized clinical trial using Opt-IVF to guide superovulation.

## MATERIALS AND METHODS

All clinical work was conducted at the Akansha Hospital and Research Institute in Gujarat, India. The institutional review board at Sat Kaival Hospital Pvt. Ltd. Ethics Committee, Gujarat, India, approved the protocol and consent forms. All participants provided written informed consent. Patient safety was reviewed throughout the study by the clinical investigators (Nayana Patel, Niket Patel, M. Patel, H. Bhadarka, P. Ghoghari, and K. Vyas), who were responsible for clinical work and data collection. U. Diwekar and S. Joag are responsible for the study design, data analysis, and interpretation and writing of this manuscript. All authors contributed to the review and editing of the manuscript and approved the final version for submission. All authors vouch for the data's accuracy and completeness and the protocol's fidelity to the trial.

### THE DECISION TOOL OPT-IVF

Opt-IVF is a unique tool that provides optimal and personalized dosage profiles for a complete superovulation cycle. The difference between this approach and the machine learning approaches<sup>7-11</sup> presented in the literature is provided in [Table 1](#).

### INITIAL DOSE

Opt-IVF provides an initial dose based on either the nomogram proposed by La Marca and Sunkara,<sup>12</sup> which predicts the initial dose based on age, day 3 serum FSH, and AMH, or based on heuristics using age, AMH, and AFC values.

### DOSAGE PROFILE FOR THE REST OF THE CYCLE

IVF's success depends on successful superovulation, defined by the number and uniformly high quality of eggs retrieved in a cycle. This requires frequent monitoring of follicular development using ultrasound and blood tests to decide day-to-day dosage. Although there are general guidelines for stimulatory hormone dosage, individualization of dosage is primarily driven by the physician's experience and clinical judgment. To overcome the shortcoming of this system, we developed a mathematical procedure that can provide a personalized model of this stage for each patient by considering the change in the distribution of follicles due to the chemical interactions of the drugs used. The aim is to obtain the maximum number of mature follicles (18-22 mm) at the end of the cycle. Optimal control theory decides personalized, optimized dosages for each patient.<sup>13,14</sup>

Opt-IVF creates a personalized model using day 1 and day 5 follicular size distribution data (as shown in [Table 2](#), obtained by ultrasound), and the initial dosage is given to the patient. Thus, the model is customized for that patient, that cycle, and the FSH dose used on days 1 to 4. We used data from 150 patients (70 agonist protocol and 80 antagonist protocol patients) from three IVF centers in India and one IVF center in the United States to validate the model. The individualized model for a cycle is then used to optimize the dosage for the remaining days using optimal control theory. This approach reduced dosage and testing, with similar or better outcomes regarding the number of mature follicles. The model, theory and initial validation details are published elsewhere.<sup>13,14</sup>

### THE CLINICAL TRIAL

The trial was registered on [ClinicalTrials.gov](#) (ID NCT05564702). We use Simple Randomization of all patients registered for the trial. A 'lottery method' was used to assign patients to test and control. Based on a previous non-randomized clinical trial,<sup>6</sup> a sample size of 45 patients in each arm was considered sufficient. We conducted power analyses for two important outcomes, the total dosage and the number of high-quality embryos. To get a power of 0.95 with a significance level of 0.05 for an average total dosage to be 20 % lower in the test than in controls, we needed 18 subjects in each arm. At the same power level, for high-quality embryos to be 60% higher in the test than the control group, we required 38 subjects in each arm. Therefore, a sample of 45 in each arm was more than sufficient for our analysis.

