Sharing data and best practice within a group of clinics

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Contents

- CARE Fertility Group of 9 clinics
  - Structure and scientific function
- Examples and approaches to add-ons
  - Time lapse and the power of big data
  - PGT-A – Best practice process
  - Culture media e.g. Embryogen
- Monitoring results and KPI

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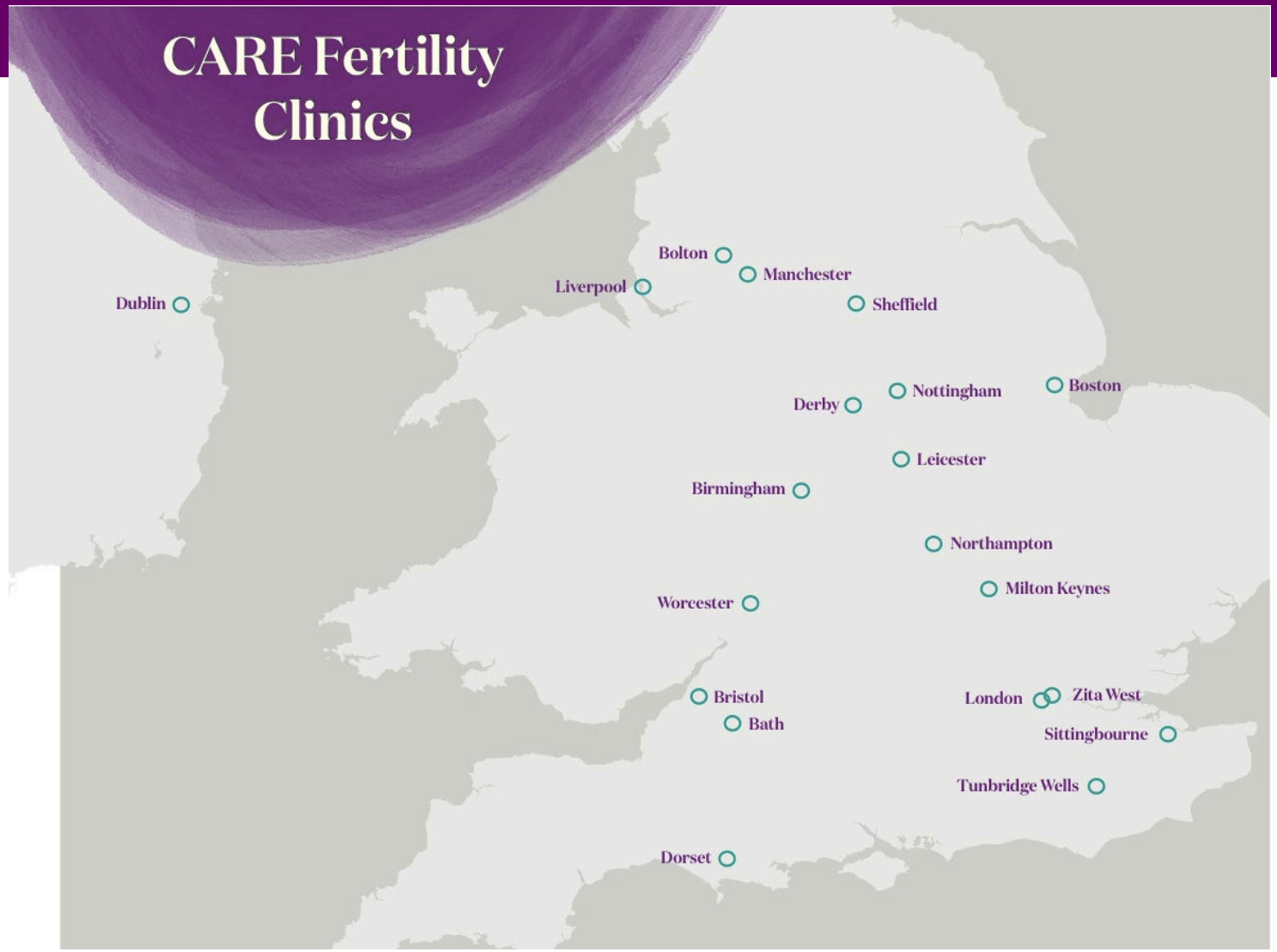

