

Benefits of Time-Lapse Technology: Beyond Embryo Selection

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Apple Computer Design Evolution

with Base Prices



Apple I – \$667
1976



Apple II – \$1298
1977



Apple III – \$7800
1980



Apple Lisa – \$9995
1983



Macintosh – \$1995
1984



Apple IIGS – \$999
1986



Macintosh II – \$5500
1987



PowerMac 5200 – \$1900
1995



iMac G3 – \$1299
1998



iMac G4 – \$1299
2002

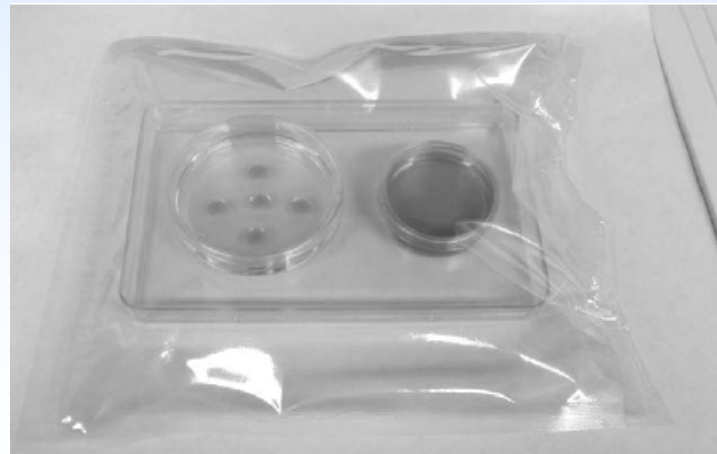


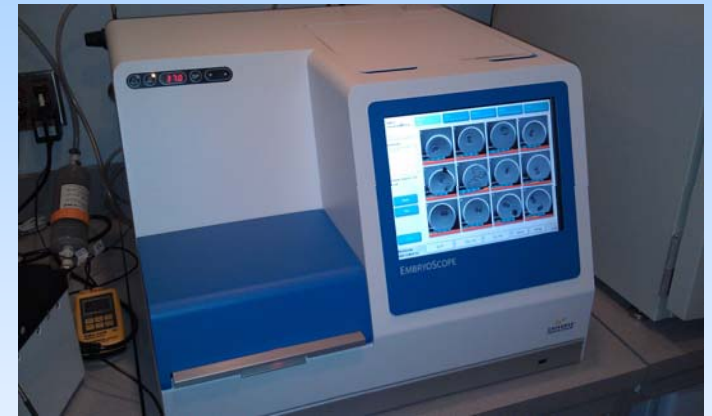
iMac G5 – \$1299
2004



iMac Unibody – \$1199
2009







1978

1988

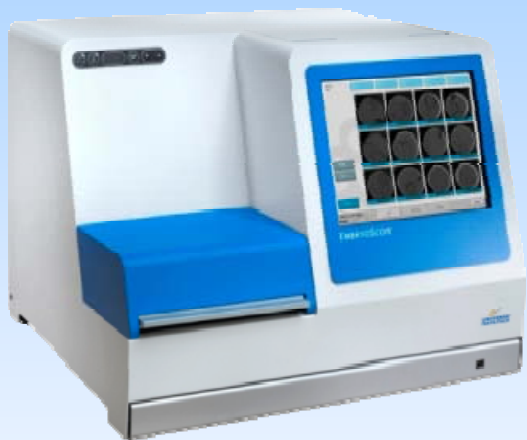
1998

2008

2011



The Era of Time-Lapse



Why Time-Lapse?