An Antagonist protocol was used for all patients, using Recombinant FSH (Gonal – F, Merck), R-Hu-LH (Merck), and Cetrorelix 0.25 mg (Bharat Serum and Vaccines Lim-

**Table 1. Comparison between Opt-IVF and machine learning approaches.**

Features	Opt-IVF	Machine Learning Approaches
Initial dose	Prediction based on nomogram & heuristics. Validated using clinical trials.	Prediction based on machine learning. Validated using existing data only. No clinical trial has been reported.
Customized daily dose	Predicts based on day 1 and day 5 follicle size distributions using the moment model. Provides dosage profile for the complete cycle on day 5. Successful clinical trials result in reduced dosage, reduced testing, and better outcomes.	Does not have such capability at this stage.
Trigger day	Predicts using the moment model. Validated using clinical trials.	Predicts using machine learning. Validated using existing data sets only.

**Table 2. An example of follicular size distribution in a patient.**

Follicle Size Bins (mm)	No. of Follicles on different days	
	Day 1	Day 5
0-4	10	2
4-8	3	8
8-12	0	2
12-16	0	0
16-20	0	0
20-24	0	0

ited). Participants were categorized before enrollment as expected poor responders (PR), expected normal responders (NR), and PCOS based on Age, AMH, and clinical presentation. All participants had transvaginal ultrasound exams (US) to quantify the number and size of follicles on day 1 and day 5 of the cycle. This information was entered into the Opt-IVF decision support tool for test group patients, which suggested FSH doses for day 5 and all subsequent days of the cycle. All recommendations of the decision support tool were made available to the clinical investigators before day 1 and on day 5.

Control participants also had US on days 7 and 9. The participating clinical investigators retained the ability to override Opt-IVF dose recommendations based on their clinical judgment but did not do so in any patient. For control group participants, the hormone doses each day were based on the participating clinical investigators' choice. Although Opt-IVF recommended trigger days, this feature was not tested in this trial. The trigger days in all test and control participants were entirely based on the participating clinical investigators' choice. There were no differences in the dosing of trigger hormones. Mii oocytes were considered mature if at least one polar body was present.

The primary outcomes measured were the cumulative FSH dosage, the number of mature and Mii oocytes retrieved, the total number of embryos, and the number of high-quality (Grade A) embryos obtained after in-vitro fertilization in each cycle. High-Quality Embryos were assessed with the Recent Gardner Grading. Morphologically Normal is known to be good quality (Grade A). Clinical pregnancy rates for patients were measured. 80% of em-

bryos transferred were frozen embryos. Statistical analyses were performed using Microsoft Excel. For statistical analysis of cumulative doses, total and Mii oocytes, total embryos, and grade A embryos, we used two-tailed t-tests with unequal variance (heteroscedastic). For pregnancy data, we used the chi-square statistic. The statistical significance level was kept at  $p < 0.05$  for all analyses.

**RESULTS**

Test and control participant groups were similar in age, and the proportions of expected normal responders, poor responders, and participants with PCOS are given in [Table 3](#)

[Table 4](#) presents the results for cumulative total average FSH dosage. The cumulative FSH doses administered to test participants were lower than the doses administered to control participants. The differences in dosage were statistically significant overall and also for each subgroup. On average, the cumulative FSH dose in test participants was 26% lower than in controls. Although clinical investigators had the discretion to override Opt-IVF recommended doses, they did not do so on any day for any participant.

The number of oocytes retrieved and Mii oocytes were statistically similar among test participants and control in total and each subgroup ([Table 5](#)). The total embryos were significantly higher in test participants than in controls ([Table 6](#)). On subgroup analysis, the total numbers of embryos were significantly higher for test group poor responders, though no statistical differences were observed among normal responders and PCOS patients. The number of high-

**Table 3. Participant Characteristics**

	Test Group	Control group
Normal responders	14	21
Poor responders	15	13
Polycystic Ovarian Syndrome	19	11
Total Participants	48	45
Age, Years $\pm$ SD	32.7 $\pm$ 5.1	33.9 $\pm$ 4.3

**Table 4. Average Cumulative Total FSH Dosage (IU)**

Patients/Results	Test	Control	% Reduction	t-test
PCOS	1775	2933	39%	p <0.01
Poor responder	1803	2207	18%	p <0.01
Normal responder	2108	2418	13%	p <0.05
Group Total	1883	2530	26%	p <0.01