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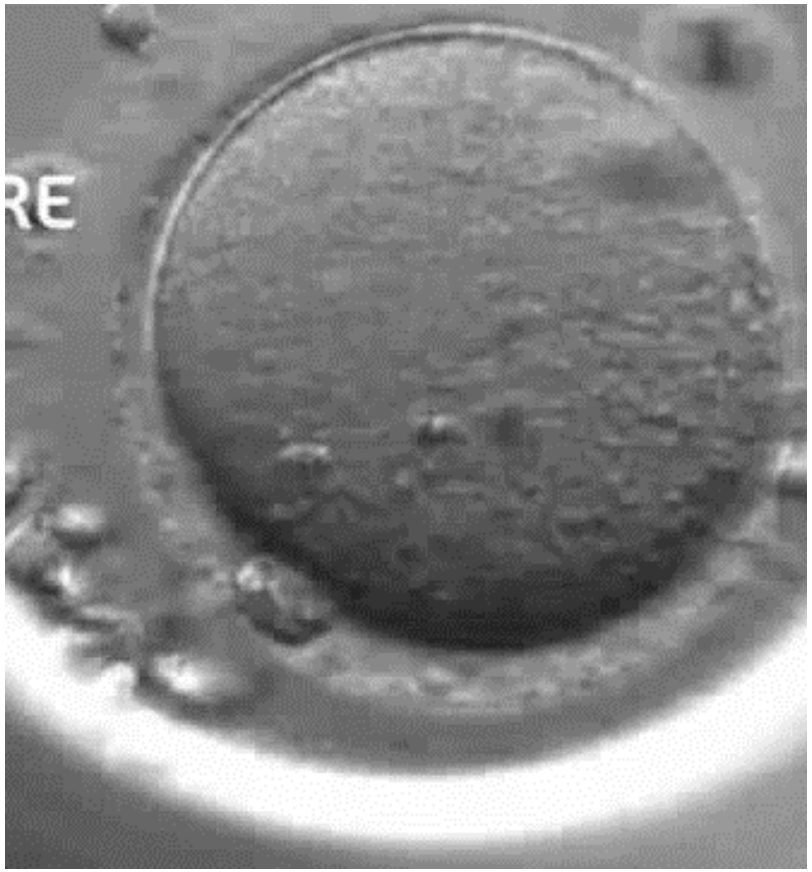
Suggested benefits of time lapse imaging?

a. Quality and **quantity** of information
b. Consistency & objectivity
c. Clinical outcome improvements
   Some dispute!
d. Undisturbed, more stable, embryo culture



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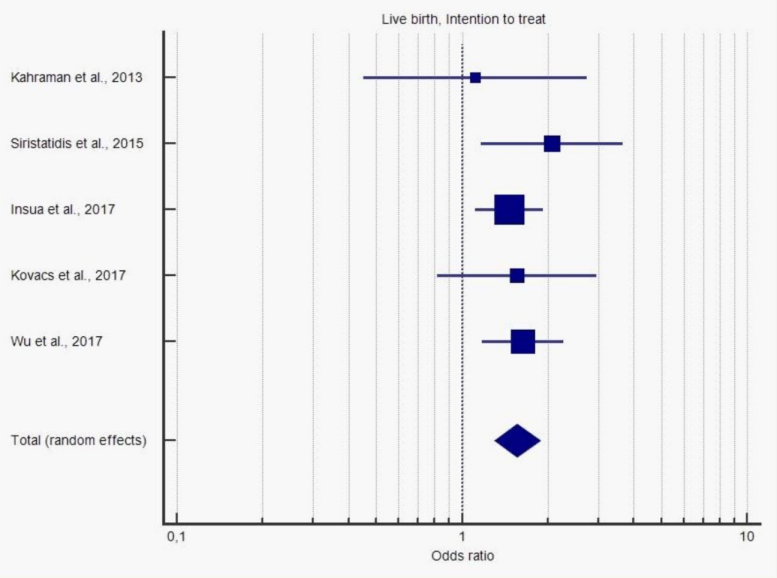
Time lapse RCTs increasing

'Use of Time-lapse information to evaluate embryos improves outcomes'.