17 hrs



25 hrs



42 hrs



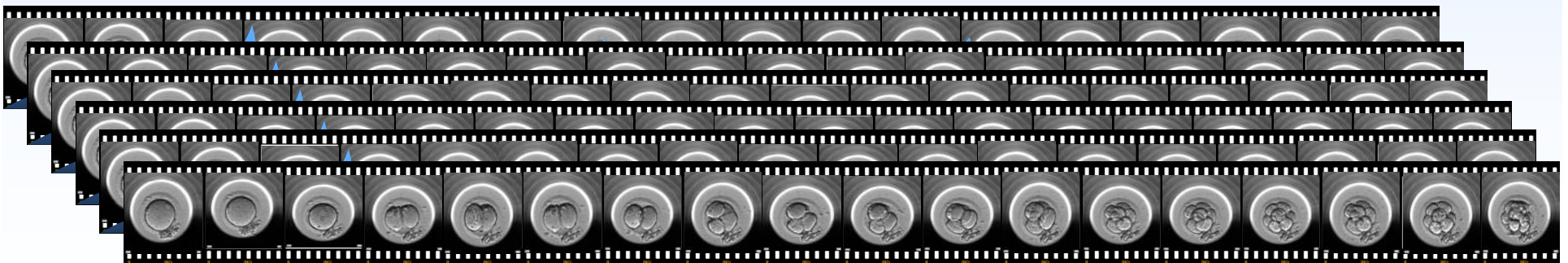
66 hrs

*More
Observations
Better Selection*



*Less Disturbance
Better
Development*

>1500 images over 3 days per embryo





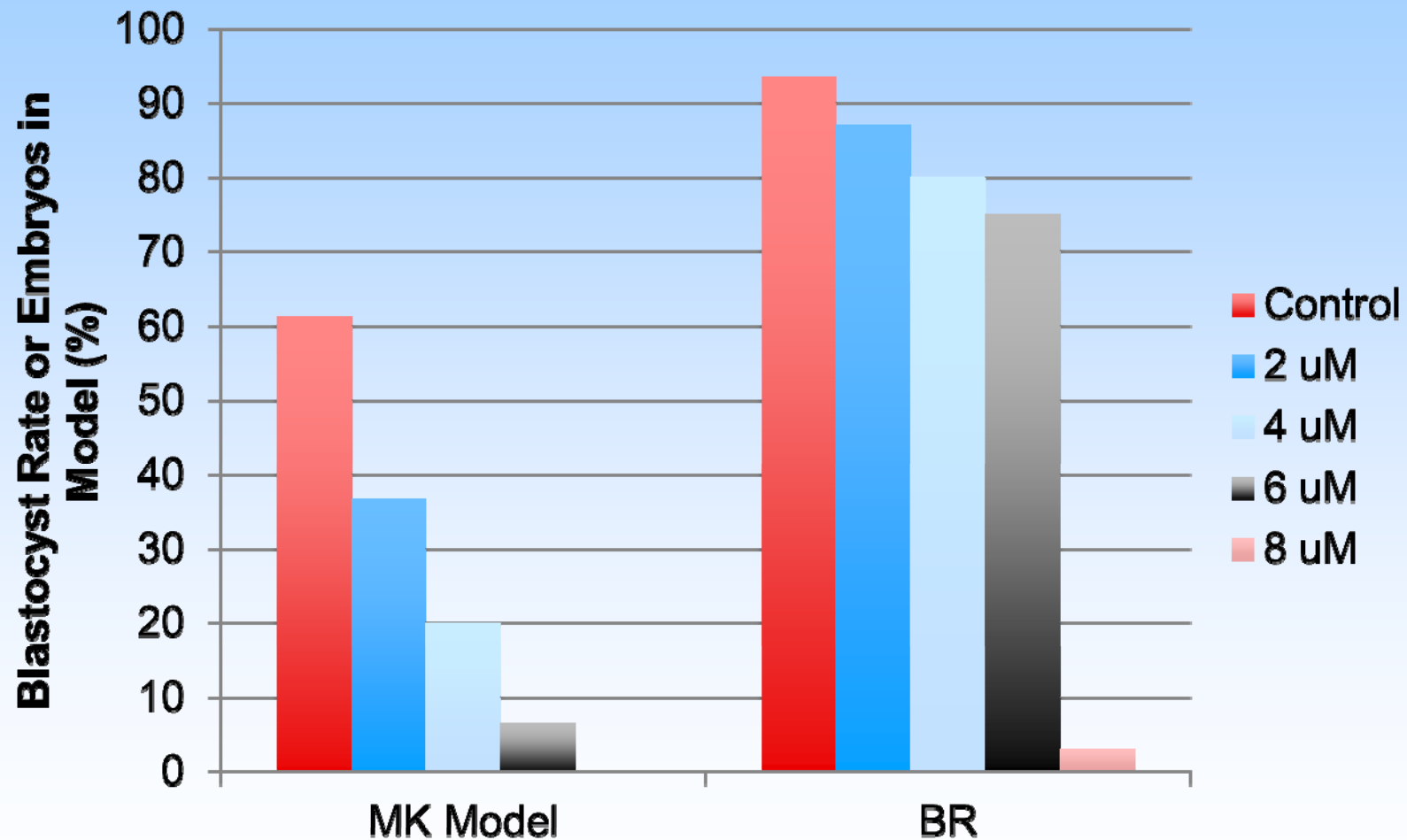
Pros

- **Stable environment**
- **Improved embryo selection**
- **New knowledge!**
- **Improved quality management**
- **Standardization across labs**
- **Better QC Assay**

Cons

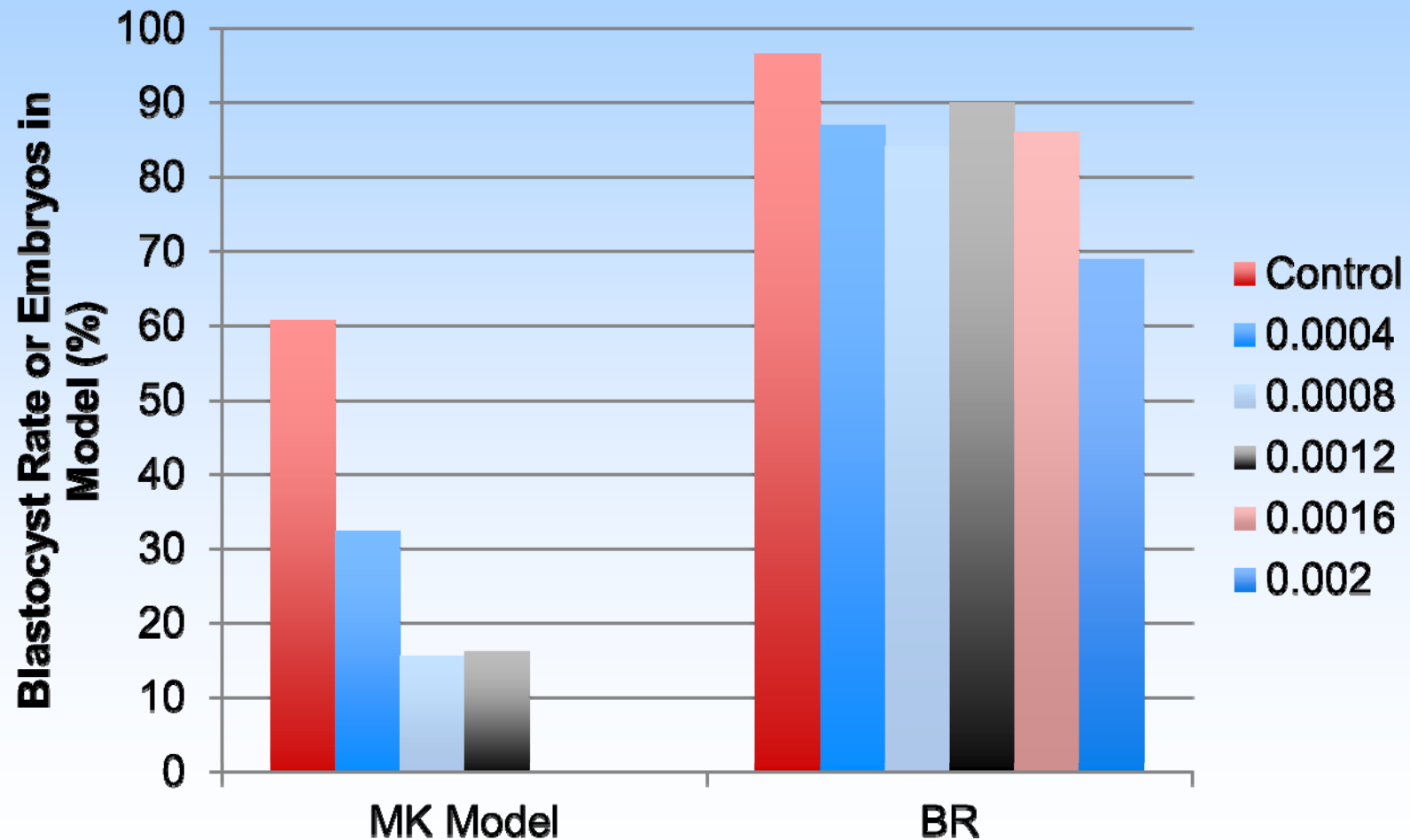
- **Price**
- **6 slides/patient limit**
- **Time intensive annotations**

Time-lapse As A Supply QC Tool Peroxide in Oil



Time-lapse As A Supply QC Tool

Triton X-100 in Media



Why Time-Lapse?



