Optimal IVF/ICSI today

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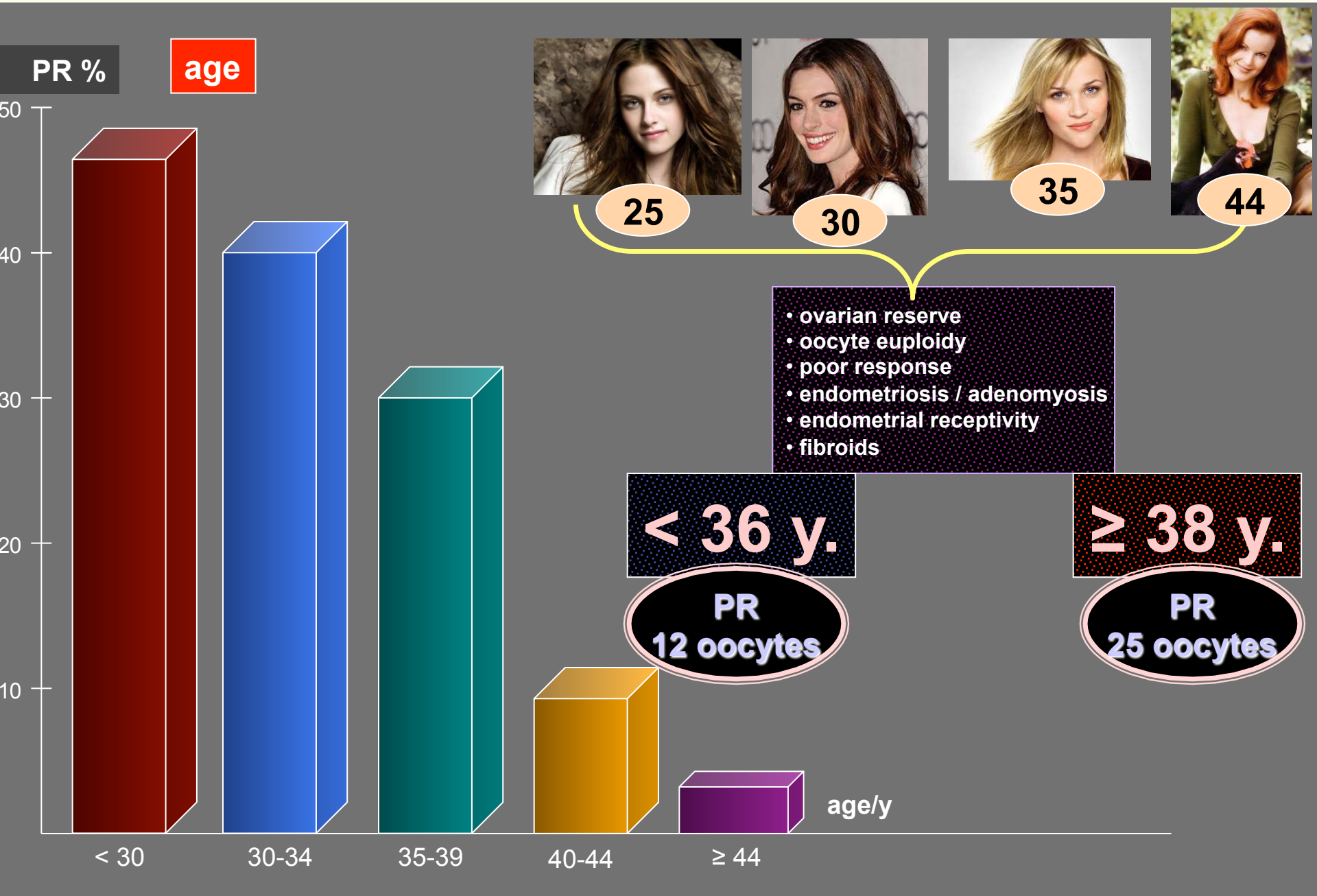
Brijuni, 2015.

LOWER IVF SUCCESS / MORE SAB

age	34,8 y.	smoking	30%
ow/obesity	> 50%	anabolic ster. drugs	?
underweight	6-8%	coffeine tein	30-40%
alcohol	15-20%	sinergism	70%

every factor - 50% success

Major contribution to unsuccessful IVF



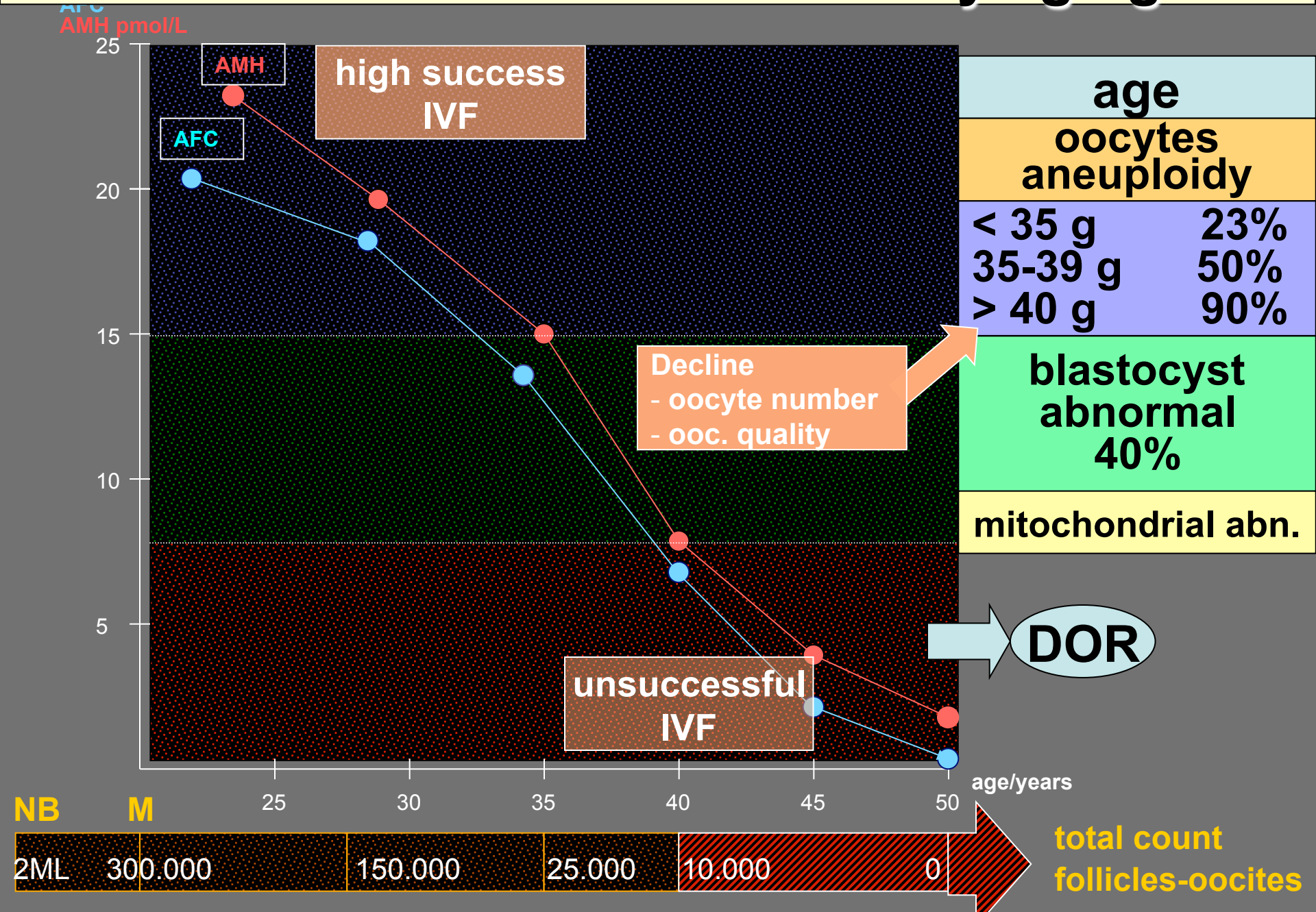
Spontaneous abortions (SAB) after IVF/ICSI

- same incidence last 20 years
- age
- oocyte/embryo quality

oocytes	ab. spont.	age (y)	ab.spont.
1-3	16,9%	< 34	18,4%
4-9	14,4%	35-37	23,1%
10-14	13,7%	38-39	29,6%
≥ 15	13,5%	40-42	40,6%

Sunkara, HR, 2014.

