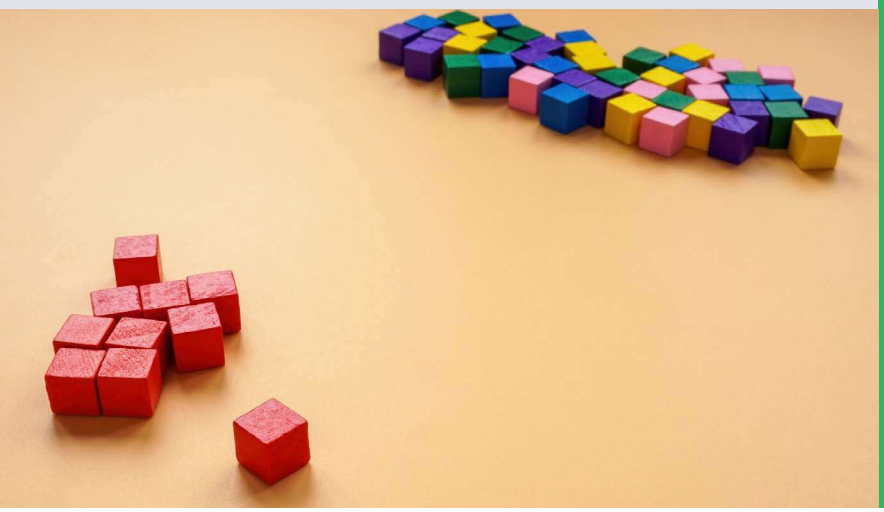
The bias is out of the bag: IVF culture dish well number influences embryo selection decision-making and implantation outcome

Oral Presentation by **Prof. Daniel Seidman** at the 2022 European Society of Human Reproduction and Embryology (ESHRE) Annual Meeting



Introduction

Substantial intra-and inter-observer variability in embryo selection, as well as differences in embryo quality assessment procedures and laboratory environment, may affect IVF success. The reasons for this are manifold: unstandardized evaluation times, differences in laboratory environment, and the use of categorical (not continuous) embryo grading schemes for relative embryo ranking may contribute. To combat this, many IVF clinics have adopted stringent guidelines to standardize laboratory workflows and control for human errors. Nevertheless, the inherent variability and biases associated with manual embryo evaluation is unavoidable. In this study, we emphasize how cognitive tendencies are inherent to the embryo selection process. We therefore demonstrate the urgent need for algorithms that streamline IVF laboratory workflows, reduce human bias, and increase objective standardization.

The AIVF Hypothesis

We hypothesize that a selection bias exists against embryos placed in higher-numbered wells inside the multi-well IVF culture dish. This selection bias alone may impact implantation outcomes.

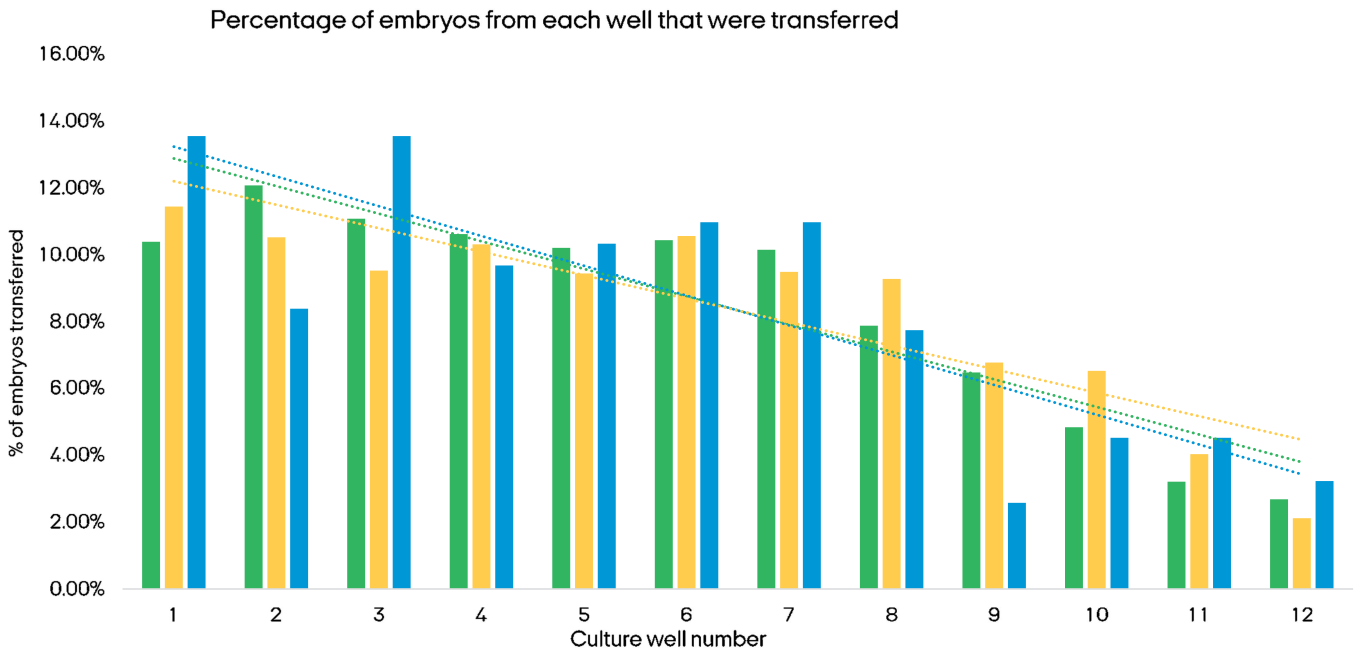
Study Design

This study used a retrospective embryo dataset from three highly experienced fertility clinics (Spain, USA, and Israel). A total of 4,275 Fresh IVF treatment cycles were included in this study. For each treatment cycle, embryo quality grades, corresponding embryo well number, Day-5 selection and implantation outcomes were documented. All cycles were performed using the EmbryoSlide® 12-well culture dish and Embryoscope™ Time-Lapse System. All three datasets were analyzed separately and also combined.