17 hrs



25 hrs



42 hrs



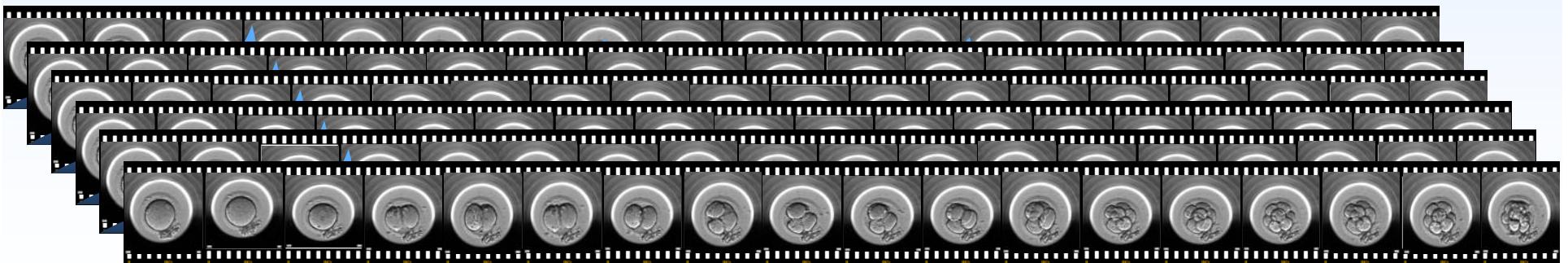
66 hrs

Standardization

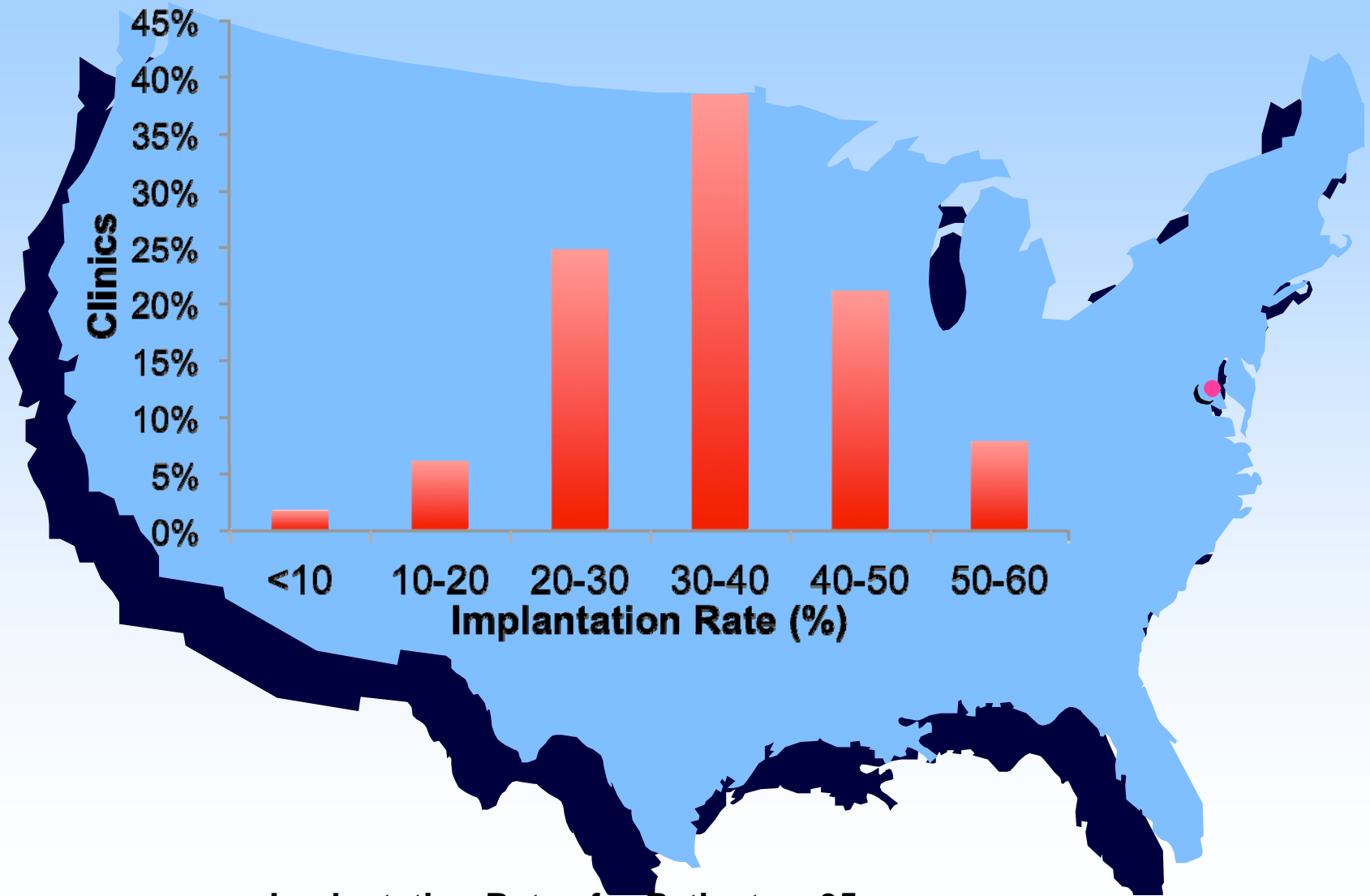


KPIs
Key Performance
Indicators

>1500 images over 3 days per embryo

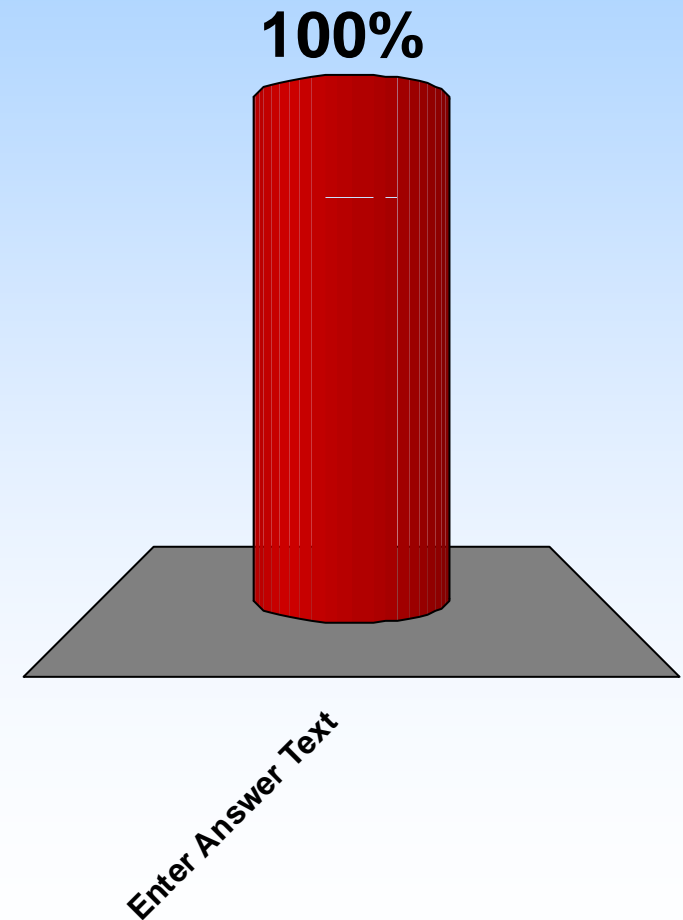


How Do You Know You Have a Quality Laboratory?



Assessing Your Laboratory's Quality: Which variable do you consider best?

- A. Fertilization Rate
- B. Cleavage Rate
- C. Good Quality Blastocyst Rate
- D. Implantation Rate
- E. Clinical PR
- F. Delivery Rate

