The Future is Bright:
Better Beer and Better Embryos

Jacques Cohen

Disclosures

- Co-Founder of Life Global & Reprogenetics
- Co-founder of Althea Science – IVFqc
- Lecturer for Cooper Surgical & Cooper Genomics
- Director ART Institute of Washington
- Advisor TMRW, KindBody
- Writer GE Healthcare
- Speaker does not drink beer – sincere apologies

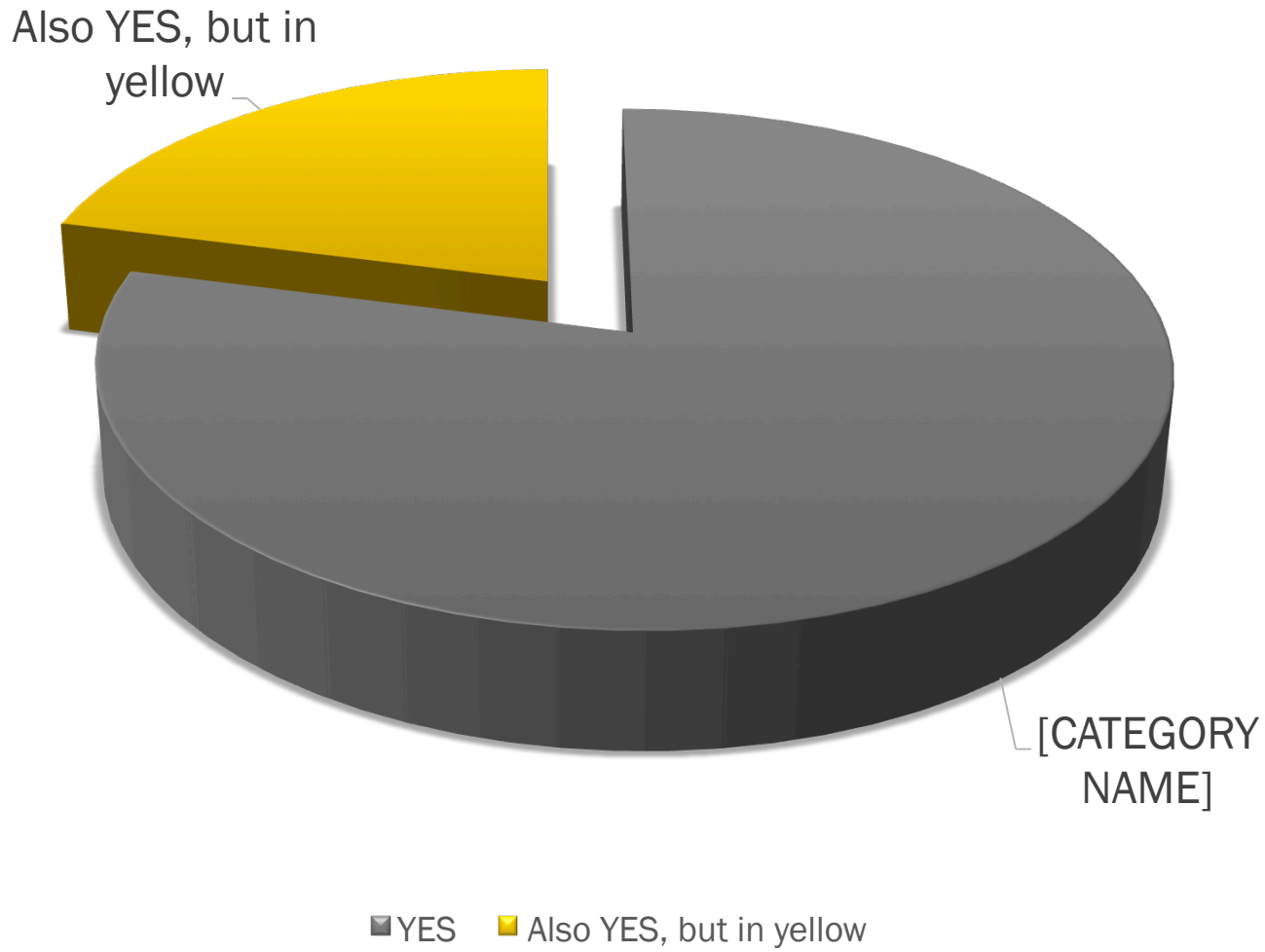
Belgium – land of innovation

- Plastic
- Smurfs
- ICSI
- Frieten
- Saxophone
- BMI
- Asphalt
- Beer Sumerian apparently (don't believe it – fake news?)


