

# There is significant unexplained inter-cycle variation in ovarian performance during IVF treatment

Thanos Papathanasiou, Nausheen Mawal, Phil Snell. Bourn Hall Clinic, UK

## Summary:

**Q:** Does amending the stimulation dose in consecutive IVF cycles produce the expected response?

**A:** More than 1 in 2 women experience unexpected ovarian response and about 1 in 8 women experience paradoxical ovarian response during subsequent IVF treatment.

## Introduction

The aim of this study was to investigate the extent of inter-cycle variation in the oocyte yield between successive treatments, which cannot be explained by modifications in the drug regime.

## Materials

Data from consecutive patients who had undergone at least two oocyte retrievals within the same year were retrospectively analysed. Poor responders were excluded.

We measured the frequency of two outcomes that support the presence of unexplained inter-cycle variation:

### Unexpected ovarian response

- Increased stimulation dose with no increase in egg yield
- Lower stimulation dose with no reduction in egg yield
- Same stimulation dose with increased/reduced egg yield

### Paradoxical ovarian response

- Higher stimulation dose with reduced egg yield
- Lower stimulation dose with increased egg yield

Multivariable analysis was performed for both outcomes, adjusting for the operator, changes in drug protocol, the woman's age and the egg yield during the 1st retrieval.

Sensitivity analysis was performed for detecting a 30% and a 10% difference in the egg yield between treatments. For example, for a yield of 10 eggs in the initial cycle, a 30% difference would correspond to  $\leq 7$  or  $\geq 13$  eggs during repeat IVF. Likewise, a 10% difference would correspond to  $\leq 9$  or  $\geq 11$  eggs during repeat treatment.

	Increase dose (n=1085)	Same dose (n=1302)	Decrease dose (n=165)
Higher egg yield	41% (441)	25% (321)	17% (28)
No change	43% (467)	48% (634)	40% (66)
Lower egg yield	16% (177)	27% (347)	43% (71)

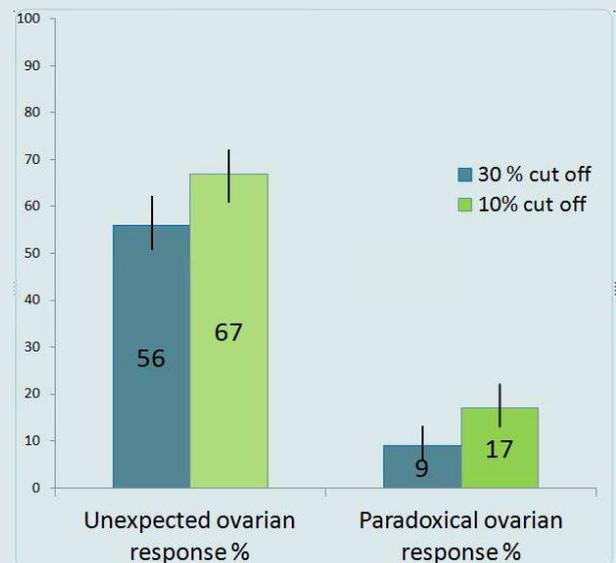
**Table 1**

**Dose refinement and observed changes in egg yield (30% cut-off, desired response in green)**

## Results

A total of 2552 patients were included. Table 1 depicts changes in the egg yield according to changes in dosing during subsequent stimulation.

After adjusting for confounders, 56%-67% of women experienced unexpected ovarian response (for detecting a 30% and 10% difference in egg yield respectively). In addition, 9%-17% of women experienced paradoxical ovarian response (Figure 1).



## Conclusion

As this original study suggests, the ovaries exhibit substantial intrinsic inter-cycle variability (and unpredictability) with regard to their potential to recruit oocytes. This should be considered when counselling couples who require repeated IVF treatments.

## Strengths of the study

- Large sample size
- Data adjusted for protocol type and operator
- Patients acted as their own controls