Some debate on quality of data within and design of these studies

How much weight can be given to first hand experience and huge data?

Favors control ← → Favors time-lapse

(OR: 1.56; CI = 1.30–1.88; *P* < 0.001; based on 1945 cases, intention-to-treat analysis;

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Pribenszky, C., Nilselid, A-M, Montag, M.,RBM online, March 2018 Volume 36, Issue 3, Pages 290–292

Power of numbers – CARE example

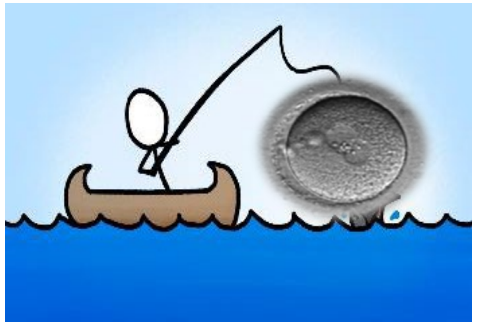
Accuracy in fertilization assessment.

- At18h post ICSI we will miss 1 in 25 without it!
- Large analysis of CARE wide data

These would be scored as 'unfertilized' 0PN without time lapse

Where PNf was completed by 18 hpi, implantation rate was 35.2% (n=142)
50 babies!

Within the whole CARE reto-analysis cohort **6402** embryos were transferred, that have a known clinical outcome (+/-)