For each dataset, three analyses were conducted: (1) the total number of selected embryos were calculated for each corresponding well number; (2) the proportion of implanted embryos, relative to the total number of selected embryos, were quantified to calculate the "success rate" for each well number; (3) the distribution of top-quality embryos amongst all the wells were quantified and compared. Results were normalized by the total number of transferred embryos and implantation rates reported for each clinic.

Results

A negative trend was found between well number, ranging from 1-12, and number of embryos selected for transfer. This trend was significant ($p<0.05$) and occurred independently in each dataset.

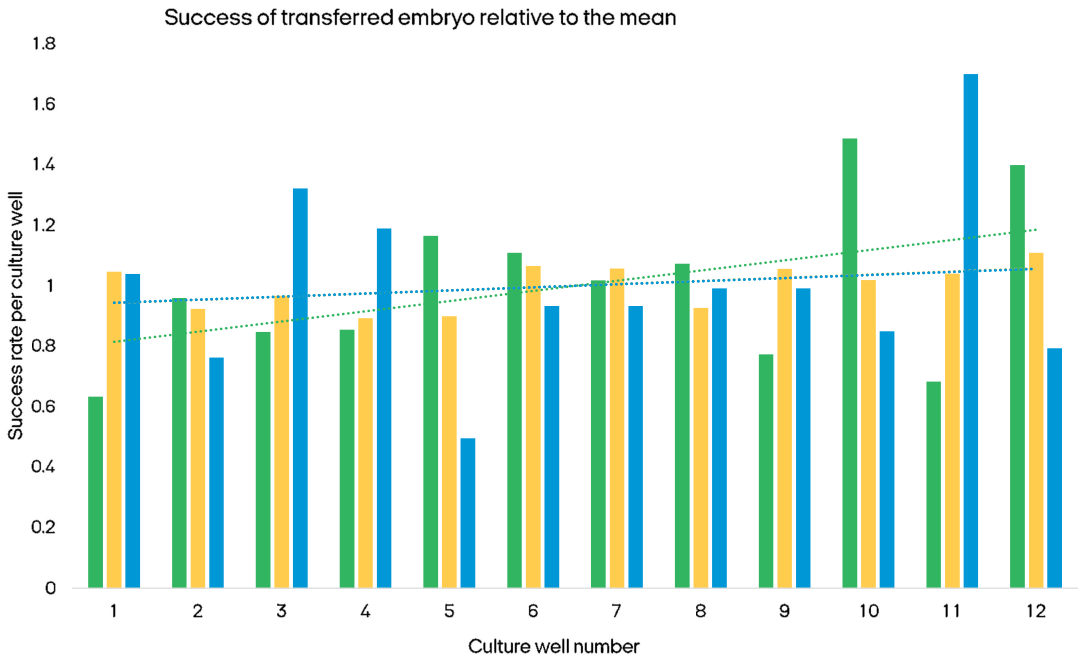


A negative trend was found between well number (ranging from 1-12) and number of embryos selected for transfer. This trend was significant ($p<0.05$) and occurred independently in each dataset.

Odds ratios (OR) for the relation between selecting embryos for transfer from wells 1-5, and from 8-12		
Clinic A	Clinic B	Clinic C
2.16	1.78	2.45

To rationalize these results, two alternative hypotheses were tested: (1) top-quality embryos are clustered in lower-numbered wells during culture; (2) enhanced embryo quality and conditions are found in lower-numbered wells, which should manifest in higher rates of implantation.

Results for each clinic showed an even distribution of top-quality embryos between wells (within 2 standard deviations from the mean; not significant).



Embryos from higher wells had similar chances of implanting as embryos transferred from lower numbered wells.

Odds ratios [OR] for the relation between 'success rate' of transferred embryos from wells 1-5, and from 8-12		
Clinic A	Clinic B	Clinic C
1.19	1.06	1.08

We conclude that embryologists may tend to select the first acceptable embryo for transfer. Embryos from higher numbered wells were highly likely to implant, since they overcame this bias when equitably evaluated and selected for transfer.

Study Takeaways

- Embryologists may tend to select the first acceptable embryo for transfer.
- Embryos from higher-numbered wells are highly likely to implant, since they overcame this bias when equitably evaluated and selected for transfer.
- This study demonstrates that inherent human bias affects decision making in the IVF lab.

Conclusions

This study emphasizes the inherent human error that exists inside IVF clinics. AI-powered systems that reduce human bias and improve objective decision-making inside the IVF laboratory, even if they are not inherently better than embryologists, would improve implantation rates. Future studies should be directed toward the validation of AI based technologies that can accomplish this.

AIVF™

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