Embryologists display low levels of agreement in predicting fertilization and blastocyst development success from a set of mature oocyte images, highlighting the need for a standard oocyte assessment tool

Natalie Mercuri[1], Sergey Corsac[2], Jullin Fjeldstad[1], Nadia Siddique[1], Isabel Puerta Vega[1], Dan Nayot[3]
[1]Clinical Embryology and Scientific Operations, Future Fertility, Toronto, Canada [2]Data Science, Future Fertility, Toronto, Canada [3]Medical, Future Fertility, Toronto, Canada

OBJECTIVE

To investigate the effects of a lacking standard oocyte assessment by evaluating the base level of agreement (LOA) between experienced embryologists in their predictions of fertilization and blastocyst development of metaphase II (MII) oocytes

METHODS

Study design

- 17 experienced embryologists
  - 3 clinics; average experience: 8.5 ± 4.3 years
- Prospectively evaluated 300 single-plane, 2-D, high-quality images of fresh denuded MII oocytes
- Blinded to true outcomes, predicted whether each oocyte would fertilize + develop into a blastocyst based on their best judgement
- Exclusion criteria was severe male factor infertility

Statistical analysis

- *Fleiss' kappa (Fκ):* inter-observer LOA between all embryologists (κ=0 is no agreement, κ=1 is perfect agreement)
- *Cohen's kappa coefficient (Cκ):* LOA between 2 embryologists on predicting successful fertilization + blastocyst development (κ≤0.4 is poor agreement, 0.4<κ≤0.75 is fair/good agreement, κ>0.75 is excellent agreement)

MAIN RESULTS

- When assessing the 300 MII oocyte images, the Embryologists had an average accuracy of:
  - 0.77, specificity of 0.41, and sensitivity of 0.86 in predicting Fertilization
  - 0.53, specificity of 0.35, and sensitivity of 0.78 in predicting Blastocyst development
- Greater lab experience was very weakly correlated with lower Fertilization + higher Blastocyst prediction accuracies (PCC= -0.13 and 0.12, respectively)
- Between all embryologists: Fair/moderate LOA on predicting Fertilization outcomes (Fκ=0.41) + Fair LOA on predicting Blastocyst development (Fκ=0.36)
- Each of the 17 embryologists was compared with one another to calculate the Cκ → a total of 136 LOA comparisons
  - 60 (44%) were of poor, 72 (53%) were of fair/good, and 4 (3%) were of excellent agreement for Fertilization predictions
  - 77 (57%) were of poor, 59 (43%) were of fair/good, and 0 were of excellent agreement for Blastocyst development predictions
- Similar results were found when assessing embryologists by clinic location

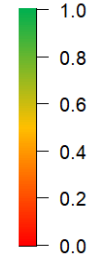
Embryologist

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q
A	1.00	0.44	0.43	0.37	0.46	0.52	0.36	0.49	0.52	0.51	0.56	0.57	0.42	0.53	0.48	0.42	0.34
B	0.44	1.00	0.47	0.38	0.32	0.37	0.19	0.27	0.48	0.49	0.37	0.30	0.20	0.33	0.27	0.27	0.47
C	0.43	0.47	1.00	0.35	0.36	0.45	0.24	0.33	0.46	0.43	0.36	0.37	0.28	0.45	0.35	0.36	0.44
D	0.37	0.38	0.35	1.00	0.36	0.55	0.38	0.36	0.45	0.54	0.56	0.40	0.44	0.39	0.45	0.44	0.30
E	0.46	0.32	0.36	0.36	1.00	0.49	0.34	0.45	0.43	0.42	0.45	0.44	0.37	0.43	0.45	0.39	0.28
F	0.52	0.37	0.45	0.55	0.49	1.00	0.56	0.36	0.49	0.40	0.64	0.66	0.60	0.63	0.67	0.62	0.27
G	0.36	0.19	0.24	0.38	0.34	0.56	1.00	0.34	0.30	0.23	0.53	0.56	0.80	0.47	0.80	0.72	0.15
H	0.49	0.27	0.33	0.36	0.45	0.36	0.34	1.00	0.39	0.33	0.40	0.48	0.34	0.44	0.38	0.37	0.30
I	0.52	0.48	0.46	0.45	0.43	0.49	0.30	0.39	1.00	0.45	0.44	0.43	0.32	0.45	0.39	0.36	0.42
J	0.51	0.49	0.43	0.54	0.42	0.40	0.23	0.33	0.45	1.00	0.41	0.37	0.25	0.35	0.33	0.33	0.41
K	0.56	0.37	0.36	0.56	0.45	0.64	0.53	0.40	0.44	0.41	1.00	0.58	0.61	0.53	0.69	0.64	0.27
L	0.57	0.30	0.37	0.40	0.44	0.66	0.56	0.48	0.43	0.37	0.58	1.00	0.60	0.55	0.64	0.56	0.27
M	0.42	0.20	0.28	0.44	0.37	0.60	0.80	0.34	0.32	0.25	0.61	0.60	1.00	0.47	0.78	0.71	0.15
N	0.53	0.33	0.45	0.39	0.43	0.63	0.47	0.44	0.45	0.35	0.53	0.55	0.47	1.00	0.62	0.54	0.25
O	0.48	0.27	0.35	0.45	0.45	0.67	0.80	0.38	0.39	0.33	0.69	0.64	0.78	0.62	1.00	0.84	0.19
P	0.42	0.27	0.36	0.44	0.39	0.62	0.72	0.37	0.36	0.33	0.64	0.56	0.71	0.54	0.84	1.00	0.19
Q	0.34	0.47	0.44	0.30	0.28	0.27	0.15	0.30	0.42	0.41	0.27	0.27	0.15	0.25	0.19	0.19	1.00