BEER
HELPING UGLY PEOPLE
HAVE SEX SINCE 1862!
Be
alls

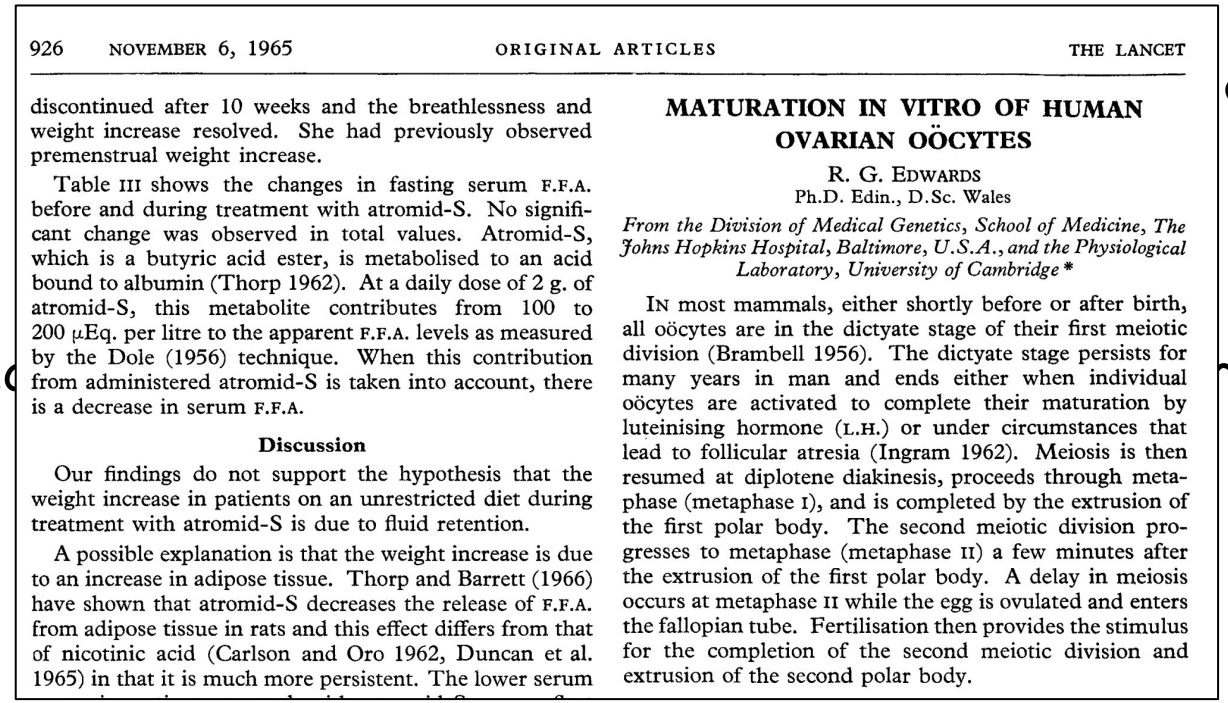
OPTIMIST	PESSIMIST	REALIST
“Mijn glas is halfvol!”	“Mijn glas is halfleeg!”	“Nog een biertje alstublieft!”

Should I have a BEER tomorrow ?



Predicting The Future – The CONVENTIONAL Approach

- Develop a **wish-list** of things you like or do not like (Edwards, 1965)
- Look for
- Look for
- Maybe d



926 NOVEMBER 6, 1965 ORIGINAL ARTICLES THE LANCET

discontinued after 10 weeks and the breathlessness and weight increase resolved. She had previously observed premenstrual weight increase.

Table III shows the changes in fasting serum F.F.A. before and during treatment with atromid-S. No significant change was observed in total values. Atromid-S, which is a butyric acid ester, is metabolised to an acid bound to albumin (Thorp 1962). At a daily dose of 2 g. of atromid-S, this metabolite contributes from 100 to 200 μEq. per litre to the apparent F.F.A. levels as measured by the Dole (1956) technique. When this contribution from administered atromid-S is taken into account, there is a decrease in serum F.F.A.

Discussion

Our findings do not support the hypothesis that the weight increase in patients on an unrestricted diet during treatment with atromid-S is due to fluid retention.