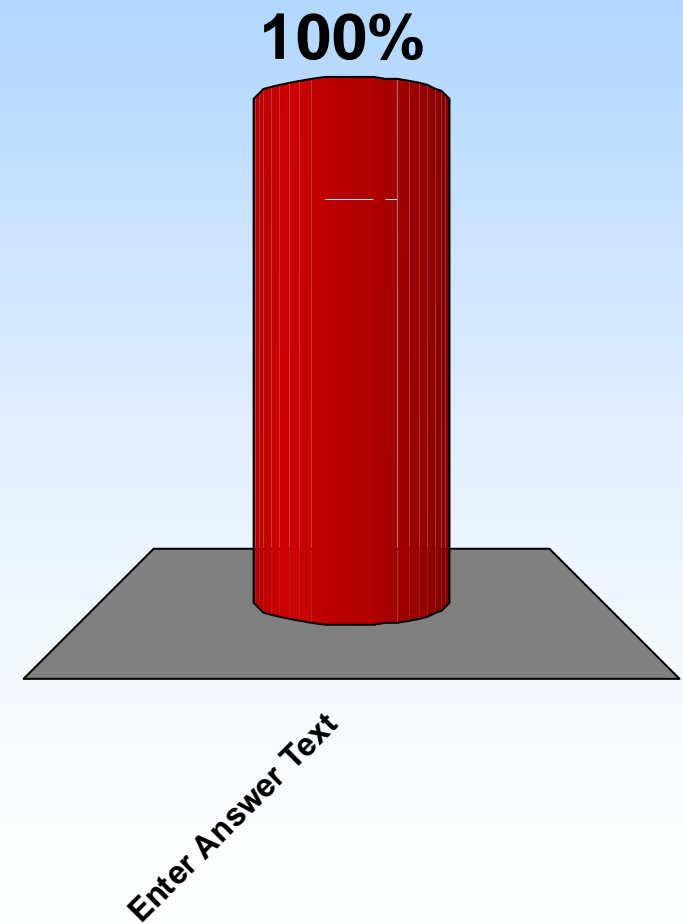


Key Performance Indicators (KPI)

- **How do we, as IVF laboratories, know we are good?**
- **Quality management program should utilize metrics that are both sensitive and easy to obtain.**

In your quality management plan, which KPI best reflects your lab's quality?

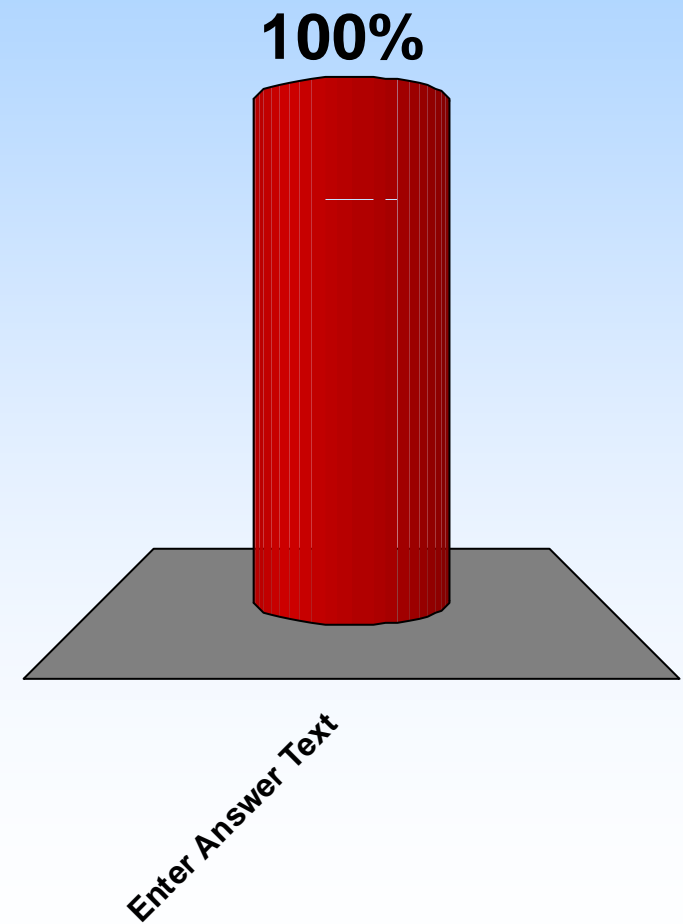
- A. Fertilization Rate**
- B. Early Cleavage Rate**
- C. Day 2 Cell Number**
- D. Day 3 Cell Number**
- E. Good Quality Blastocyst Rate**



Have you ever used early cleavage for embryo selection?