Cohen's kappa for Fertilization Prediction – Level of Agreement between Two Raters

Embryologist

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q
A	1.00	0.43	0.30	0.43	0.37	0.53	0.31	0.38	0.40	0.45	0.53	0.49	0.39	0.55	0.35	0.48	0.37
B	0.43	1.00	0.40	0.44	0.34	0.27	0.24	0.30	0.43	0.54	0.41	0.37	0.31	0.42	0.24	0.42	0.42
C	0.30	0.40	1.00	0.25	0.23	0.22	0.12	0.20	0.38	0.35	0.23	0.27	0.19	0.30	0.14	0.29	0.37
D	0.43	0.44	0.25	1.00	0.45	0.33	0.22	0.26	0.36	0.51	0.41	0.37	0.27	0.37	0.23	0.41	0.45
E	0.37	0.34	0.23	0.45	1.00	0.34	0.20	0.30	0.30	0.41	0.35	0.31	0.24	0.34	0.24	0.35	0.37
F	0.53	0.27	0.22	0.33	0.34	1.00	0.52	0.35	0.28	0.36	0.57	0.49	0.53	0.51	0.57	0.52	0.26
G	0.31	0.24	0.12	0.22	0.20	0.52	1.00	0.33	0.20	0.24	0.48	0.42	0.58	0.41	0.74	0.45	0.17
H	0.38	0.30	0.20	0.26	0.30	0.35	0.33	1.00	0.40	0.32	0.42	0.52	0.40	0.43	0.32	0.44	0.29
I	0.40	0.43	0.38	0.36	0.30	0.28	0.20	0.40	1.00	0.39	0.35	0.36	0.26	0.41	0.20	0.30	0.36
J	0.45	0.54	0.35	0.51	0.41	0.36	0.24	0.32	0.39	1.00	0.46	0.39	0.34	0.38	0.26	0.43	0.44
K	0.53	0.41	0.23	0.41	0.35	0.57	0.48	0.42	0.35	0.46	1.00	0.55	0.53	0.50	0.54	0.50	0.30
L	0.49	0.37	0.27	0.37	0.31	0.49	0.42	0.52	0.36	0.39	0.55	1.00	0.55	0.52	0.43	0.54	0.28
M	0.39	0.31	0.19	0.27	0.24	0.53	0.58	0.40	0.26	0.34	0.53	0.55	1.00	0.43	0.66	0.57	0.17
N	0.55	0.42	0.30	0.37	0.34	0.51	0.41	0.43	0.41	0.38	0.50	0.52	0.43	1.00	0.39	0.43	0.36
O	0.35	0.24	0.14	0.23	0.24	0.57	0.74	0.32	0.20	0.26	0.54	0.43	0.66	0.39	1.00	0.53	0.16
P	0.48	0.42	0.29	0.41	0.35	0.52	0.45	0.44	0.30	0.43	0.50	0.54	0.57	0.43	0.53	1.00	0.29
Q	0.37	0.42	0.37	0.45	0.37	0.26	0.17	0.29	0.36	0.44	0.30	0.28	0.17	0.36	0.16	0.29	1.00



Cohen's Kappa for Blastocyst Prediction – Level of Agreement between Two Raters

CONCLUSION

High inter-observer variability was observed among embryologists' opinions on the same MII oocytes with low LOA in predicting fertilization or blastocyst development - even within the same clinic, where standardized lab practices can be expected.

Results emphasize the need for a standard oocyte assessment tool to better evaluate oocyte quality

 Corresponding author: nataliem@futurefertility.com