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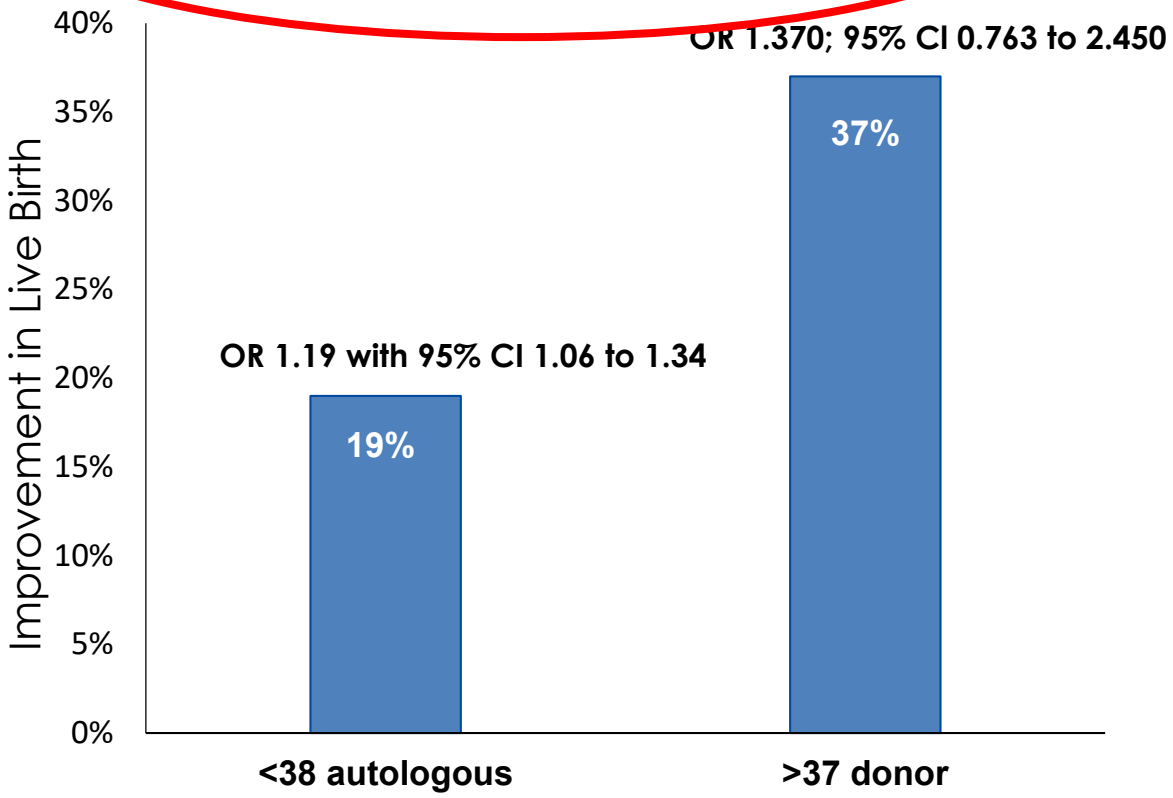
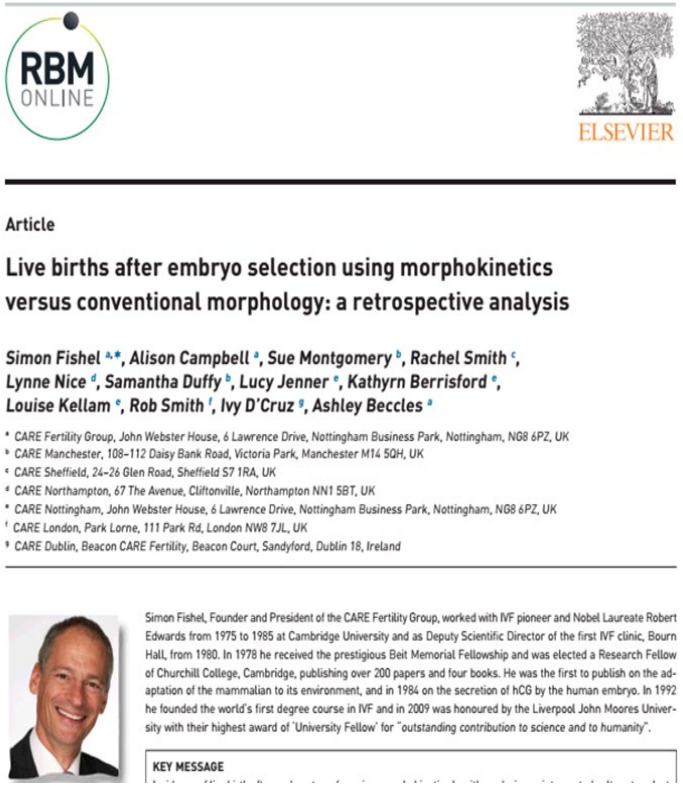
Power of numbers – CARE example
relative improvements in birth rates

Retrospective analysis of 23,762 cycles highlights





RBM ONLINE

ELSEVIER

Article

Live births after embryo selection using morphokinetics versus conventional morphology: a retrospective analysis

Simon Fishel [a,], Alison Campbell [a], Sue Montgomery [b], Rachel Smith [c], Lynne Nice [d], Samantha Duffy [b], Lucy Jenner [e], Kathyrn Berrisford [e], Louise Kellam [e], Rob Smith [f], Ivy D'Cruz [g], Ashley Beccles [a]*

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Simon Fishel, Founder and President of the CARE Fertility Group, worked with IVF pioneer and Nobel Laureate Robert Edwards from 1975 to 1985 at Cambridge University and as Deputy Scientific Director of the first IVF clinic, Bourn Hall, from 1980. In 1978 he received the prestigious Beit Memorial Fellowship and was elected a Research Fellow of Churchill College, Cambridge, publishing over 200 papers and four books. He was the first to publish on the adaptation of the mammalian to its environment, and in 1984 on the secretion of hCG by the human embryo. In 1992 he founded the world's first degree course in IVF and in 2009 was honoured by the Liverpool John Moores University with their highest award of 'University Fellow' for "outstanding contribution to science and to humanity".