**Table 5. Average Total Oocytes and Mii Oocytes**

Patients/Results	Test	Control
PCOS - oocytes	13.3	12.5
PCOS - Mii oocytes	9.6	10.4
PR - oocytes	6.5	3.8
PR - Mii oocytes	5.1	3.5
NR - oocytes	7.1	8.6
NR - Mii oocytes	6.1	6.9
Overall - oocytes	9.4	8.0
Overall - Mii oocytes	7.2	6.8

**Table 6. Total Number of Embryos**

Patients/Results	Test	Control	t-test
Poor responders	3.4	1.8	p < 0.05
PCOS	7.4	6.5	p = 0.47
Normal responders	4.7	3.0	p = 0.14
Total	5.4	3.5	p < 0.01

**Table 7. Number of Grade A Embryos**

Patients/Results	Test	Control	t-test
Poor responders	2.5	0.8	p <0.01
PCOS	3.7	1.2	p <0.01
Normal responders	2.9	1.5	p <0.05
Total	3.1	1.2	p <0.01

quality embryos ([Table 7](#)) was significantly higher in test participants than in controls. A statistically significant difference was found in all three subgroups.

NR and PR - Normal responders and poor responders, respectively.

We could not get clinical pregnancy results for all participants because the travel schedule of some patients did not allow the transfers to be completed. Currently, we have data for 44 of 48 test group patients and 31 of 45 control group patients. The clinical pregnancy rates were signifi-

Patients/Results	Test	Control
PCOS - pregnant	9	1
PCOS -not pregnant	10	6
% Pregnant	47%	13%
PR - pregnant	7	2
PR -not pregnant	8	8
% Pregnant	47%	20%
NR - pregnant	7	5
NR -not pregnant	3	8
% Pregnant	70%	38%
Total- pregnant	23	8
Total -not pregnant	21	23
% Pregnant	52%	26%

**Table 8. Clinical Pregnancy Rates**

cantly higher (chi-square statistic 3.92,  $p = 0.048$ ) in test patients as compared to control patients, as shown in [Table 8](#). For poor responders and PCOS patients, pregnancy rates in the test group are higher than clinical pregnancy rates reported in the literature.<sup>15-18</sup>

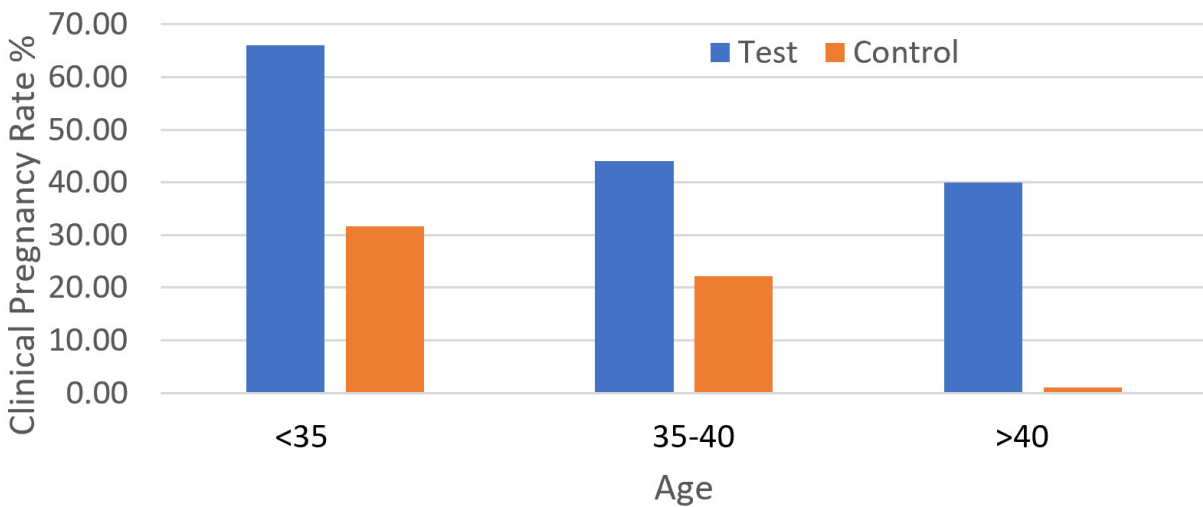
The clinical pregnancy rate was higher in test patients than in controls at all ages ([Figure 1](#)).