A possible explanation is that the weight increase is due to an increase in adipose tissue. Thorp and Barrett (1966) have shown that atromid-S decreases the release of F.F.A. from adipose tissue in rats and this effect differs from that of nicotinic acid (Carlson and Oro 1962, Duncan et al. 1965) in that it is much more persistent. The lower serum

MATURATION IN VITRO OF HUMAN OVARIAN OÖCYTES

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IN most mammals, either shortly before or after birth, all oöcytes are in the dictyate stage of their first meiotic division (Brambell 1956). The dictyate stage persists for many years in man and ends either when individual oöcytes are activated to complete their maturation by luteinising hormone (L.H.) or under circumstances that lead to follicular atresia (Ingram 1962). Meiosis is then resumed at diplotene diakinesis, proceeds through metaphase (metaphase I), and is completed by the extrusion of the first polar body. The second meiotic division progresses to metaphase (metaphase II) a few minutes after the extrusion of the first polar body. A delay in meiosis occurs at metaphase II while the egg is ovulated and enters the fallopian tube. Fertilisation then provides the stimulus for the completion of the second meiotic division and extrusion of the second polar body.

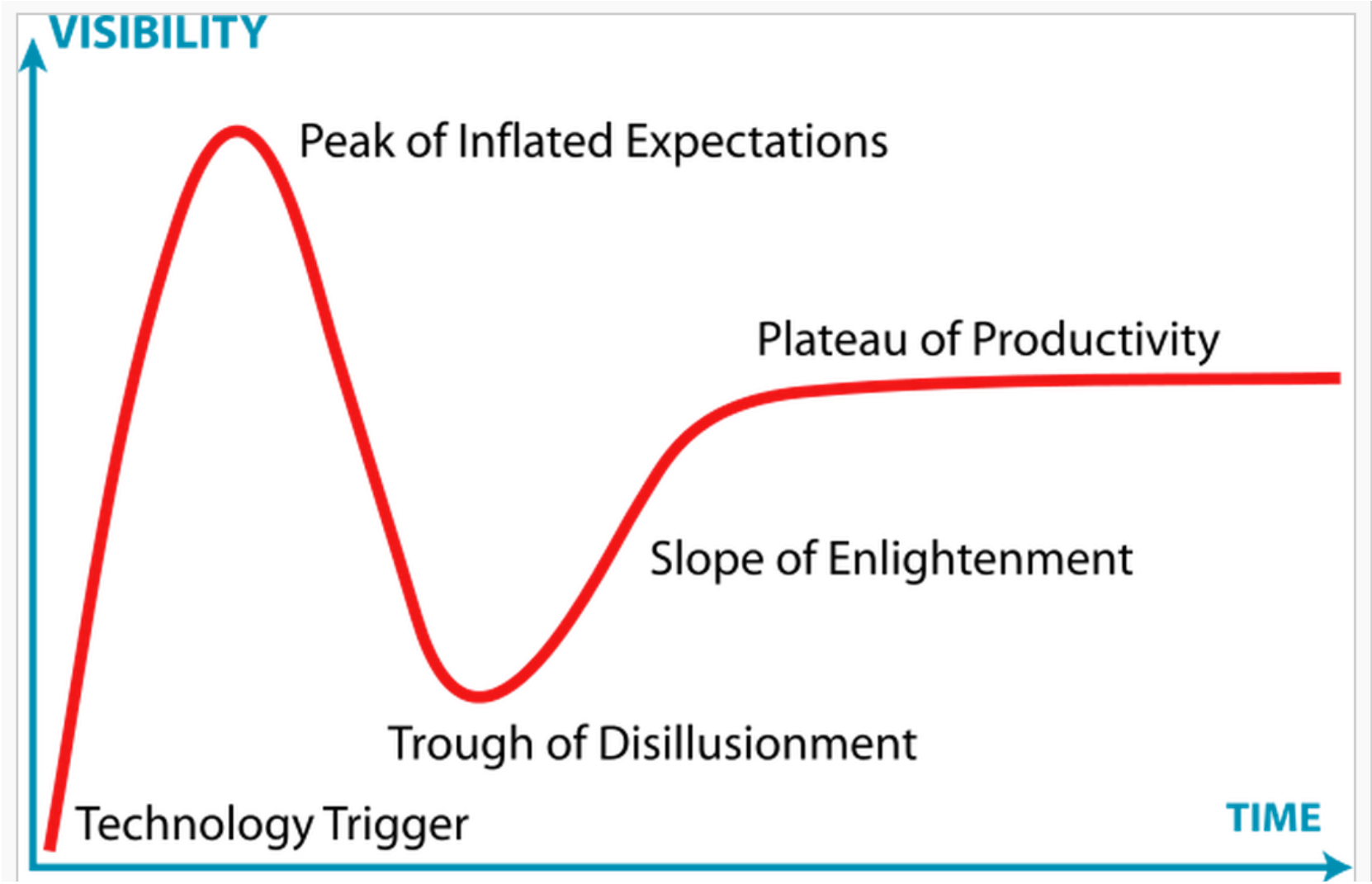
engineering)

m)