A. Yes

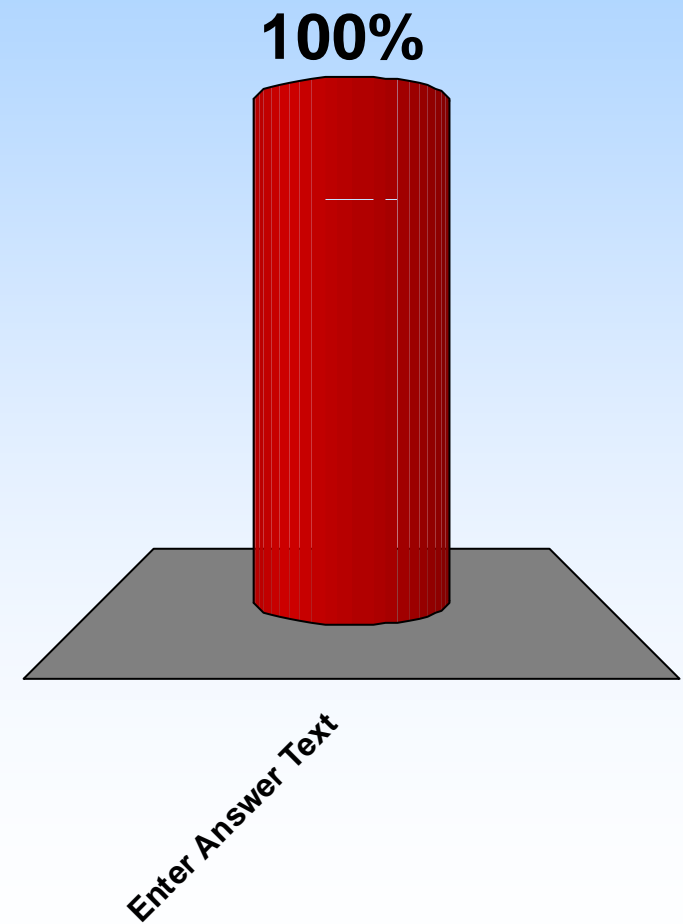
B. No



Do you currently use early cleavage for embryo selection?