KEY MESSAGE

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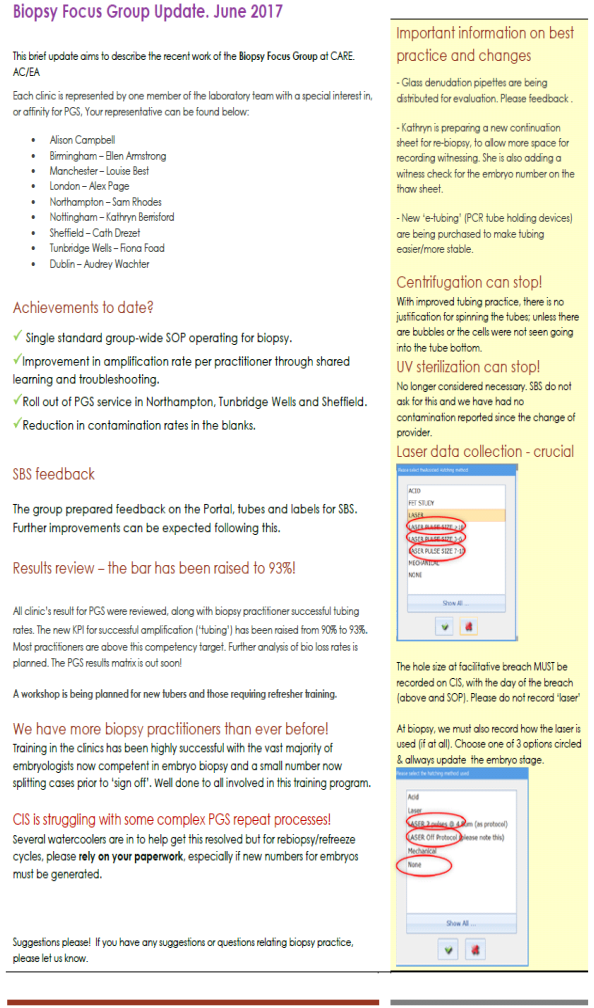
Fishel et al., RBM Online 2017

CARE Fertility:
Data collection and scrutiny

e.g. PGT-A

- Single lab SOP
- Focus Group
- Aspirational KPI
- ‘Broadshoulders’ comparisons
- Group and local results matrices
- Communication of changes and progress



Biopsy Focus Group Update. June 2017

This brief update aims to describe the recent work of the **Biopsy Focus Group** at CARE. AC/EA

Each clinic is represented by one member of the laboratory team with a special interest in, or affinity for PGS, Your representative can be found below:

- Alison Campbell
- Birmingham – Ellen Armstrong
- Manchester – Louise Best
- London – Alex Page
- Northampton – Sam Rhodes
- Nottingham – Kathryn Berrisford
- Sheffield – Cath Drezet
- Tunbridge Wells – Fiona Foad
- Dublin – Audrey Wachter

Achievements to date?

✓ Single standard group-wide SOP operating for biopsy.

✓ Improvement in amplification rate per practitioner through shared learning and troubleshooting.

✓ Roll out of PGS service in Northampton, Tunbridge Wells and Sheffield.

✓ Reduction in contamination rates in the blanks.

SBS feedback

The group prepared feedback on the Portal, tubes and labels for SBS. Further improvements can be expected following this.

Results review – the bar has been raised to 93%!

All clinic's result for PGS were reviewed, along with biopsy practitioner successful tubing rates. The new KPI for successful amplification ('tubing') has been raised from 90% to 93%. Most practitioners are above this competency target. Further analysis of bio loss rates is planned. The PGS results matrix is out soon!

A workshop is being planned for new tubers and those requiring refresher training.

We have more biopsy practitioners than ever before!

Training in the clinics has been highly successful with the vast majority of embryologists now competent in embryo biopsy and a small number now splitting cases prior to 'sign off'. Well done to all involved in this training program.

CIS is struggling with some complex PGS repeat processes!

Several watercoolers are in to help get this resolved but for rebiopsy/refreeze cycles, please **rely on your paperwork**, especially if new numbers for embryos must be generated.

Suggestions please! If you have any suggestions or questions relating biopsy practice, please let us know.

Important information on best practice and changes

- Glass denudation pipettes are being distributed for evaluation. Please feedback .

- Kathryn is preparing a new continuation sheet for re-biopsy, to allow more space for recording witnessing. She is also adding a witness check for the embryo number on the thaw sheet.