OVARIAN FUNCTION: DOR by aging



Vitamin D deficiency and IVF/ICSI

25 OH vit D < 20 ng/ml

OR 0,61 (0,39-0,95) CPR

OR 0,56 (0,33-0,93) CPR (SET)

Polyzos,HR,2014.

Low vit D ⇒ reduced IVF success

↑ RPL / APA / NK-cells **no consensus**

Th: vit D 800 IU/d

Irani,FS,2014.
Ota,HR,2014.
Bischoff-Ferrari,NEJM,2012.
Perissin-Chevallier,HR,2014.

Brakta,FS, in press

Subclinical hypothyroidism - SCHT

Normal TSH ≤ 4,12 mIU/L

SCHT > 4,5 mIU/L
fT4⇒ normal
incidence: 5-8%

If TSH ≤ 2,5 mIU/L
SCHT incidence: 18%

anti-TPO autoimmunity
incidence: 10-12%

Pregnancy / max TSH mIU/L

- I trimester 2,5
- II trimester 3,0
- III trimester 3,5

gest.HT incidence: 20-25%

No assoc: Polyzos,HR,2015.
SCHT and ovarian reserve

General screening ⇒ no consensus

De Groot, J CEM,2012 / ACOG, 0G,2007 / Garber, EP, 2012 / Hammond,FS,2015.

Subclinical hypothyroidism - SCHT

Associations with SCHT	TSH > 4	TSH 2,5-4,0
• SAB • Infertility (ovul/unexpl) • IVF – lower LBR/SAB • adverse obstetrical • adverse neonatal • neurodevelopment	good evidence	no evidence
TH: Levothyroxine improvement		

- TSH > 4,0 m IU/L
- PR I trim. ⇒ TSH > 2,5 m IU/L
- infertility treatm. – IVF/ICSI → TSH > 2,5 m IU/L
- anti TPO ⊕ TSH > 2,5 m IU/L

PC-ASRM, 2015.

Williams,JCEM,2012 / Vissenborg,HRU,2012 / Kim,FS,2011 / Benaglia,EJOG,2014.

Anti-phospholipid antibodies APA

*** effect on fertility** *** screening**

- anticardiolipin antibodies
- lupus anticoagulant
- anti-β_2 glycoprotein I

APA do not affect IVF success
CPR OR 0,99 (0,64-1,53)
LBR OR 1,07 (0,66-1,75)

Screening only with clinical criteria

NK cells – tests and immune th. – NO EVIDENCE

Kovach,2011.
PC-ASRM, 2008.
Sacks,HR,2015.

Thrombophilia
LMWH effect on IVF outcome

Coagulation defects inherited and acquired
- more prevalent in RIF / IVF populations

- **> 3 high quality ET → no PR**
- **≥ 10 embryos – multiple ET → no PR**

- **≥ 3 pregnancy losses**
- **unexplained recurent PR losses**
- **late pregnancy pathology**

- **IVF and venous thrombosis (VTE)** — **1-2%**
  - **IVF PR** — **OR 4,3 (2,0-9,4)**
  - **IVF PR I trim.** — **OR 9,8 (6,7-14,3)**
  - **IVF PR and OHSS** — **OR 14,5 (6,8-16,1)**
  - **OHSS (ascites)** — **RR 5,4 (2,1-13,7)**

Jacobson,JTR,2008.
Henriksson,BMJ,2013.

Hansen,HR,2014.
Rova,FS,2012.

Heparin effect on IVF outcome inconsistent

- studies with RIF, thrombophilia (inh/aqui), IVF

Observational studies – significant improvement

- CPR RR 1,83 (1,04-3,23)
- LBR RR 2,64 (1,84-3,80)
- ab.spont. RR 0,84 (0,49-1,43)

Urman,2009.
Garido,2013.

RCT – no improvement

- IR RR 1,39 (0,96-2,01)
- LBR RR 1,27 (0,89-1,81)
- ab.spont. RR 0,77 (0,24-2,42)

de Jong,Cochrane,2013.
Emson,Cochrane,2005.

LMWH indications – high VTE risk

- family / personal history
- proven thrombophilia
  - defic. antitrombin
  - protrombin mutations
  - FVL mutations

* IVF and OHSS (PF)
* OHSS and pregnancy
* other risk factors
  - PCOS
  - multiple pregnancy

LIVE-ENOX st.,2005
SPIN st.,2010.

Akhtar,Cochrane,2015.
Potdar,HRU,2013.
Seshadri, Sunkara,RBO,2012.

Surgery and IVF success

Surgery before ART improvement of success

Hydrosalpinx – salpyngectomy
OR 2,31 (1,48-3,62)

Endometrial polypectomy
IUI
RR 2,10 (1,5-2,9)

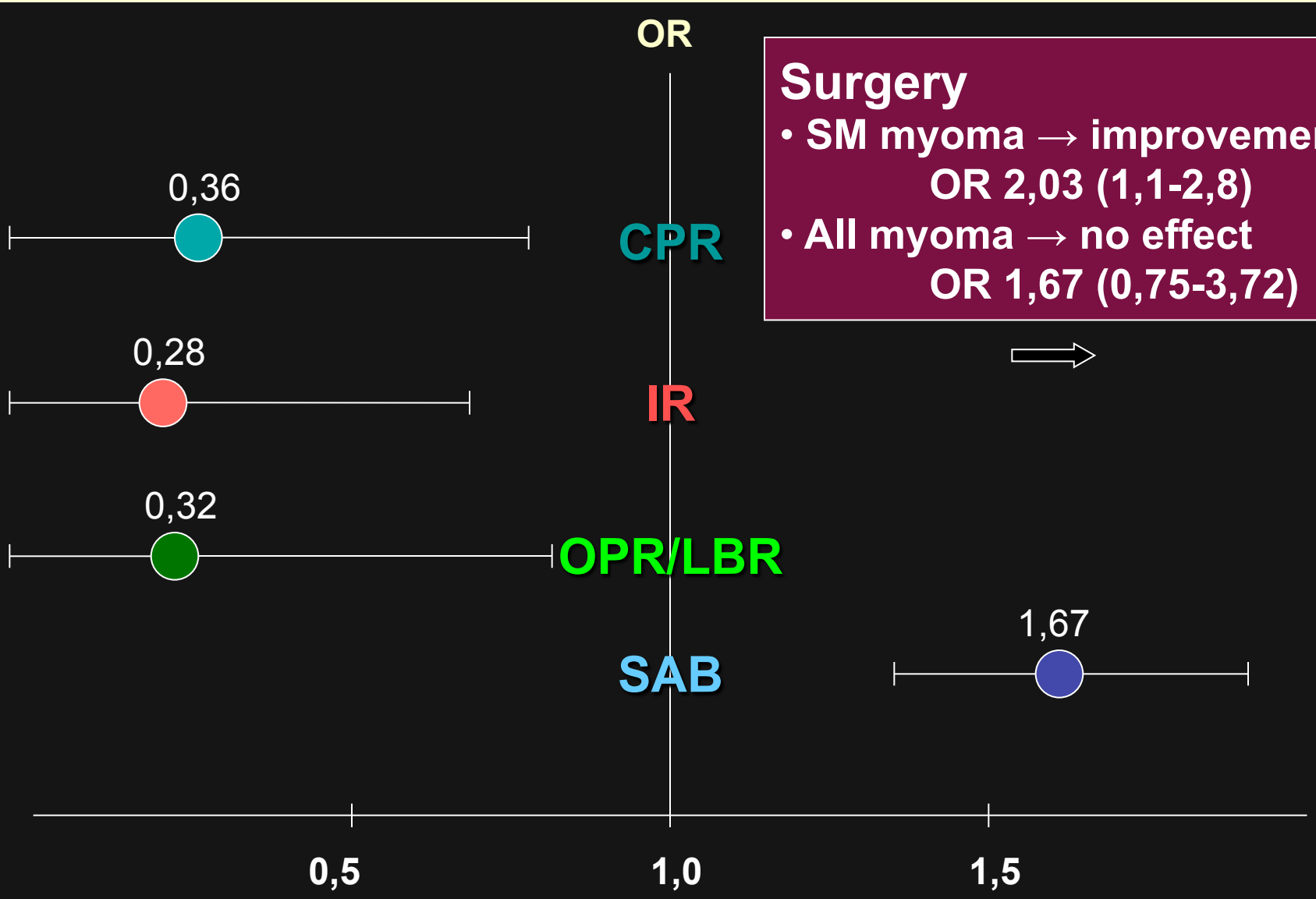
Uterine septum resection
OR 2,67 (1,2-3,6)

Submucous myoma enucleation
OR 2,03 (1,1-2,8)

Endometrioma ablation (> 4 cm)
OR 1,76 (1,1-2,8)

Kovach 2011 / Johnson Coch. SR 2010 /Lieng AOG 2010 / Perez-Medina HR 2005 / Galliano HRU 2015 / Pritts FS 2009

SUBMUCOUS MYOMA: effect on fertility/IVF



Surgery

- SM myoma → improvement
  OR 2,03 (1,1-2,8)
- All myoma → no effect
  OR 1,67 (0,75-3,72)

Pritts, FS, 2009.