A. Yes

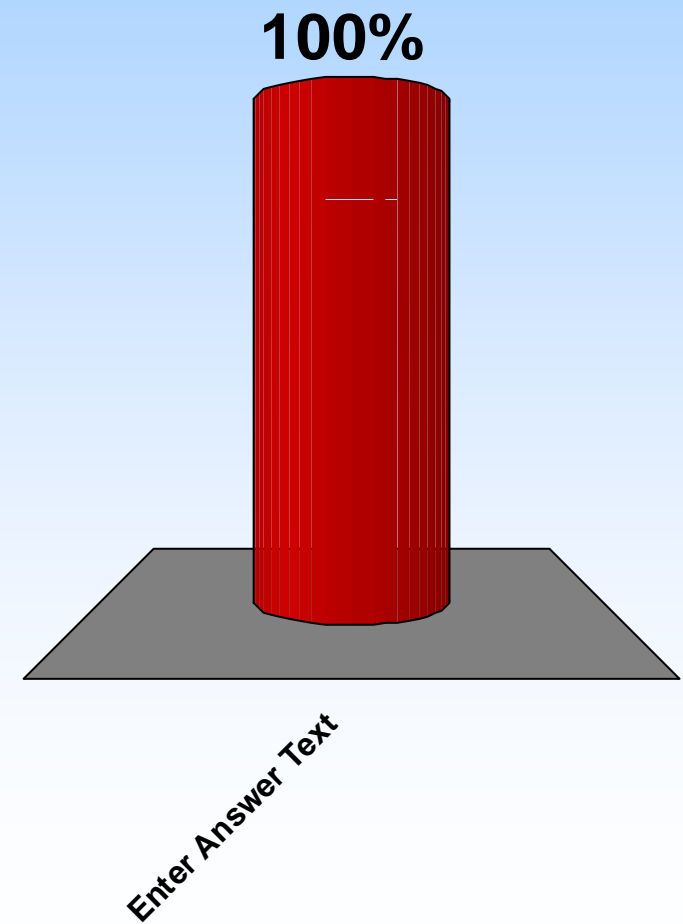
B. No



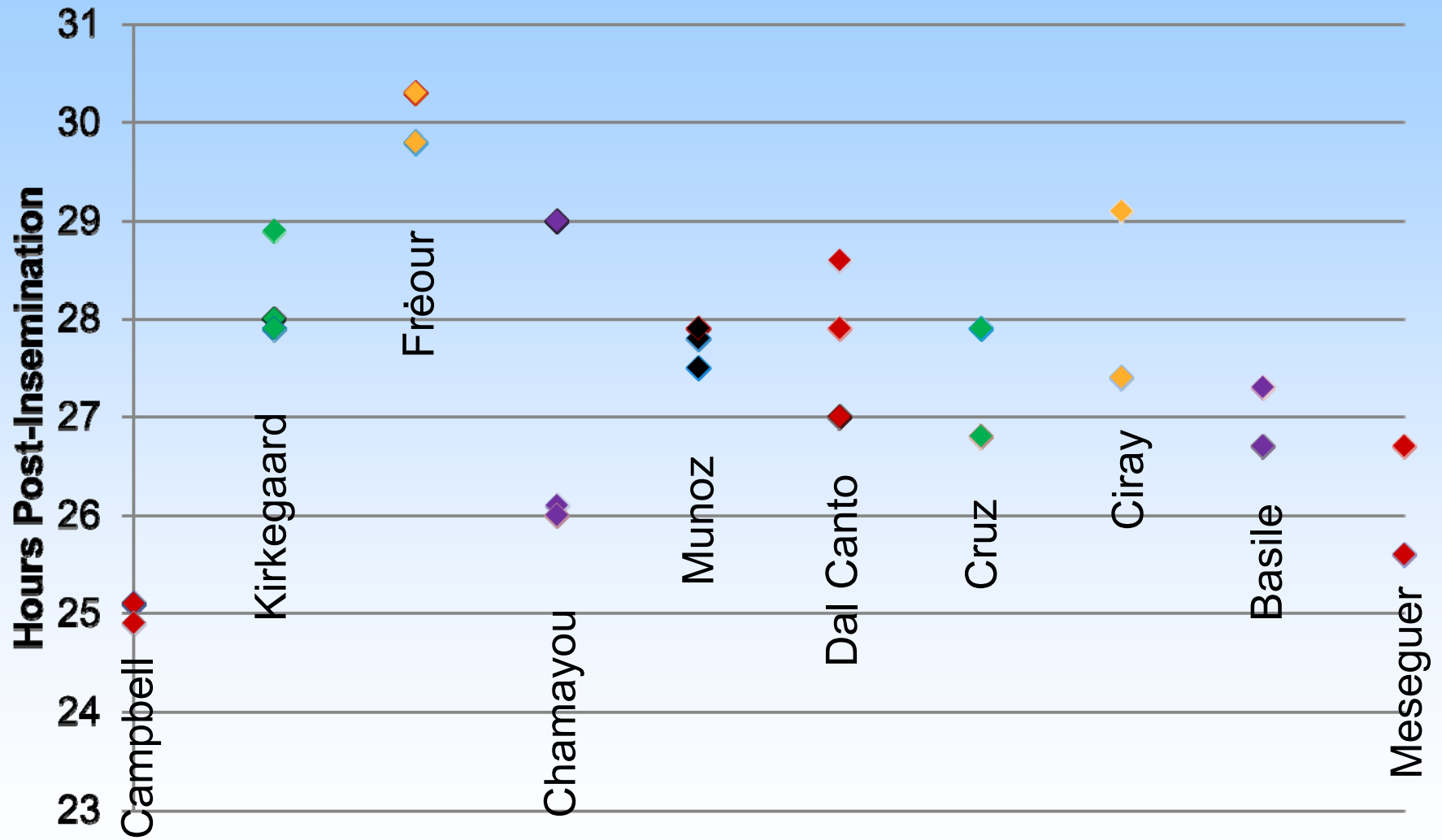
Do you track early cleavage data in your quality management plan?

A. Yes

B. No

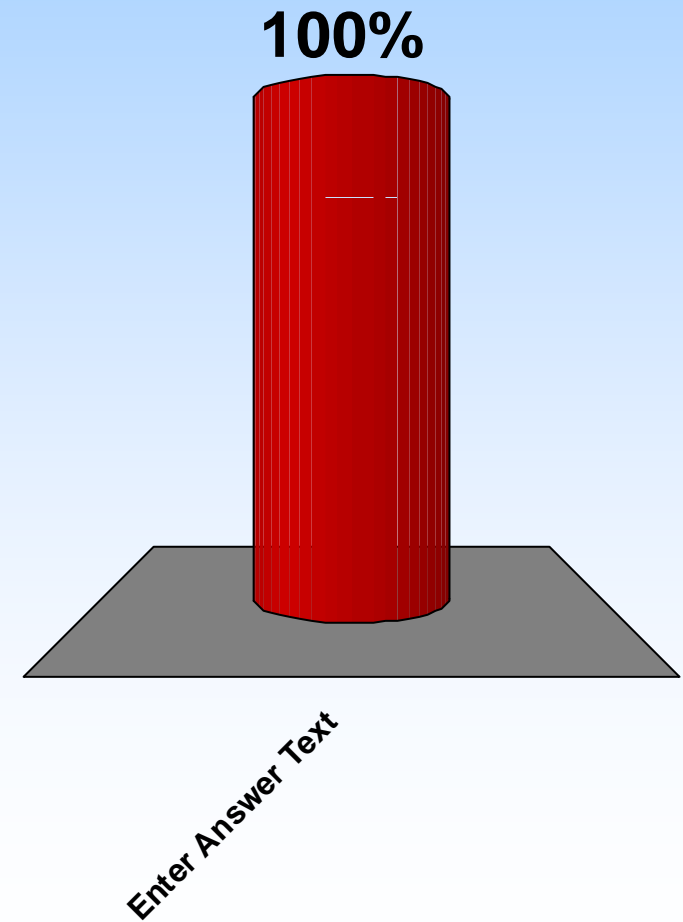


Timing of First Cleavage



Which describes your laboratory's QM Plan?

- A. We only track clinical outcomes**
- B. Includes fert rate, cleavage rate and blastocyst rate**
- C. A and B plus d2 and/or d3 embryo quality**
- D. We only use embryo utilization rate (good quality blastocysts)**