Predicting The Future – The NUMERICAL Approach

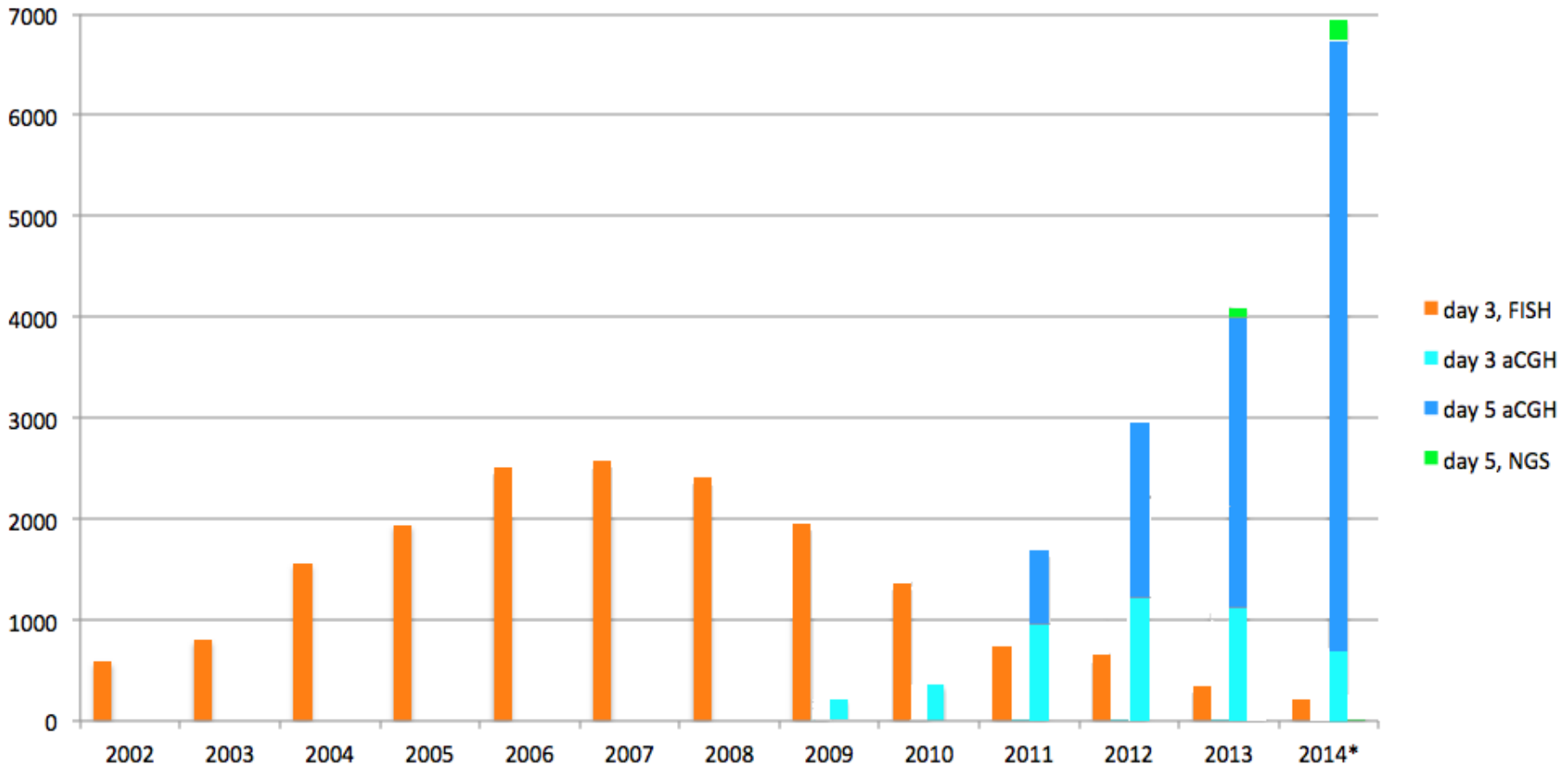
- Consider past developments as a prologue to the future, and translate into **mathematical assumptions**, if possible.
- **'Gartner / Palmer' Hype Cycle:** market forces at work after introduction of new technology
- **Timeline & Duration**: the time it takes to go from (A) **hypothesis**, to (B) basic **experimental** work, to (C) clinical **application** and finally (D) **routine**
- **Moore's Law** and derivatives: association between success rate and time