IM myoma and IVF success

- incidence 10-30%
- IVF patients **26,7%** Hart ,2001
  12,6% Klatsky, 2008

Significant reduction of OPR/LBR

- all IM myomas
  - CPR 35% vs. 43%
  - RR 0,79 (0,7-0,88)
- IM not distorting cavity

Pritts,2009
Khalaf,2006
Sunkara,2011
Tanos,2014

Do not affect IVF results

- SS myomas
- IM myomas – not distorting cavity
  - < 3 cm
  - ≤ 5 cm

Metwally,2011.
Bulletti,2004.
Klatsky,2007.
Somigliana,2011.
Yan,2014

Th: surgery / UPA / GnRH ag

Galliano,2015

Donnez,2015

inconsistent studies

Endometriosis: first IVF or surgery

* Incidence: 30-40% infertile w.
* 50% for IVF treatment
* 10-18% in IVF

Kawwas,2015.

Negative effects on fertility – reduced IVF success

Fecundity lower 2-5x
SAB OR 1,7 (1,1-2,6)
Surgery better than pasive – spont PR

Hughes,1993.
Omland,2005.
Niezhat 1989 / Vercellini 2006.

CPR lower in IVF (E vs. control)

- ↓ 50% / 15,3% vs 37,3%
- OR 0,46 (0,28-0,74)
- oocyte donation
- lower success E III/IV

Simon,1994.
Barnhart,2002.
Garrido,2002.
ESHRE,2005.

Same IVF success – surgery no benefit

- Endometriosis vs. control
  - CPR 39,1% 33,2%
  - same results
- Endometrioma unilat/bilat
  - same nbr. oocytes, FR, EQ, CPR
  - same response OS - both ovaries
  - competent oocytes
- Endometrioma ø 2,5 cm
  - same response / same AMH
- Endometrioma surgery ≤ 4cm / > 3cm / deep PE
  - no benefit
- Endometrial receptivity - same

SART,2012.
HFEA
Jacobson, Cochrane,2010.
ESHRE,2014.
Benaglia 2013/2010.
Filipi,2014.
Somigliana,2015/2012.
Hart,2008.
Gupta,2006.
Donnez,2001.
Benchop,2010.
Garcia-Velasco,2004/2009.

Surgery before IVF no benefit →

Jacobson,Cochrane,2010. / PC ASRM – 2012. / ESHRE 2014 / Somigliana, 2015.

Endometrioma surgery

Negative effects of surgery – reduced IVF success

- Lower ovarian reserve
  - less spontaneous ovulations
  - ↓ AMH ≈ 10 pmol/L
  - reduced response on OS → Θ 50%
  - DOR / POF 15%
- Recurrences – higher risk in younger age
  - 2y ≈ 20%
  - 5y ≈ 40-50%
- Bilateral endometrioma surgery
  - OR 0,34 (0,1-0,9)
- Second operation
  - OR 0,29 (0,15-0,86)

Raffi,2015.
Somigliana,2006/2008/2015.
Esincler,2006.
Benaglia,2010.
Coccia,2011.
Ćorić,2011.

When surgery is an option - consensus

- Symptomatic endometriosis – proven dg
  - pain, tubal damage, adhesions
  - finding on work-up laparoscopy
- Endometrioma > 4 cm
- After IVF success
- After self donation
  - fertility preservation

Donnez,2011.
PC-ASRM, 2012
ESHRE q, 2014
Somigliana, 2015

Endometrioma and conservative therapy: risks in IVF

CONSISTENT

1. **Ovarian response**
   - same in E and intact ovary
2. **Oocyte competence**
   - similar FR, high Q E, IR, CPR
3. **OPU risks** 2-4%
   - difficul OPU (endometrioma > 4 cm)
   - injury
   - infection – despite antibiotic profilaxis
   - cyst rupture – chemical peritonitis
   - contamination of follicular fluid
     - reduced CPR
     - washing oocytes

INCONSISTENT

4. **Progression of endometriosis**
   - minor risk
   - OS and IVF ⇒ no risk
5. **Pregnancy complications**
6. **Occult malignancy**

Benaglia,2012/2014.
Kobayaski,2007.
Somigliana,2015.

Endometrial polyps

Incidence

• 15,6-32%		*Onalan,FS,2008.*
• Rec SAB / BMI > 30	15-50%	*Galliano,HRU,2015.*
• IVF naive p. / asimptomatic	6%	*Fatemi,HR,2010.*

Size

• < 10 mm	→ spont. regression	*Lieng,JMIG,2009.*
• > 15 mm	→ low chance for regression	*Isikoglu,RBO,2006.*
• ≤ 20 mm	→ does not affect CPR	*Lass,JARG,1999.*

Treatment

- Pasive – 1-3 months
- Polypectomy
- Cancellation and freeze all
- Polypectomy in IVF cycle

Galliano,HRU,2015.
Batioglu,RBO,2005.

No consensus – size effect, treatment

Intrauterine adhesions - synaechie

Causes

- infections
- surgery- iatrogenic
- SAB, SC, post P
  - HSC
  - electrosurgery

Incidence

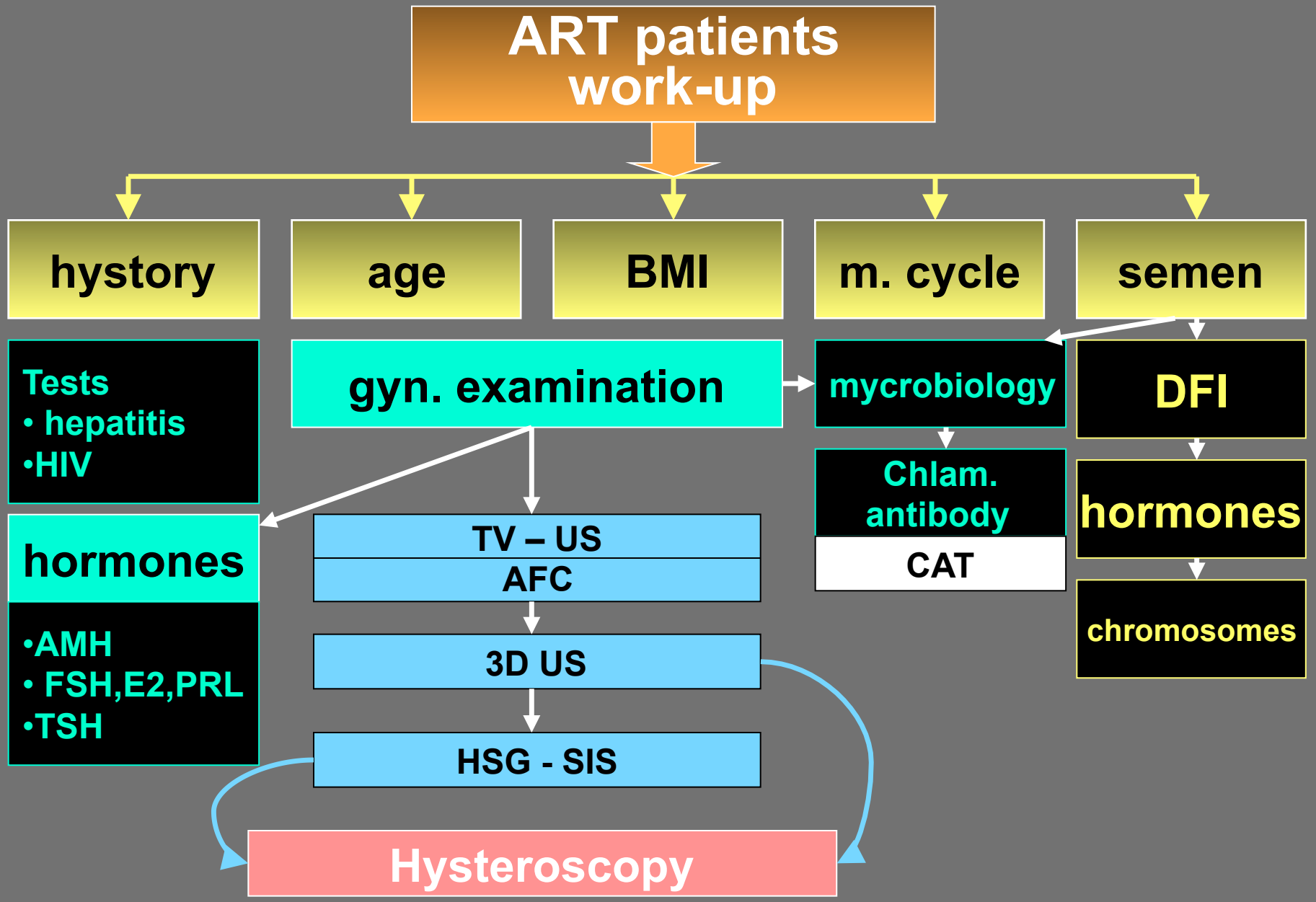
- post surgery → 5-40%
- post SAB → 19,1%
- ART patients → 2-16%