Mayo Clinic IVF Clinical Practice

OR setting
Shared air

2PN freeze
Keep 2 embryos in culture

Use D2 Cell Number
as Benchmark



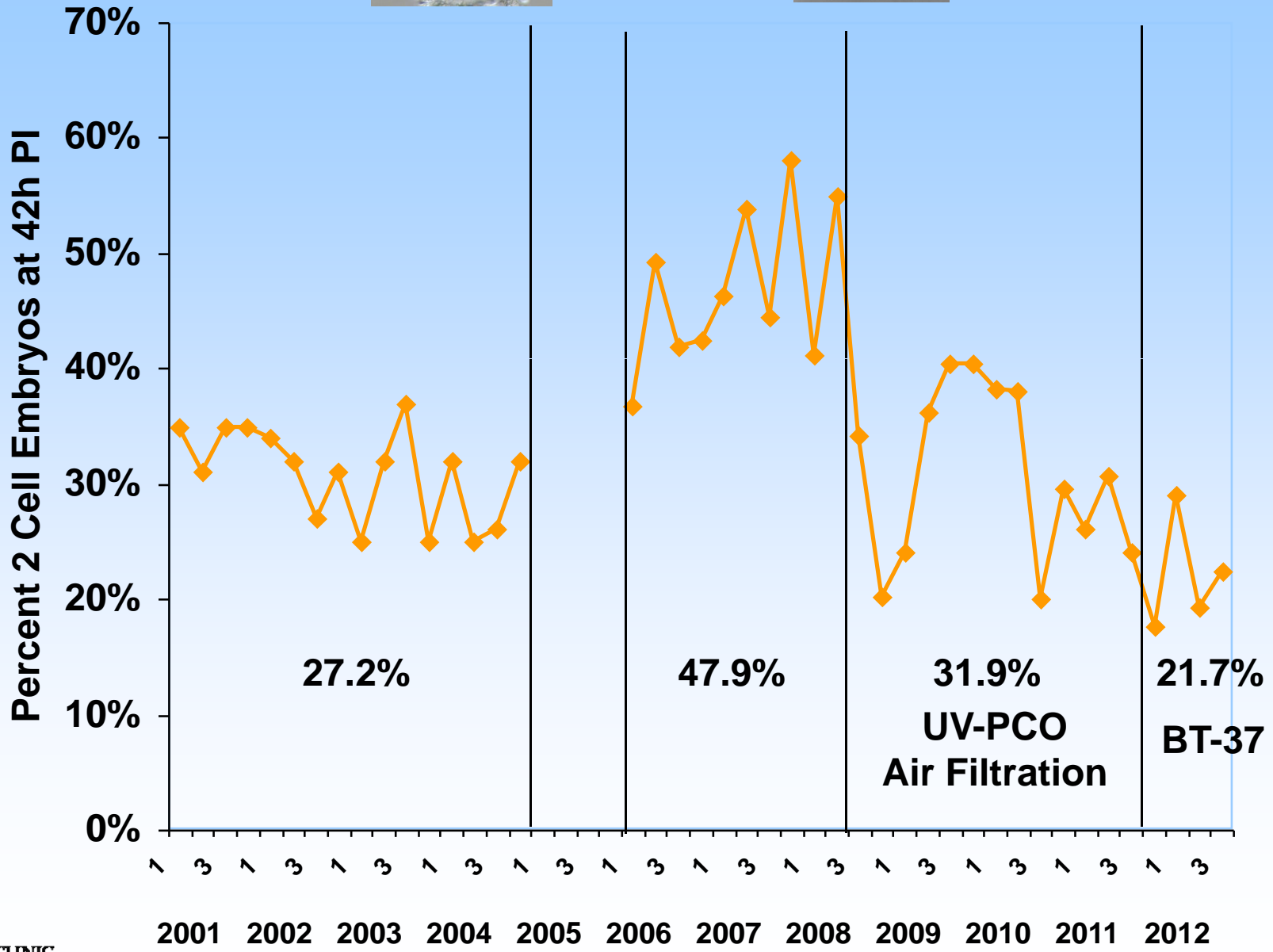
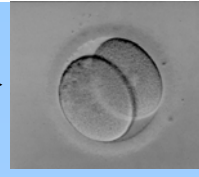
Benchmark
30% < 4 Cell
42h Post-Insemination



Benchmark
50% 4-Cell
42h Post-Insemination



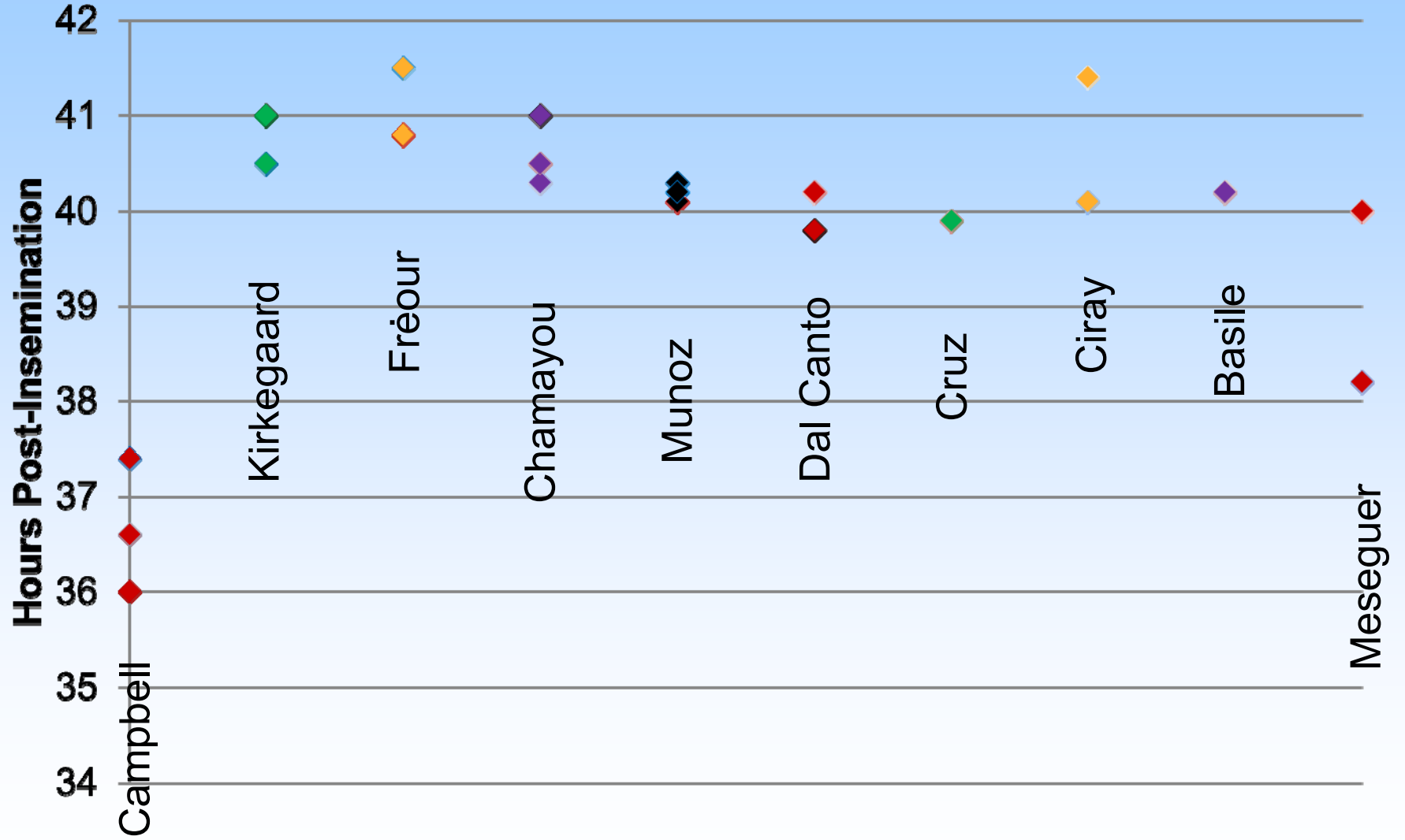
42h



Problems with EC or 4 Cell Rate as KPI

- **Time post insemination varies depending on day and workload**
- **Timing of events may depend on method of insemination**
- **The optimal time to assess varies by laboratory**