- New 'e-tubing' (PCR tube holding devices) are being purchased to make tubing easier/more stable.

Centrifugation can stop!

With improved tubing practice, there is no justification for spinning the tubes; unless there are bubbles or the cells were not seen going into the tube bottom.

UV sterilization can stop!

No longer considered necessary. SBS do not ask for this and we have had no contamination reported since the change of provider.

Laser data collection - crucial

The hole size at facilitative breach MUST be recorded on CIS, with the day of the breach (above and SOP). Please do not record 'laser'

At biopsy, we must also record how the laser is used (if at all). Choose one of 3 options circled & allways update the embryo stage.

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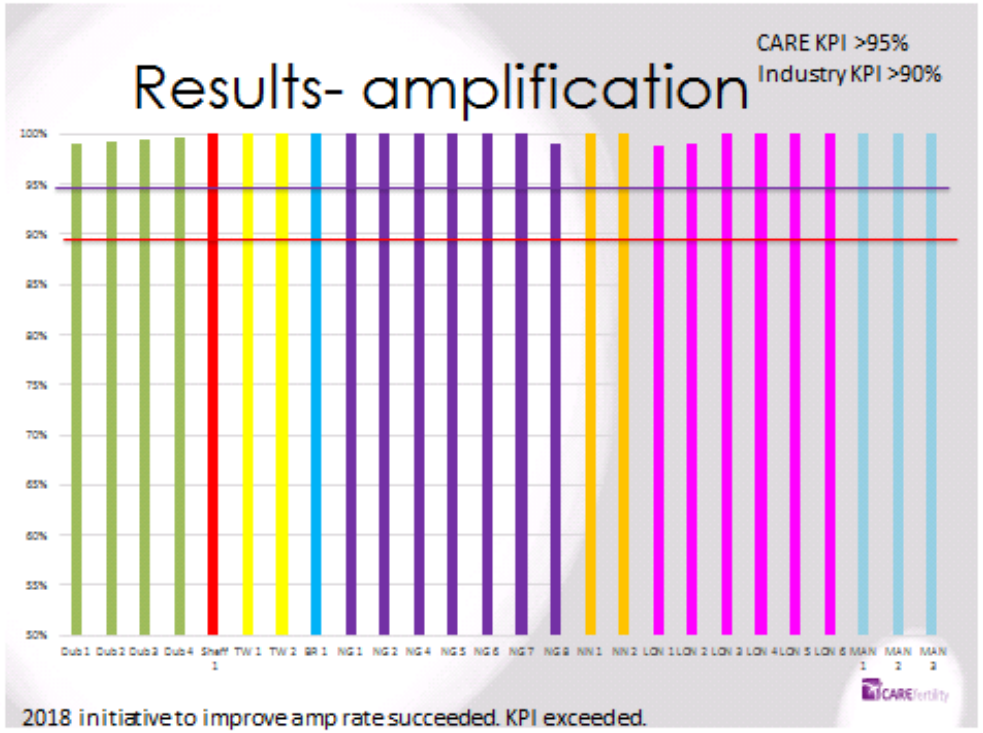
Quality assurance and analytics



- 27 biopsy practitioners
- Compared against each other
- Shared best practice
- Continuous improvement
- Aspirational targets