Therapy

- screening hysteroscopy
- second look hysteroscopy
- ⊕ IUD / gel

CPR OR 1,57 (0,98-2,11)

Hooker,HRU,2014.
Mazzon,FS,2014.
Galliano,HRU,2015.



Šimunić,2014.

Fatemi,HR,2010.
Seshadri,HRU,2015.

Hysteroscopy and ART

cervix

- stenosis, abnormalities, lenght

cavum uteri

- chronic endometritis
- endometrium – mycrobiology, histology
- adhesions – synaechie
- polyps
- submucous myoma
- second look

ET preparation

- dimensions, place for ET
- endometrial injury (scratching)
- endometrial “washing”

Fatemi, Popović-Todorović,RBO,2013.

Hysteroscopy – first line screening

?

Unsuspected uterine abnormalities - incidence

- Lit. → 20-45%
- ART first attempt → 11-22%
- RIF → 26-45%

Karayalcin,RBO,2010.
Kilic, AGO, 2013.
Galliano, HRU, 2015.

IVF/ICSI p. first attempt/ 34,4 y/ no US suspition

- Screening HSC → 11% uterine abnormalities

Fatemi, HR, 2010.

Sono HSG (SIS) → 22% undetected abnormalities

Karayalcin, RBO, 2012.

Not first-line investigation ESHRE 2000. / RCOG 2004.	Today Hysteroscopy 60 – 70% IVF p.

Male causes

Sperm DNA damage

- **oxydative stress – DNA damage**

Reactive oxygen species – ROS ⇒ antioxydance balance

DNA fragmentation index – DFI > 30%

- **lower fertility /unexplained infertility – 15-30%**

Tomlinson,HF,2013.

CPR	DFI > 30%	control
IUI	1,3%	12,5%
IVF	17%	36%
ICSI	32%	35%
Ab.spont.	35%	18%
	OR 2,48 (1,52-4,04)	

DFI testing – no consensus for routine use

ICSI → no benefit

Osman,El-Toukhy,2015.

Wright,RBO,2014.
Lewis,RBO,2015.
Drobnis,RBO,2015.
PC-ASRM,FS, 2013.

Varicocele surgery

* surgery * embolization

- 2-3 sperm analysis → infertile / DFI
- complaints → testicular size / pain / A deficiency
- relationship – female fertile
- male age
- palpable varicocele

surgery – fertility improvement
- density / motility

Abdel,EU,2011.
Nork,FS,2014.

Return of sperm → 35% pat. NOA
OPR (1y) 33% vs. 16%

Schlegel,FS,2011.

- surgery no effect → may improve CPR
- ICSI for combined infertility

PC-ASRM,2014.
Cochrane SR 2004 / 2006 / 2012

No consensus

IMSI vs. ICSI

Inconsistent – conflicting findings

Observational / RCT studies – improvement

- vacuoles → DNA-F / aneuploidy
- fertilization improved?
- improved only blastocyst Q not cleveage
- previous ICSI failures – better FR / IR / CPR
- better IR, CPR
- better SAB rate

Antinori 2011 / Oliveira 2011 / Knez 2012 / Souza Setti 2010/2013.

RCT – no advantage

- surface irregul. ⇒ no relation DNA-F / aneuploidy
- sperm vacuoles cannot differentiate...
- same fertilization rate / embryo Q
- same CPR / SAB rate
- same LBR

Perdrix 2013/Balaban 2011/Leandri 2013/Delaroshe 2013/Palermo 2011,2014/Gatimel 2014 / De Vos 2013.

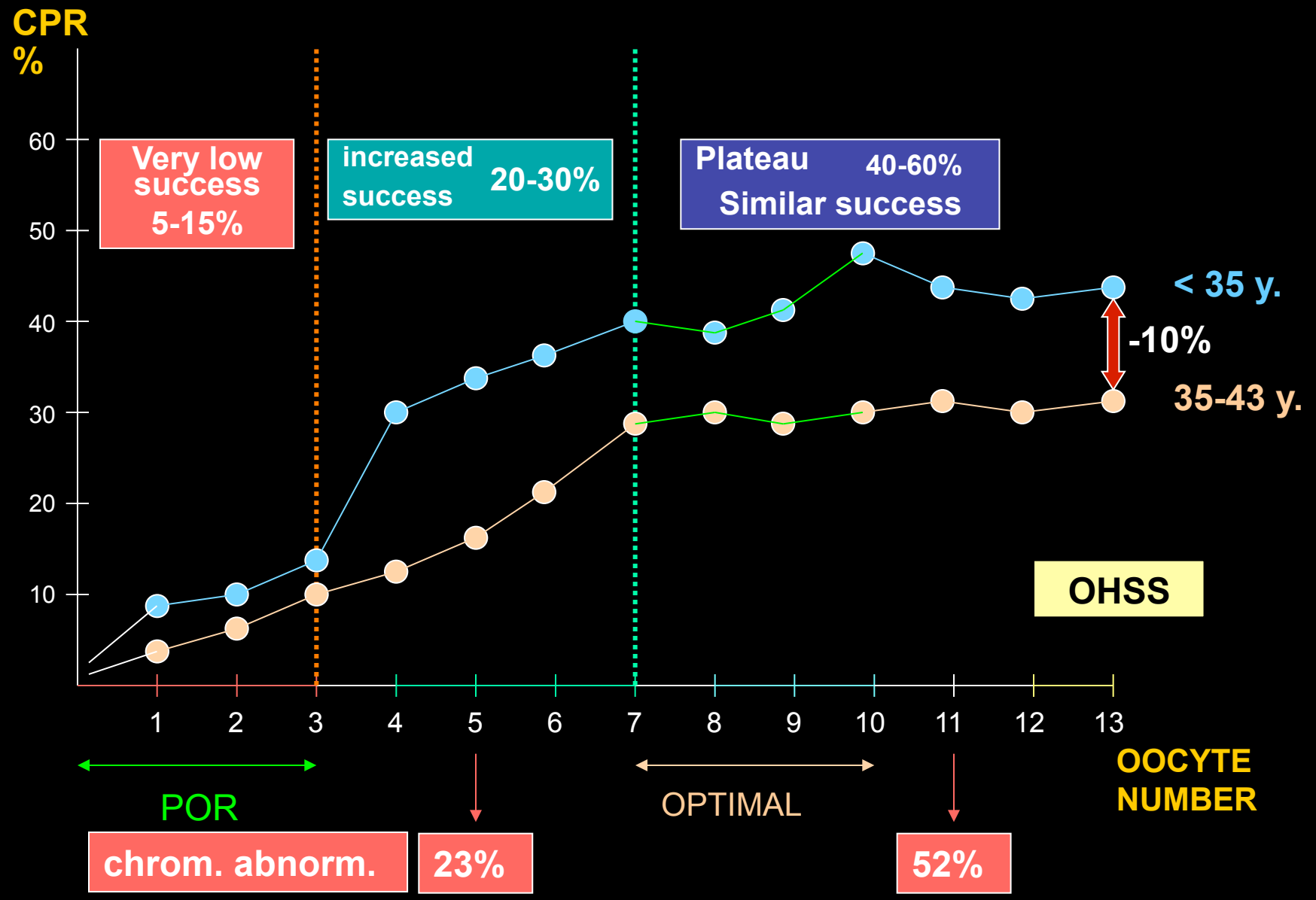
Ovarian stimulation

How many oocytes we need?

or

Can you ever collect to many oocytes?