The Hype Cycle



Gartner – Palmer* Hype Cycle

USA data - PGD & PGS cycles

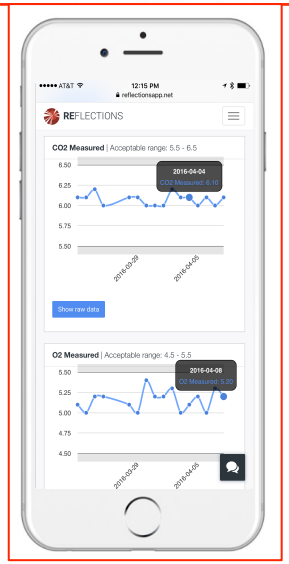


Reprogenetics 2002-2014

Timeline Approximation

(speed of acceptance of technology and routine application)

None of this existed 7 years ago



Predicting the future using time intervals from basic model to first clinical application

Technology	Animal Model	Clinical application	Interval
IVF	1959	1978	19
Foll. Stim.	1927	1960	33
Cryopreservation	1972	1983	11
PGD	1968	1989	21
Vitrification	1985	2005	20
Assisted fertilization	1980	1988	8
ICSI	1989	1992	3
Nuclear Transplantation	1983	2016	33

Predicting the future using time intervals from basic science model to clinical application

Towards clinical application	-	3 to 33 years
The average interval	-	18.6 years

Predicting the future using time intervals from basic science model to EFFECTIVE clinical application

Technology	Animal Model (year)	**Effective** application (year)	Interval (years)
IVF	1959	2010	31
Foll. Stim.	1927	1990	63
Cryo	1972	2011	>44
PGD	1968	not yet	>48
Vitrification	1984	2015	31
ICSI	1989	1997	9
Nuclear Transplantation	1983	not yet	>33

Predicting the future using time intervals from basic science model to clinical efficacy

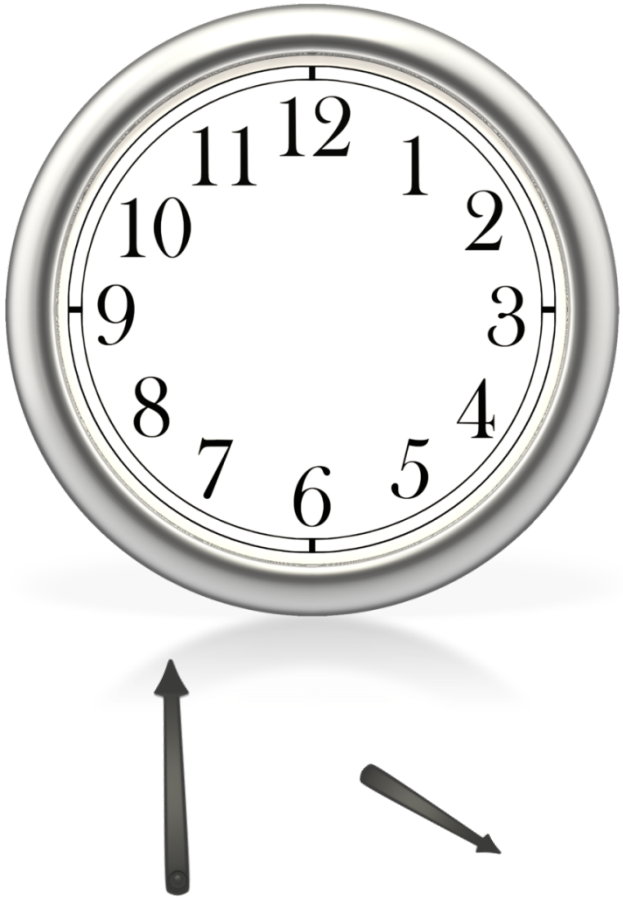
Towards **effective** clinical application	-	9 to >48 years
The average interval	-	>34.2 years

THREE MAJOR TECHNOLOGIES.

What is their timeline?