**DISCUSSION**

This paper described a clinical decision support tool for predicting the complete dosage profile from day 1 to the

end of the cycle using modeling and optimization. The tool is based on a physics-based model<sup>13,14</sup> that can be personalized for each patient based on the cycle’s follicle size distribution data for day 1 and day 5. Optimal control theory is then used to predict the optimal dosage profile for the complete cycle to minimize the variance in follicle sizes at the end of the cycle. This paper presents the first randomized trial to study the effectiveness of the decision support tool, Opt-IVF. This trial aimed to investigate the use of Opt-IVF, a clinical decision support tool, in guiding superovulation to reduce the need for US testing and lowering hormone dosage while maintaining comparable outcomes regarding oocyte retrieval, embryo quality, and pregnancy rates. The model was previously validated and showed that using the tool could reduce hormonal dosage and testing and improve outcomes. Our study with 93 patients was sufficient to provide statistically significant results for hormone dosage and embryos obtained. The trial utilized a personalized approach to hormone dosing based on optimal control theory, a new approach in the field of in-vitro fertility.

Our results showed that using a clinical decision support tool eliminated the need for transvaginal US exams after day 5 of a superovulation cycle. Test participants had US only on days 1 and 5, while controls required the US on days 1, 5, 7, and 9. This represents a 50% reduction in US testing during a superovulation cycle. Using the tool significantly reduced stimulatory hormone doses in all three subgroups - normal responders, poor responders, and PCOS participants, which is likely to lower the overall costs of treatment, especially in resource-poor settings. None of the participants in the trial developed OHSS or other significant side effects. These results were similar to those of a previous clinical trial with retrospective controls.<sup>6</sup> We had calculated that a sample size of 189 in each arm would be re-



**Figure 1. Clinical pregnancy rates for different age groups.**



quired for a power of 0.8 with a significance level of 0.05 for a 15% higher oocyte yield in the test than in controls. The numbers of oocytes retrieved and MII oocytes did not differ significantly between the test and control groups, and the study was underpowered to detect differences in this measure.

Although the trial's aims did not include pregnancy rates, an unexpected result was that the test group had significantly higher numbers of high-quality embryos and clinical pregnancy rates than the control group. The higher pregnancy rates and high-quality embryo numbers were particularly noticeable in poor responders and PCOS patients. The clinical pregnancy rate in older patients compares favorably with published reports.<sup>19</sup> Our results suggest that using this clinical decision support tool will be particularly valuable in more challenging cases: PCOS, poor responders, and relatively older women.

Among the limitations of this study are that it is a single-center trial and that the patients were all from a single ethnic background (Indian), which might limit the generalizability of our results. However, the model underlying the clinical decision support tool was validated in patients from India and the US, suggesting that the results likely apply to patients of other ethnicities. As the model is individualized for each patient, other confounding factors are unlikely to affect the results.

## CONCLUSION

The clinical trial demonstrated that utilizing the clinical decision support tool, Opt-IVF, to guide hormone dosing during superovulation resulted in lower hormone doses and eliminated the need for ultrasound testing after day 5 of the cycle. This approach led to increased total and high-quality embryos and higher pregnancy rates in the test group compared to prospective control.

.....