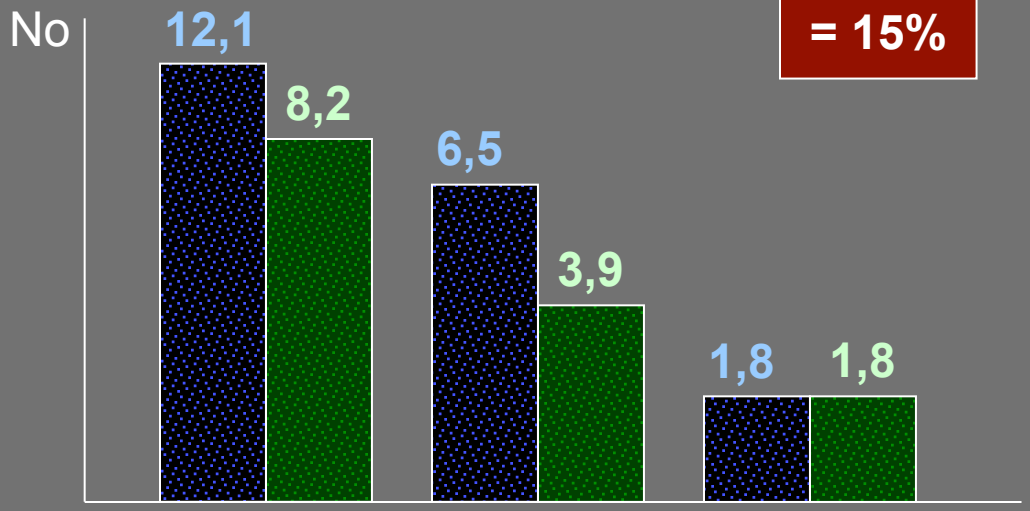
IVF: oocyte number for success?



Mild IVF protocols: aneuploidy reduction

➡ embryo biopsy → FISH

	standard IVF	mild
Oocytes	12,1	8,2
Embryos / patient	6,5	3,9
E – normal morphology	35%	51%
E – chromos. abnormal.	73%	55%
E – chromos. normal. (No)	1,8 = 15%	1,8 = 22%



Baart et al,HR,2007.

Number of eggs and LBR

1999-2007. (N=400135)

eggs	≤ 34 y	35-37y	≥ 40 y
1-3	15,3%	13%	4%
4-6	29,3%	24,3%	9,7%
7-10	35%	30,7%	12,7%
11-14	38,7%	34,7%	15,7%
15	40%	41%	17%

> 15 ⟹ plateau

> 20 ⟹ decline

Sunkara,HR,2011.

Oocyte number: what is optimum?

9 – 12 oocytes → **optimal CPR**

Gaast,2006 / Devroey,2009.

6 and 10 oocytes
8 and 12 oocytes → **same results**

Bart,2007 / Hoomans,2002 / Tan,2005 / Pelicer,2010

> 15 oocytes

- **same results**
- **no further benefit**
- **lower CPR**

Baker,2015,
Tremellen,2014 / Sunkara,2011 / Briggs,2015 / Hamdine,2015

High response ⇒AMH and PCOM / PCOS

- HR incidence 15-25%
- PCOM/PCOS 18-30%

→ same oocyte quality

	Population	AMH pmol/L	top Q embryos
	General / NR	15 – 20	37,3%
	PCOM	40 – 60	38,6%
HR PCOS	• normal cycle	50 – 60	34,5%
	• oligomenorrhoea	70 – 80	
	• amenorrhoea	90 - 120	

Sigala,FS,2015.

- 15% PCOS → AMH < 30 pmol/L
- AFC ≥ 25 per ovary
- AF produces more AMH in PCOS

Pigny,HR,2006.
Homburg,HR,2013.
Dewailly,HR,2014.
Bhide,FS,2015.

High ovarian response effects

Engage n=1506 / reanalysis

		OOCYTES				
		0-5	6-9	10-13	14-18	> 18
ELONVA	Patients (%)	12,5%	18,1%	22,9%	21,8%	24,8
	Progest. elevat.	4,3%	1,5%	7,1%	9,2%	12,9%
	Embryos (n)	2,0	4,6	6,6	9,4	13,5
	OPR / ET	44,1%	40,9%	43,7%	41,1%	48,4
	Embryos cryopr.	0,2	0,8	1,4	2,6	4,9
recFSH	Patients (%)	12,8%	22,9%	25,1%	20,8%	18,2
	Progest. elevat.	4,2%	3,5%	5,3%	14,7%	21,3%
	Embryos (n)	2,1	4,7	6,9	9,0	13,0
	OPR / ET	38,0%	41,1%	38,9%	39,7%	45,0
	Embryos cryopr.	0,2	1,2	1,8	2,7	4,2

High response

⇒ high OPR

⇒ increases cumulative PR

⇒ progest. elev. effect - lower

HR vs. POR
OPR OR 1,87 (1,34-2,59)

Fatemi, HR, 2013.

High ovarian response – not compromise PR

success		Oocytes 1 - 5	6 - 13	≥ 18
LBR	*Fatemi 2013.*	25%	34,9%	40,4%
	Jayaprakasan 2012.	23%	35,2%	> 15 44%
	Briggs 2015.	1 - 3 15,1%	28,6%	33,6%
	Sunkara 2011.	15,3%	35%	15 - 20 40%

HR

- **prediction → AMH > 26 / AFC > 16**
- **imature oocytes ≈ 22%**
- **progesteron elevation 20-25%**
- **younger patients / longer cycles**

La Marca,HRU,2014.