- Automation and AI
- Genetic modification
- Engineered gametes

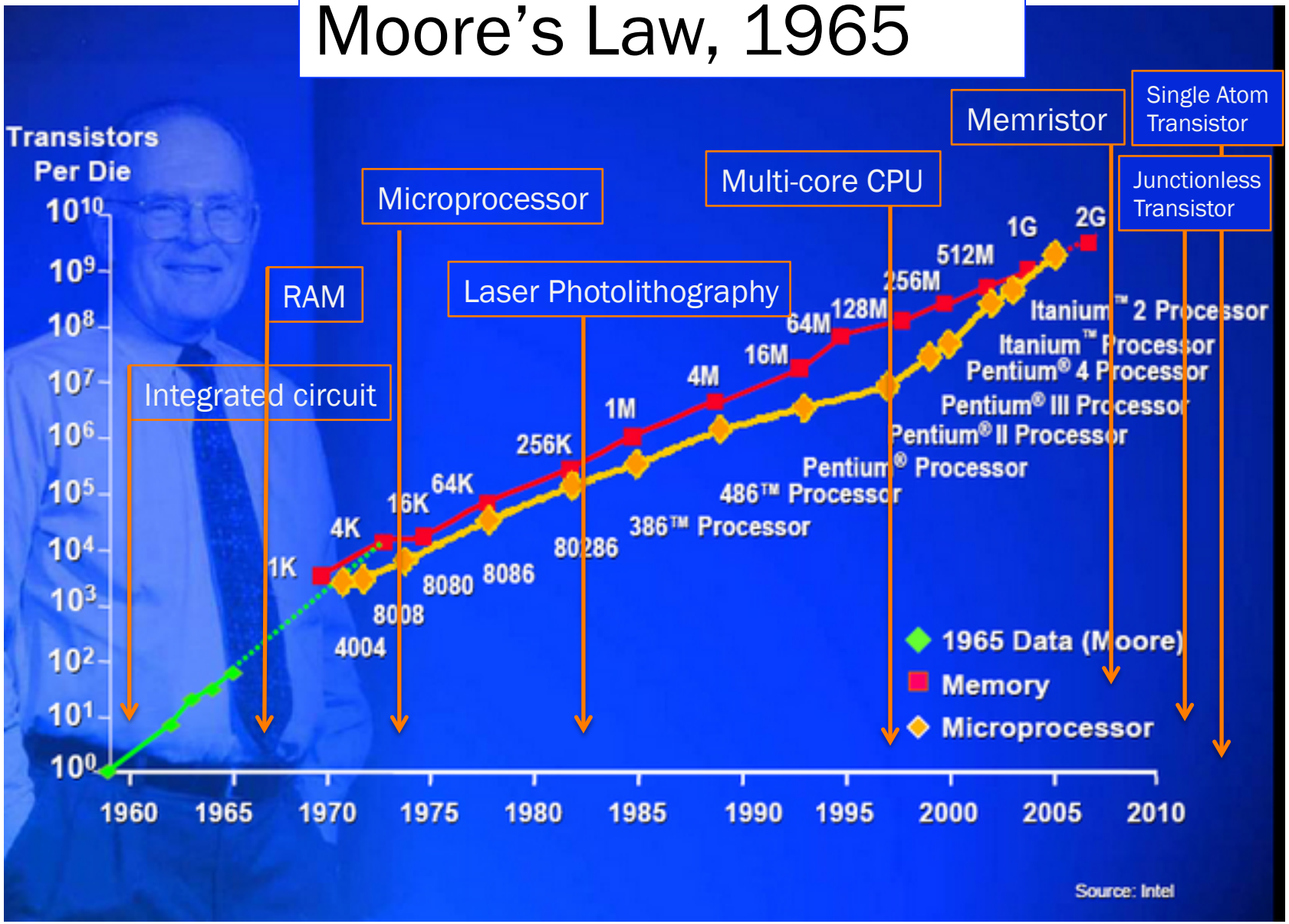
Known Influences – Unknown Effects



- Ethical debate
- Market economy
- Unexpected forces
- Political will
- Hype

Moore's Law in Assisted Reproduction

Moore's Law, 1965




IVF Success Gauge
0% SUCCESS
100% SUCCESS

In 2020 the glass will be half full

- ✓ SART data from www.sart.org
- ✓ >400 clinics
- ✓ >750
- ✓ >2,0
- ✓ USA
- ✓ <35
- ✓ Regr
- ✓ 100%
- ✓ AD 2