## AUTHORS' CONTRIBUTION – CREDIT

Conceptualization: Urmila Diwekar; Data curation: Urmila Diwekar, Sanjay Joag; Formal Analysis: Urmila Diwekar and Sanjay Joag; Investigation: Urmila Diwekar, Nayana Patel,

Niket Patel, Harsha Bhandarka, Molina Patel, Paresh Ghoghari, Kairavi Vyas, Sanjay Joag; Methodology: Urmila Diwekar, Nayana Patel, Sanjay Joag; Project administration: Urmila Diwekar; Software: Urmila Diwekar; Supervision: Urmila Diwekar and Nayana Patel; Validation: Dr. Urmila Diwekar, Sanjay Joag; Writing – original draft: Urmila Diwekar, Sanjay Patel; Writing – review & editing: Urmila Diwekar, Nayana Patel, Sanjay Joag.

## FUNDING STATEMENT

No external funding

## DISCLOSURE STATEMENT

Urmila Diwekar and Sanjay Joag have an ownership interest in Stochastic Research Technologies LLC, which owns and markets Opt-IVF. Nayana Patel, Niket Patel, Harsha Bhandarka, Molina Patel, Paresh Ghoghari, and Kairavi Vyas have no disclosures.

## FUNDING STATEMENT

No external funding

## ATTESTATION STATEMENT

- The subjects in this trial have not been involved in other randomized trials.
- Data regarding any of the subjects in the study has not been previously published unless specified.
- Data will be made available to the journal editors for review or query upon request.

## DATA SHARING STATEMENT

Data on individual patients will be shared in spreadsheet format to the corresponding author upon request.

## TRIAL REGISTRATION

[ClinicalTrials.gov](https://clinicaltrials.gov) (ID NCT05564702).

Date of Registration: Oct. 3, 2022. Date of enrolment of the first subject: Oct. 10, 2022.

Submitted: July 06, 2023 IDT, Accepted: August 06, 2023 IDT



This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CCBY-NC-ND-4.0). View this license's legal deed at <https://creativecommons.org/licenses/by-nc-nd/4.0> and legal code at <https://creativecommons.org/licenses/by-nc-nd/4.0/legalcode> for more information.