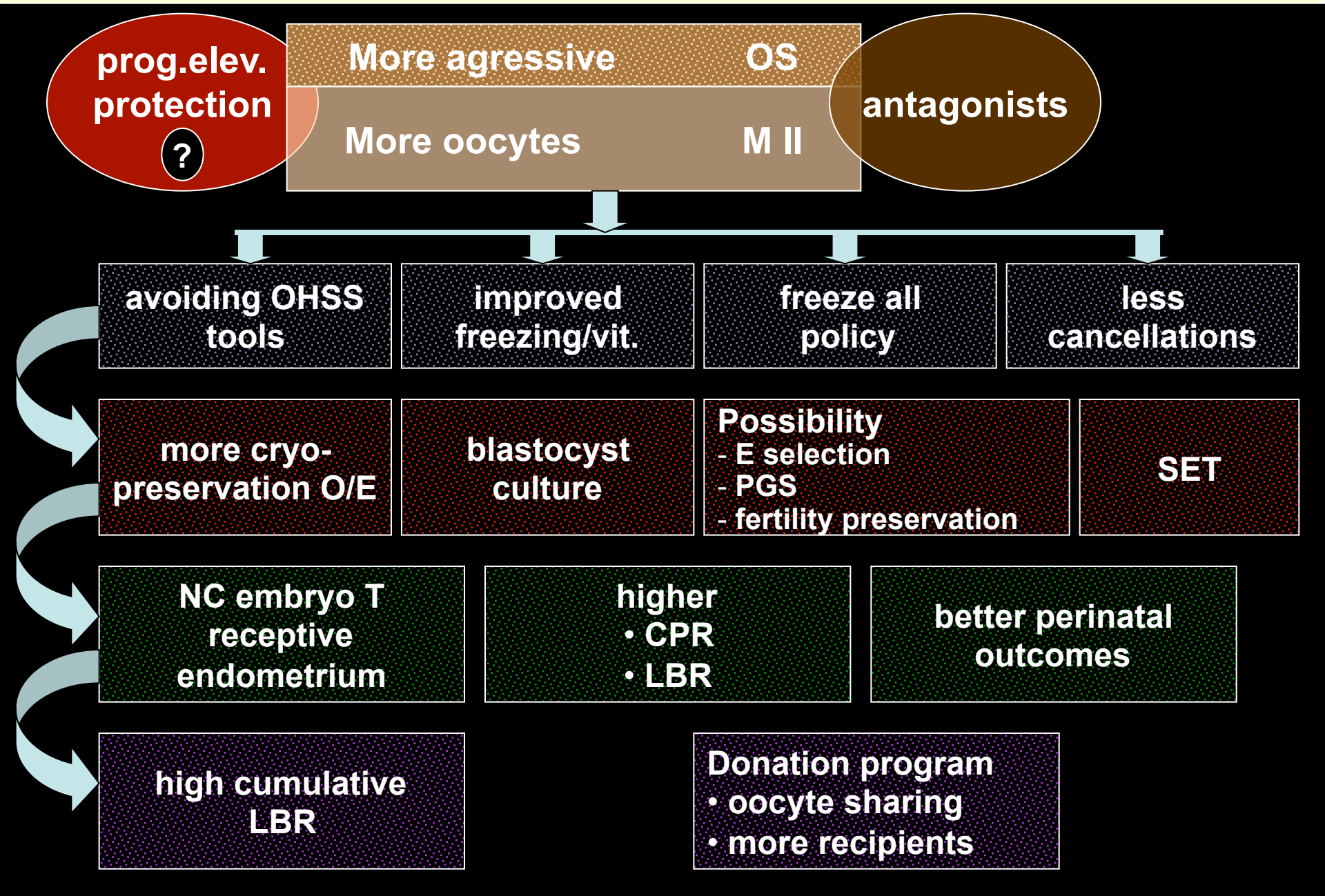
- **↑ preterm births / IUGR**

Sunkara,HR,2015.
Baker,FS,2015.

cum PR 33% vs 60,8%

Fatemi,HR,2013.

More is better – new technologies / new philosophy



Technologies

ICSI

- for non-male infertility
- for all patients

		IVF	ICSI
C	unexplained infertility	32 %	38 %
		OR 0,83 (0,48 – 1,45)	
P	POR	17,3 %	21,1 % st. not sign.
R	for all NNT 33	33 %	26 %
		RR 1,27 (0,95 – 1,72)	

congenital abnormalities
OR 1,11 | OR 1,57

inconsistent

Van Rumste, Cochrane SR, 2003.
PC ASRM, FS, 2012.
Luna, JARG, 2011.
Davies, NEJM, 2012./Carrell,Andr,2015.

ICSI is not justified:

- for all
- unexplained infertility
- for POR
- older women

Blastocyst transfer
extended culture system

- advanced IVF centers
- vitrification
- selection

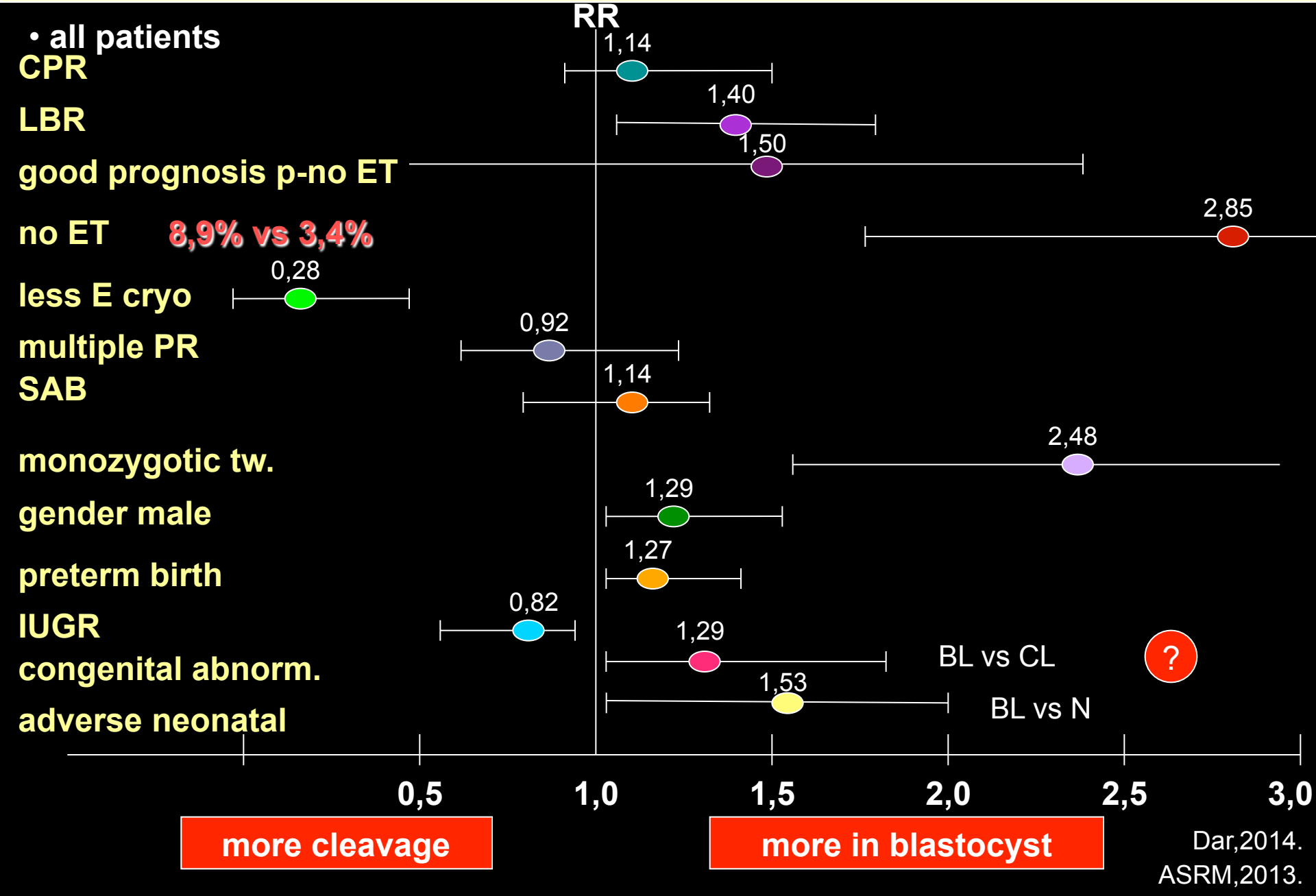
CPR	BL-ET	Cleavage ET
good prognosis p. 3. day ≥ 3 E (8 cells)	50,5%	30,1%
all patients	41,6%	38,6%

NO IMPROVEMENT	ADVERSE EFFECT?
• low oocyte number • nonselected patients • poor prognosis patients	• less ET / less FET • preterm birth • EPH gestosis • monozygotic twining ↑ • congenital abnormalities ?

Blake, Cochrane SR, 2007.
Glujovsky, Cochrane, 2012.
PC-ASRM, FS, 2013.

Papanikolaou, NEJM, 2006/2008.
Maheswari, FS, 2013.
Maalong, FS, 2014.
Dar,HRU,2014.

ET – blastocyst vs. cleavage st.



Dar,2014.
ASRM,2013.