2011	35.9%
2012	37.4%
2013	39.4%
2014	43.7%
2015	44.4%
2016	45.6%

rates

..46%

d in 35 year

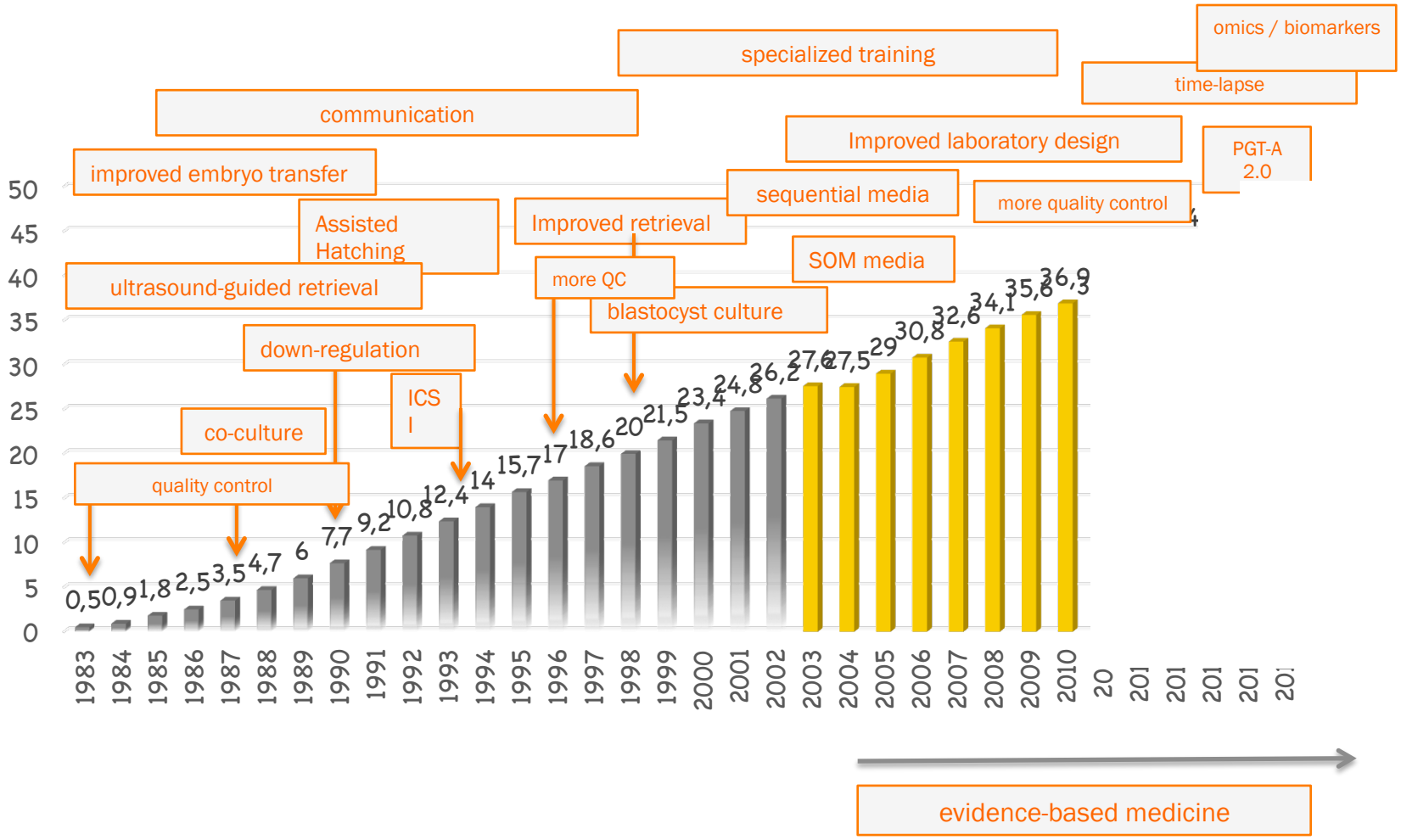
Cohen, Alikani and Bisignano, 2012

The Future of IVF - Success Rate of ALL age groups

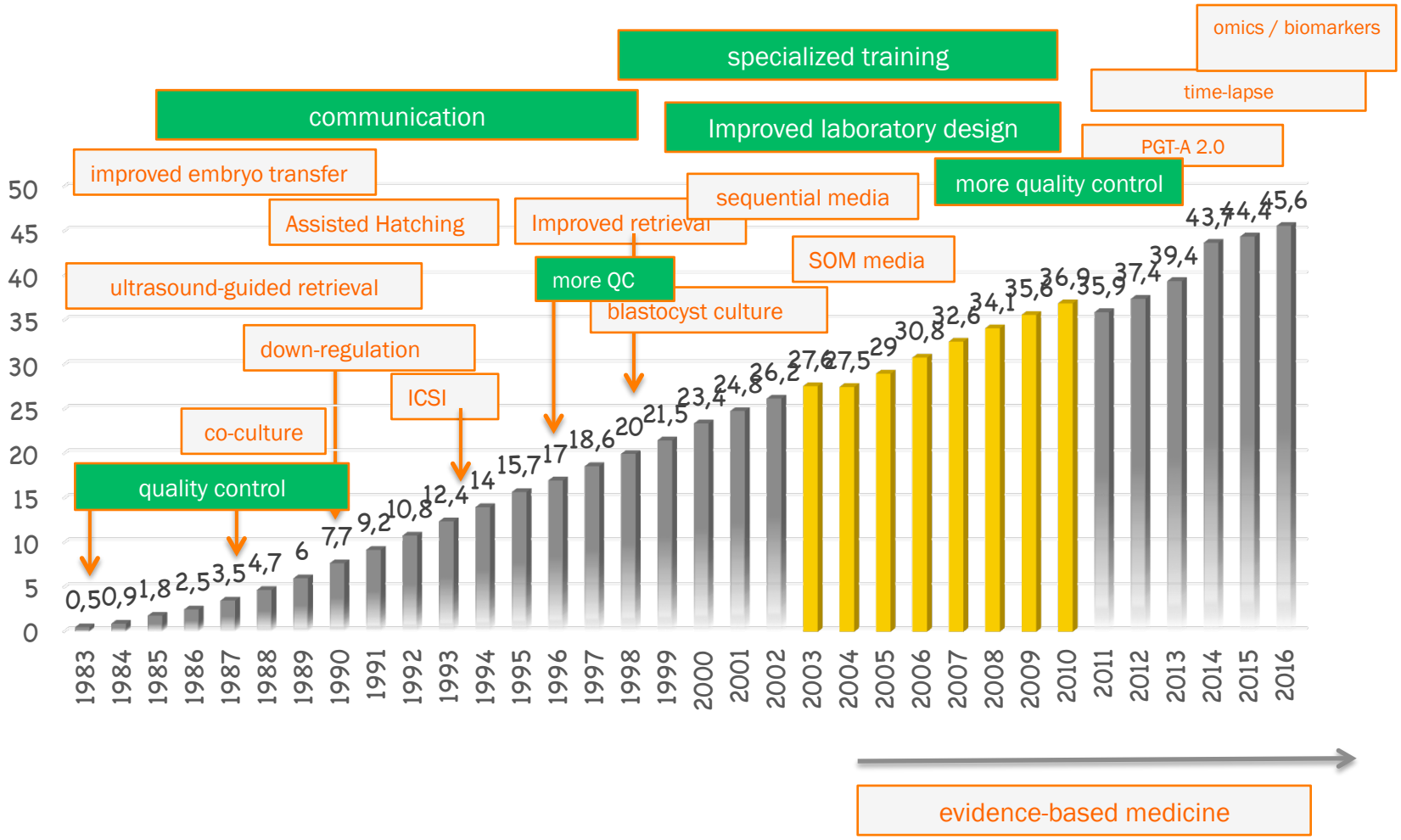
SART implantation success rate	<35	35-37	38-40	41-42
Improvement per year (%)	1.46	0.93	0.64	0.32
Years to reach 100%	35	69	121	276
Year of 100% implantation	2053	2087	2139	2294

(Based on SART data, Moore's Law and without 'paradigm shift' – Cohen et al, 2012)

implantation rate (per embryo) in patients <35 years



implantation rate (per embryo) in patients <35 years



Conclusions:

- ✓ Predictive algorithms based on current data sets
- ✓ Dependent on improvement of technology, training, communication
- ✓ Younger age group may approach 100% implantation in some clinics within 10 years (based on Moore's law) – USA data
- ✓ 100% implantation < 100% births < 100% healthy births
- ✓ TRUE paradigm shift (egg engineering?) could change that
- ✓ Automation & AI will phased in over time.
- ✓ Future IVF specialist is an engineer/geneticist/physicist
- ✓ A few hundred years from now: ART = reproduction