Timing of 4 Cell Stage



Time-Lapse and Quality Management

- **Detect changes in laboratory environment**
 - **Air quality**
- **Track lot number variation**
 - **Culture media**
 - **Protein**
 - **Oil**
 - **Plasticware**
- **Track practice drift**
 - **Stimulations**
 - **Laboratory technique**

Time-Lapse Quality Management in Action

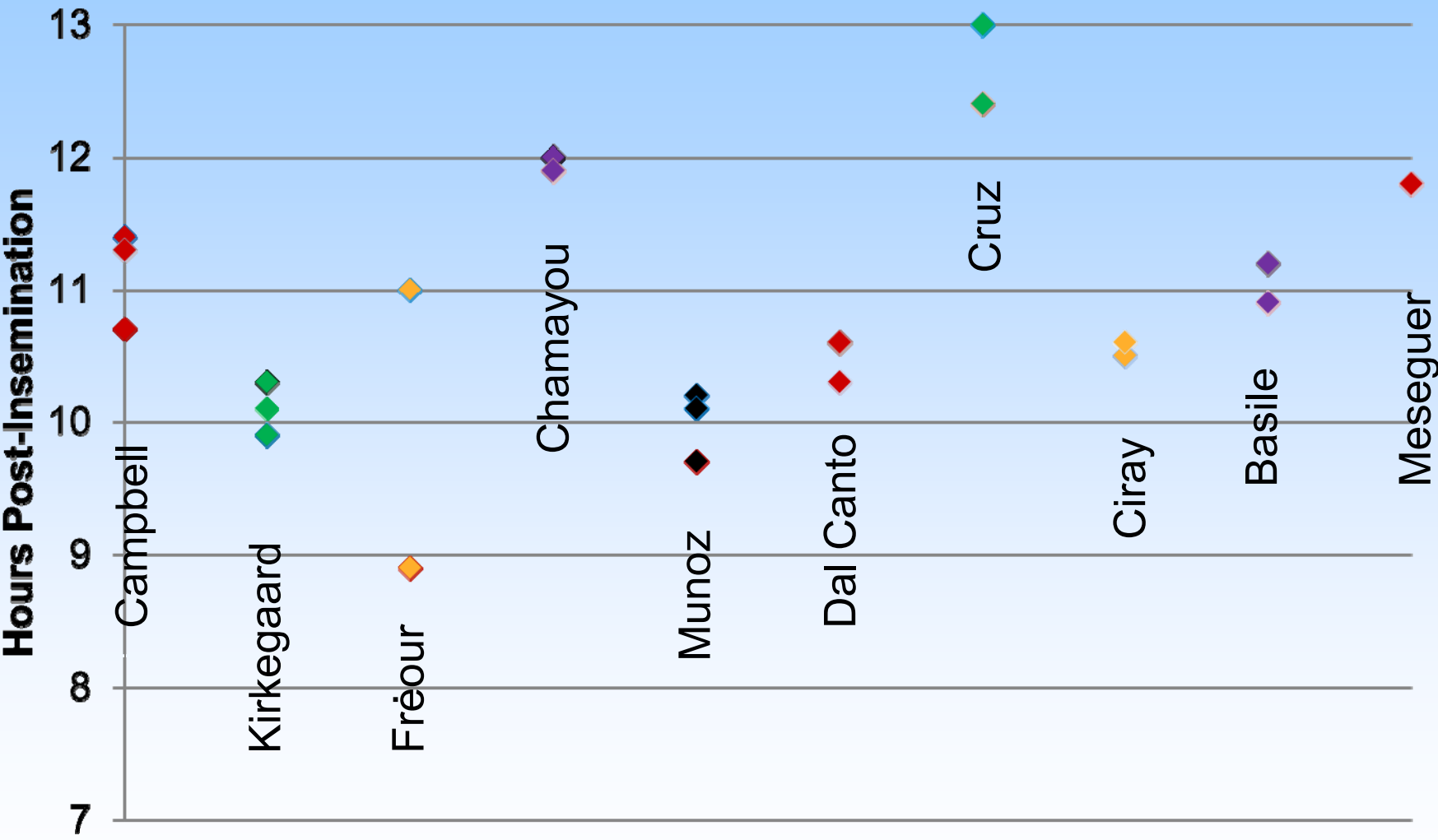
Lot variation in
protein quality

- **Decreased pregnancy rates – delayed response**
- **Shift in 4 Cell rate on D2**
- **No difference in blastocyst conversion rate**
- **Significant impact on length of cell cycles**

KPIs by Quarter - 2012

	Q1	Q2	Q3	Q4
<4 Cell (%)	31	22	21.7	21.9
4 Cell (%)	20.7	65.9	52.2	46.9
>4 Cell (%)	48.3	12.2	26.1	31.2
Cells	4.4	3.7	4	4.2
t2	28.8	28.2	26.9	27.1
t3	35.9	39.4	37.1	37.9
t5	45.8	50.7	48.7	49.8
cc2 (hours as 2 cell)	7	11.2	10.3	10.8
cc3 (hours as 4 cell)	6.6	10.4	9.9	8.8

Duration of 2 Cell Stage



Benefits of Standardization

- **Develop robust KPIs to compare among laboratories**
- **Know that embryo development is per industry standards**
- **Improved quality control of supplies**
 - **Compare data among laboratories?**

Time-Lapse Summary

Technology is
changing clinical
embryology

- **Improved culture conditions**
- **Better embryo selection**
- **Improved quality control testing**
- **New knowledge**
- **Valuable tool for quality management**