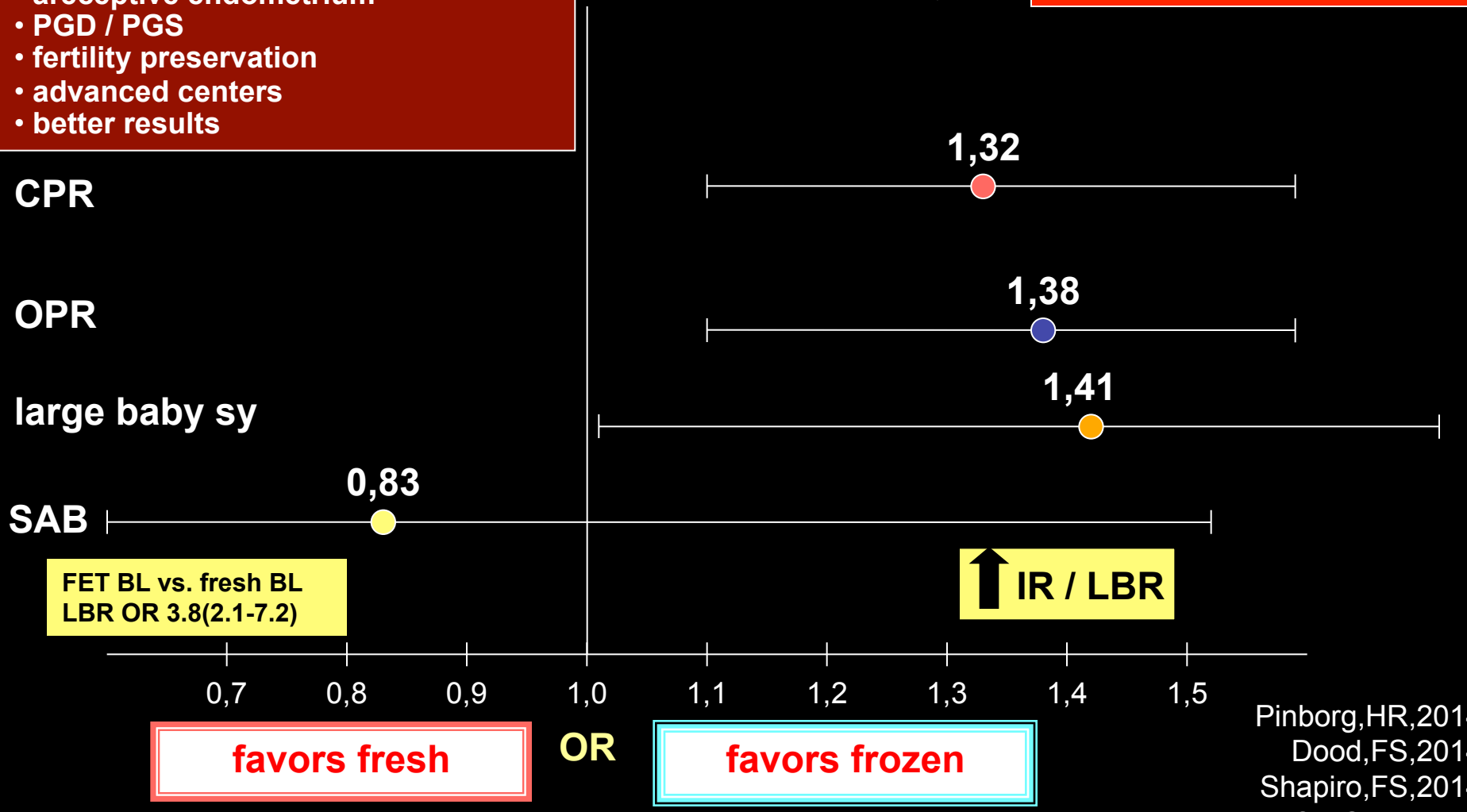
Freeze all embryos
vitrification

- actual IVF
  - avoiding OHSS
  - P4 elevation
- areceptive endometrium
- PGD / PGS
- fertility preservation
- advanced centers
- better results

Double freeze E
→ Same CPR

Koch,2011.

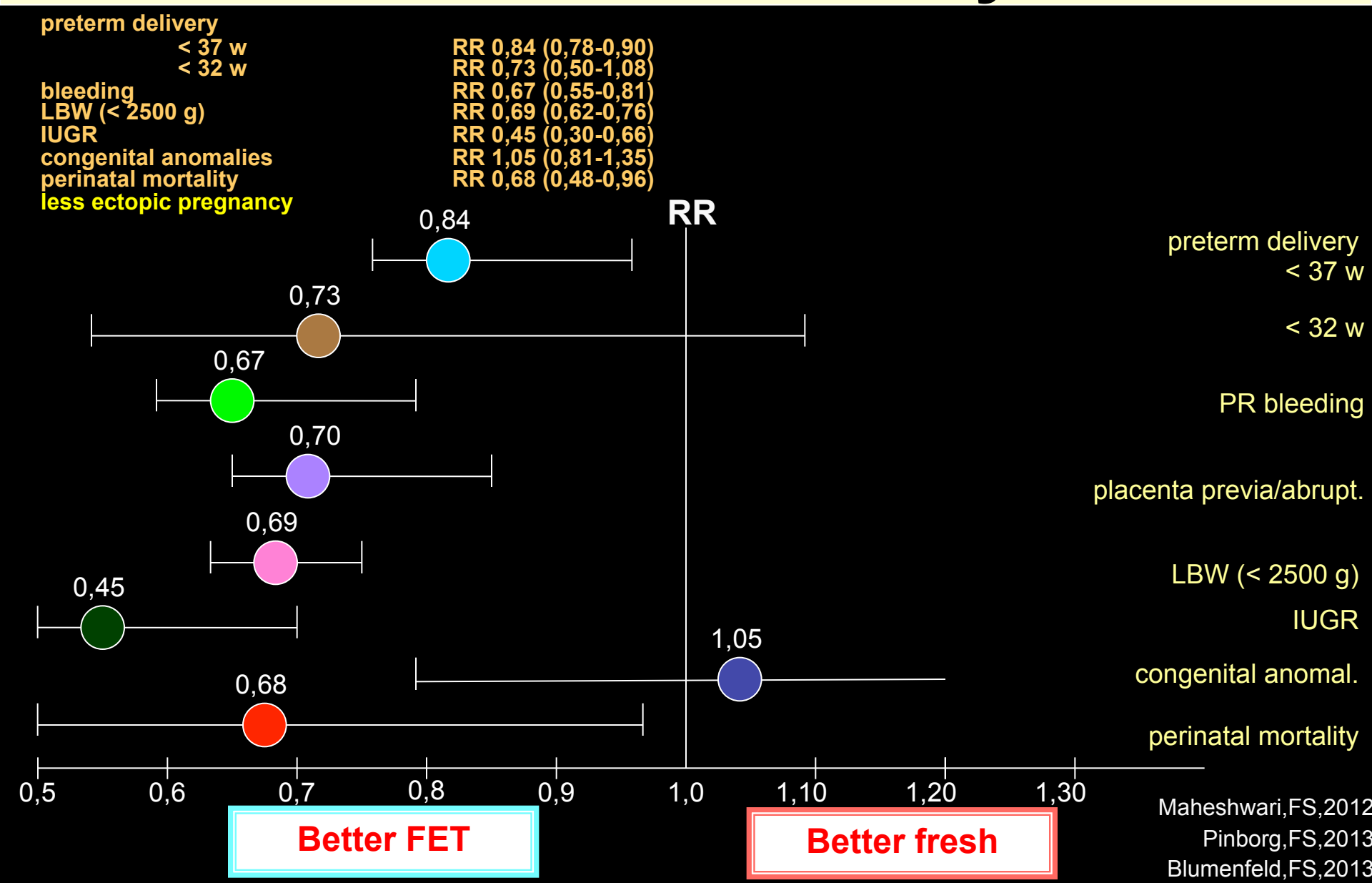
FET	2006.	2012.
	16,9%	42,4%



LBR freeze BL vs. fresh BL **OR 3,8**

Pinborg,HR,2014.
Dood,FS,2014.
Shapiro,FS,2014.
PC-ASRM,2013.
Roque, FS, 2013./2015.

Perinatal outcomes singleton PR FET vs. Fresh embryos



Maheshwari,FS,2012
Pinborg,FS,2013
Blumenfeld,FS,2013

ET – with better IVF success

PREPARATION	→	histerometry, mock ET, HSC laminaria
DIFFICULT/EASY	→	CPR OR 0,73 (0,63-0,85)
SOFT CATHETER	→	CPR OR 1,49 (1,26-1,77)
UTERINE PERISTALTY	→	≤ 3 per min. CPR OR 1,39 (1,1-1,7)
US / TACTILE	→	LBR OR 1,78 (1,19-2,67) LBR OR 1,14 (0,93-1,39)

Fanchin,RBO,2009.
Drakelly,HR,2008.
Brown,Cochrane,2010.