## REFERENCES

1. <https://www.who.int/news-room/fact-sheets/detail/infertility>
2. Conrad M, Grifo J. How much does IVF Cost? Forbes, <https://www.forbes.com/health/family/how-much-does-ivf-cost/>, last accessed. *Apr.* 2023;28.
3. Klemetti R, Sevón T, Gissler M, Hemminki E. Complications of IVF and ovulation induction. *Hum Reproduction.* 2005;20(12):3293-3300. [doi:10.1093/humrep/dei253](https://doi.org/10.1093/humrep/dei253)
4. Leahy BD, Racowsky C, Needleman D. Inferring simple but precise quantitative models of human oocyte and early embryo development. *J R Soc Interface.* 2021;18(182):20210475. [doi:10.1098/rsif.2021.0475](https://doi.org/10.1098/rsif.2021.0475)
5. Simopoulou M, Sfakianoudis K, Antoniou N, et al. Making IVF more effective through the evolution of prediction models: is prognosis the missing piece of the puzzle? *Syst Biol Reprod Med.* 2018;64(5):305-323. [doi:10.1080/19396368.2018.1504347](https://doi.org/10.1080/19396368.2018.1504347)
6. Diwekar U, Patel N, Patel N, Patel M, Bhadarka H, Ghoghari P, et al. A Non -Randomized Clinical Trial of a Decision Support Tool to Optimize Superovulation Cycles in Individual Patients. *J Fertil In vitro IVF World w Reprod Med Genet Stem Cell Biol.* 2022;10(261). <https://opt-ivf.com/paper.pdf>
7. Hariton E, Chi EA, Chi G, et al. A machine learning algorithm can optimize the day of trigger to improve in vitro fertilization outcomes. *Fertility and Sterility.* 2021;116(5):1227-1235. [doi:10.1016/j.fertnstert.2021.06.018](https://doi.org/10.1016/j.fertnstert.2021.06.018)
8. Fanton M, Baker VL, Loewke KE. SELECTION OF OPTIMAL GONADOTROPIN DOSE USING MACHINE LEARNING MAY BE ASSOCIATED WITH IMPROVED OUTCOMES AND REDUCED UTILIZATION OF FSH. *Fertility and Sterility.* 2022;118(4):e80-e81. [doi:10.1016/j.fertnstert.2022.08.246](https://doi.org/10.1016/j.fertnstert.2022.08.246)
9. Fanton M, Nutting V, Rothman A, et al. An interpretable machine learning model for individualized gonadotrophin starting dose selection during ovarian stimulation. *Reproductive BioMedicine Online.* 2022;45(6):1152-1159. [doi:10.1016/j.rbmo.2022.07.010](https://doi.org/10.1016/j.rbmo.2022.07.010)
10. Correa N, Cerquides J, Arcos JL, Vassena R. Supporting first FSH dosage for ovarian stimulation with machine learning. *Reprod Biomed Online.* Published online February 15, 2022:1472-6483. [doi:10.1101/2022.02.10.22270790](https://doi.org/10.1101/2022.02.10.22270790)
11. Curchoe CL, Farias AFS, Mendizabal-Ruiz G, Chavez-Badiola A. Evaluating predictive models in reproductive medicine. *Fertility and Sterility.* 2020;114(5):921-926.
12. La Marca A, Sunkara SK. Individualization of controlled ovarian stimulation in IVF using ovarian reserve markers: from theory to practice. *Human Reproduction Update.* 2013;20(1):124-140. [doi:10.1093/humupd/dmt037](https://doi.org/10.1093/humupd/dmt037)
13. Nisal A, Diwekar UM, Hobeika E. Personalized medicine for GnRH antagonist protocol in in vitro fertilization procedure using modeling and optimal control. *Computers and Chemical Engineering.* 2021;156,107554.
14. Nisal A, Diwekar U, Bhalerao V. Personalized medicine for in vitro fertilization procedure using modeling and optimal control. *J Theor Biol.* 2020;487:110105. [doi:10.1016/j.jtbi.2019.110105](https://doi.org/10.1016/j.jtbi.2019.110105)
15. Oudendijk JF, Yarde F, Eijkemans MJC, Broekmans FJM, Broer SL. The poor responder in IVF: is the prognosis always poor? A systematic review. *Human Reproduction Update.* 2011;18(1):1-11. [doi:10.1093/humupd/dmr037](https://doi.org/10.1093/humupd/dmr037)
16. Practice Committee of the American Society for Reproductive Medicine. Comparison of pregnancy rates for poor responders using IVF with mild ovarian stimulation versus conventional IVF: a guideline. *Fertility and Sterility.* 2018;109(6):993-999. [doi:10.1016/j.fertnstert.2018.03.019](https://doi.org/10.1016/j.fertnstert.2018.03.019)
17. Li C, He YC, Xu JJ, et al. Perinatal outcomes of neonates born from different endometrial preparation protocols after frozen embryo transfer: a retrospective cohort study. *BMC Pregnancy Childbirth.* 2021;21(1). [doi:10.1186/s12884-021-03791-9](https://doi.org/10.1186/s12884-021-03791-9)
18. Mai Z, Liu M, Pan P, et al. Comparison of Cumulative Live Birth Rate Between Aged PCOS Women and Controls in IVF/ICSI Cycles. *Front Endocrinol.* 2021;12(724333). [doi:10.3389/fendo.2021.724333](https://doi.org/10.3389/fendo.2021.724333)
19. IVF-Life-co.uk, reproductivefertility.com, ivfoptions.com, web.hksh.com, fertilitycenteroforegon.com, drtamarahunter.com.au.