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‘Broadshoulders’culture

From 01/12/2013 To 30/11/2014

Embryology Broad Shoulders Report Summary

	By Egg Recovery (ICSI & IVF)		By Hyaluronidase (ICSI only)		By Sperm Prep + Conc (Ivf ONLY - Insem Concentration)		Thaw Statistics By Freeze		Thaw Statistics By Thaw		ICSI Practitioner Data			By Embryo Transfer (ICSI & IVF)		By IVF Fertilisation Check			
Embryologist	% 2PN	% CP/ET	% Mature	% CP/ET	% 2PN	% CP/ET	% Survival	% CP/ET	% Survival	% CP/ET	% DEG	% 2PN	% CP/ET	% Bio/ET	% CP/ET	% 2PN	% DEG	% Other	% CP/ET
1	57.64%	42.11%	78.44%	60.98%							7.72%	66.88%	42.86%	53.13%	40.63%				
2	67.39%	40.79%	79.41%	49.15%			81.08%	54.29%	76.32%	36.00%	5.36%	72.16%	52.24%	60.00%	43.64%				
3	62.56%	29.89%	81.13%	52.38%	79.01%	38.24%	81.82%	45.76%	88.14%	43.90%	5.02%	77.12%	59.78%	54.87%	43.36%	67.76%	0.00%	27.96%	44.74%
4	70.77%	48.18%	82.76%	38.78%	66.85%	65.00%								63.89%	55.56%				
5	71.51%	53.27%							69.39%	27.27%	4.42%	78.23%	37.84%	49.15%	40.68%	66.53%	0.00%	29.39%	58.06%
6	68.05%	54.29%					82.26%	37.14%			3.70%	69.14%	37.50%	56.41%	52.56%				
7	65.81%	39.47%	73.98%	44.05%	67.07%	45.45%	79.10%	45.24%	89.80%	53.19%	6.48%	75.84%	42.86%	54.17%	43.23%	63.13%	0.25%	32.83%	57.14%
8	63.68%	63.64%	84.36%	51.28%			79.01%	41.46%			6.54%	74.95%	42.86%	55.95%	46.43%				
9	69.47%	41.67%												54.76%	47.62%				
10	69.94%	48.53%	78.99%	41.67%	75.89%	48.89%	72.04%	33.33%	78.67%	41.67%	3.93%	72.48%	48.65%	58.96%	48.58%	62.21%	0.67%	29.43%	35.48%
11	68.41%	50.77%	80.68%	55.56%	66.47%	45.45%	80.77%	38.89%	71.83%	46.51%	4.83%	67.94%	52.73%	57.35%	51.47%	58.55%	2.63%	34.21%	52.38%
Total	**68.12%**	**45.67%**	**79.33%**	**43.91%**	**45.88%**	**30.36%**	**70.36%**	**37.34%**	**67.76%**	**37.11%**	**5.40%**	**73.34%**	**47.85%**	**53.13%**	**40.63%**	**63.87%**	**0.50%**	**30.30%**	**50.43%**

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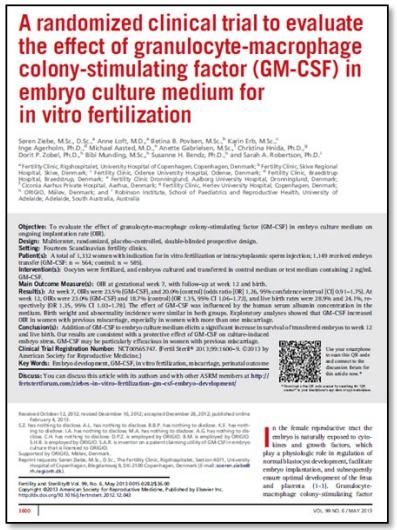
Culture media add ons: What is best practice? Why & how do CARE offer them? e.g. EmbryoGen

- ✓ Scientific rationale considered:
  - Cytokines play a key role in reproduction
  - Up-regulation occurs during pregnancy
  - Low levels associated with miscarriage and implantation failure



A randomized clinical trial to evaluate the effect of granulocyte-macrophage colony-stimulating factor (GM-CSF) in embryo culture medium for in vitro fertilization

- ✓ There is supporting data (RCT 2013)
- ✓ Careful patient selection and justification
- ✓ Transparent patient information
- ✓ Group-wide pooling of results and experiences
- ✓ Regular review of CARE data
- ✓ Continued awareness of the literature and communication with other users

Same approach for other media add-ons such as EmbryoGlue, AOA and Sper mobil. If we don't replicate published improvements, we do not offer or promote.

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Conclusions

- Decisions regarding treatment add-ons can be challenging for patients & clinics
- Robust data/RCTs not always available
- Patients often ask for them
- Transparent information is vital
- Clinics sharing experience and combining data can help build an evidence base to support decision making and progress.

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Thank you for listening

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