Thin E < 7	→	OR 0,42 (0,27-0,67) ?
Bed rest	→	short ø longer 10-30 min. OR 1,13 (0,77-1,67)
Embryos expulsion	→	less than 120 sec. → 2 cm below fundus
ET media Optimal volume adherence compounds	→	10-20 µL / hyaluronon (HA) OR 1,39 (1,21 – 1,80)
ET catheter	→	avoid neg. pressure waiting in situ – no advantage re ET – same result
Not proven benefit	→	cervical M removal / sex / full blader tenaculum / tocolitics / p. position

Kasius,HRU,2014.
Cracinnes,FS,2014.
Gargely,HR,2010.

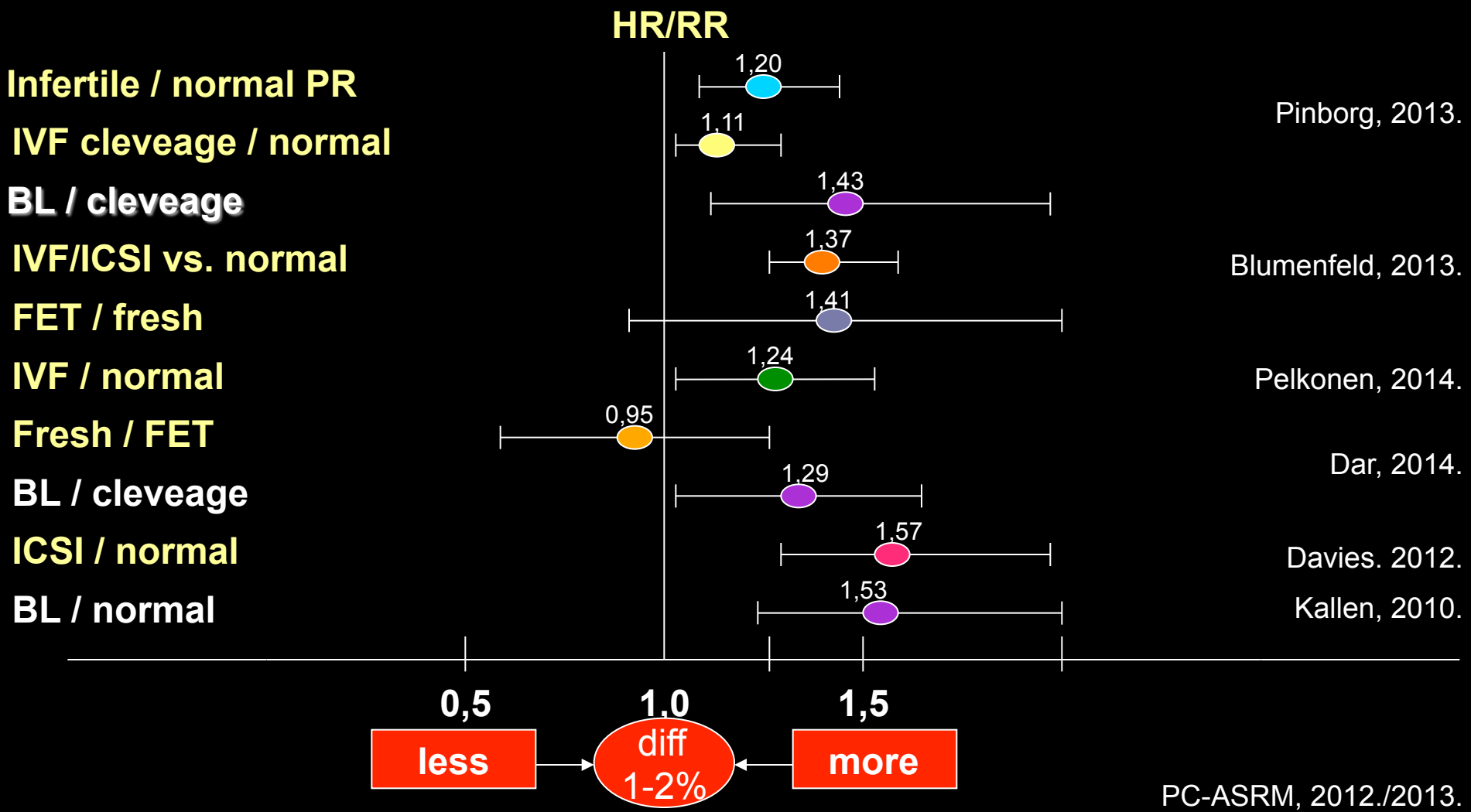
Bontekoe, Coch, 2015

Derks,Cochrane,2009.
Brown,Cochrane,2010.
Gaikwad,FS,2013.

IVF/ICSI: congenital abnormalities

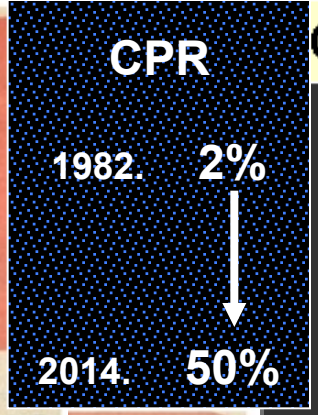
Epigenetic mutations – genomic imprinting

* infertility – 40% abnorm. due to
* paternal
* ovarian stimulation – E2, P4, VEGF
* labor. technologies



PC-ASRM, 2012./2013.

Ovarian stimulation – a hystorical view



- N=153 / 33,5y / infertility 6,9 y
- clomiphene 100-150 mg / Pergonal 670 IU
- LH SIR timing ovulation/Abd. US

CHARACTERISTIC	RESULT
Patients / cycles	153
Age ($\bar{x}$) y	33,5
Canceled/neg. OPU	18,9%
Laparoscopic OPU posit	124 (83,2%)
Oocytes No ($\bar{x}$)	4,1 (57% mature)
ET	113 (91,1%)
Embryos / ET	2,6
CPR / ET	11 (9,7%)
OPR / ET	9 (7,96%)
SAB	2 (18,2%)
twins	1 (9,1%)

Grizelj, Šimunić, DC, 1985.

IVF should not give confidence for delaying motherhood

Endometrium

Chronic endometritis

Prevalence on screening HSC:

- 30,3% *Quaas, OG, 2008.*
- 57,5% PHD
- 45% culture *Cicinelli,HR,2015.*
- 2,8% PHD *Kasius,Fatemi,FS,2011.*

Enterococ	33%
Mycopl./ureapl.	30%
E. colli	23%
Chlamidia	8%

- more intrauterine abnormalities 35% vs. 11%

Significant improvement IVF after treatment

CPR	65,2%	vs.	33%	
SAB	4%	vs.	20%	*Cicinelli*

NO CONSENSUS

No impact on fertility and IVF

CPR OR 1,45 (0,77-2,75)

Kasius,Fatemi,FS,2009.
Johnson,FS,2009.
Haggarty,AJOG,2008.

Chr. endometritis ⇒ altered contract. *Pinto,FS,2015.*

Endometrial thickness

Thin endometrium	Normal	Thick endometrium
	9-14 mm (triple line) volume ≥ 2 ml	
cut-off	7 mm 4-5 mm	≥ 15 mm
Incidence	5% younger 25% older age	5-11,5 %
IVF-PR with	< 4 mm	19-20 mm
No difference	< 6 mm vs	> 10 mm

Th: aspirin, viagra, Pentoxyfilin, vit E, G-CSF

Contradictory r. – no consensus

Dain,FS,2013.
Check,FS,2004/2011.
Zhao,RBE,2012.
Momeni,JHR,2011.
Barad,FS,2014.

Endometrial peristaltic waves

OS → E2 → oxytocin / increased contrac.

- endometriosis
- myoma
- ET difficult
- chr. endometriosis

	≤ 3 min	> 5	
OPR	53%	14%	Fanchin,HR,1998. RBO,2009.
CPR gentle ET/less p.w.	OR 1,39 (1,11-1,74)		Mansour,HR,2005.

Improvement

- ET technic
- blastocyst ET
- atosiban
- NSAID

NO CONSENSUS

Zhu,HR,2014.
Maraloglu,HR,2010.
Galliano,HR,2015.

Endometrial injury before IVF cycle

- expression of implantation factors

Cochrane SR ⇒ improved IR, CPR, LBR

Metaanalysis ⇒ OR 1,70 (0,89-2,11)

ooc. donation ⇒ no difference in LBR

NO CONSENSUS

El Toukhy, Cochrane, RBO, 2012.
Potdar, RBO, 2012.
Dain, FS, 2014.