

Embryo transfer – the elusive step

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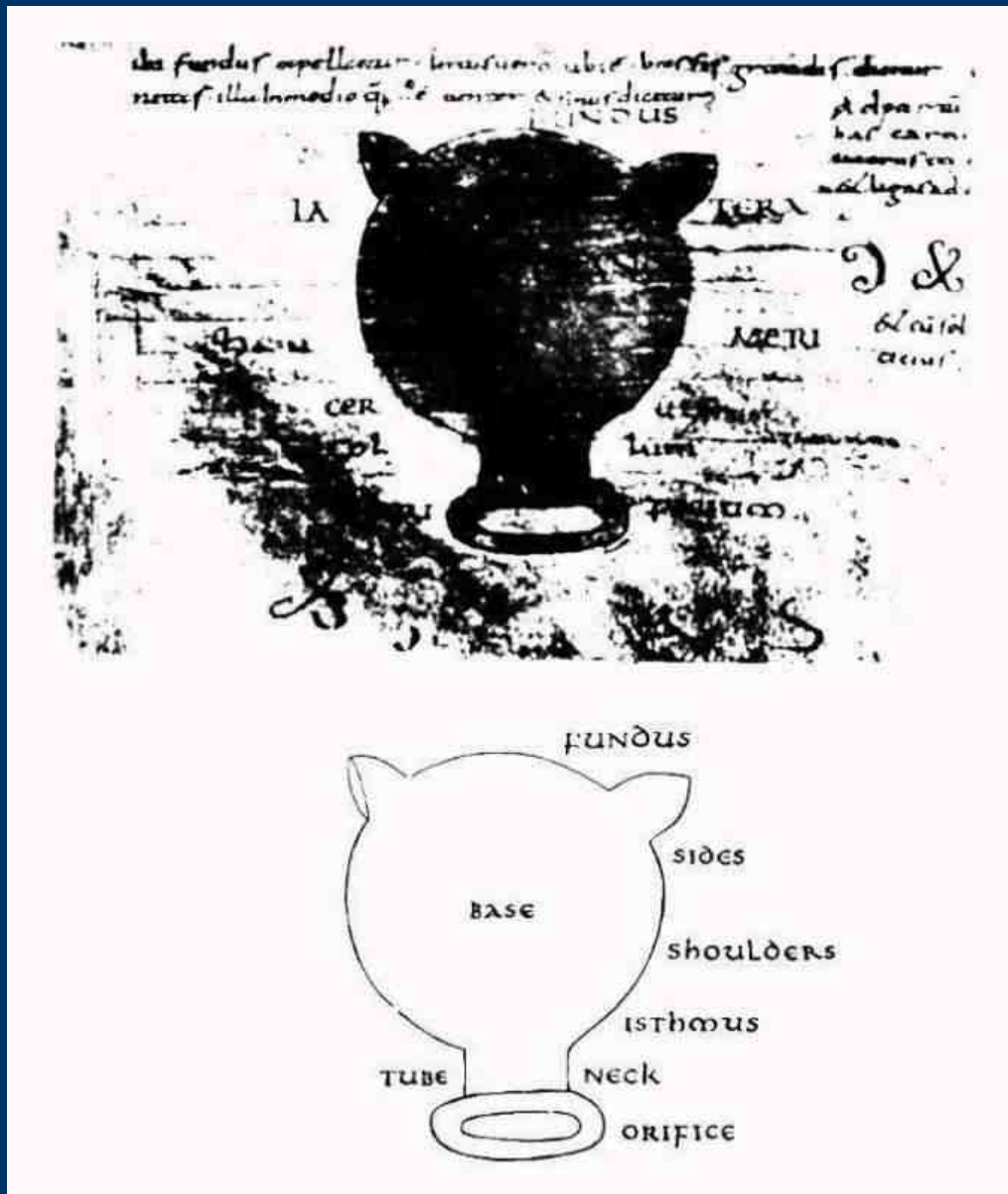
The University of Alexandria in Egypt

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for Women's Health and Development

*2nd Annual Congress of the Turkish Society for Reproductive
Medicine, 1-4 October 2009, Antalya, Turkey*

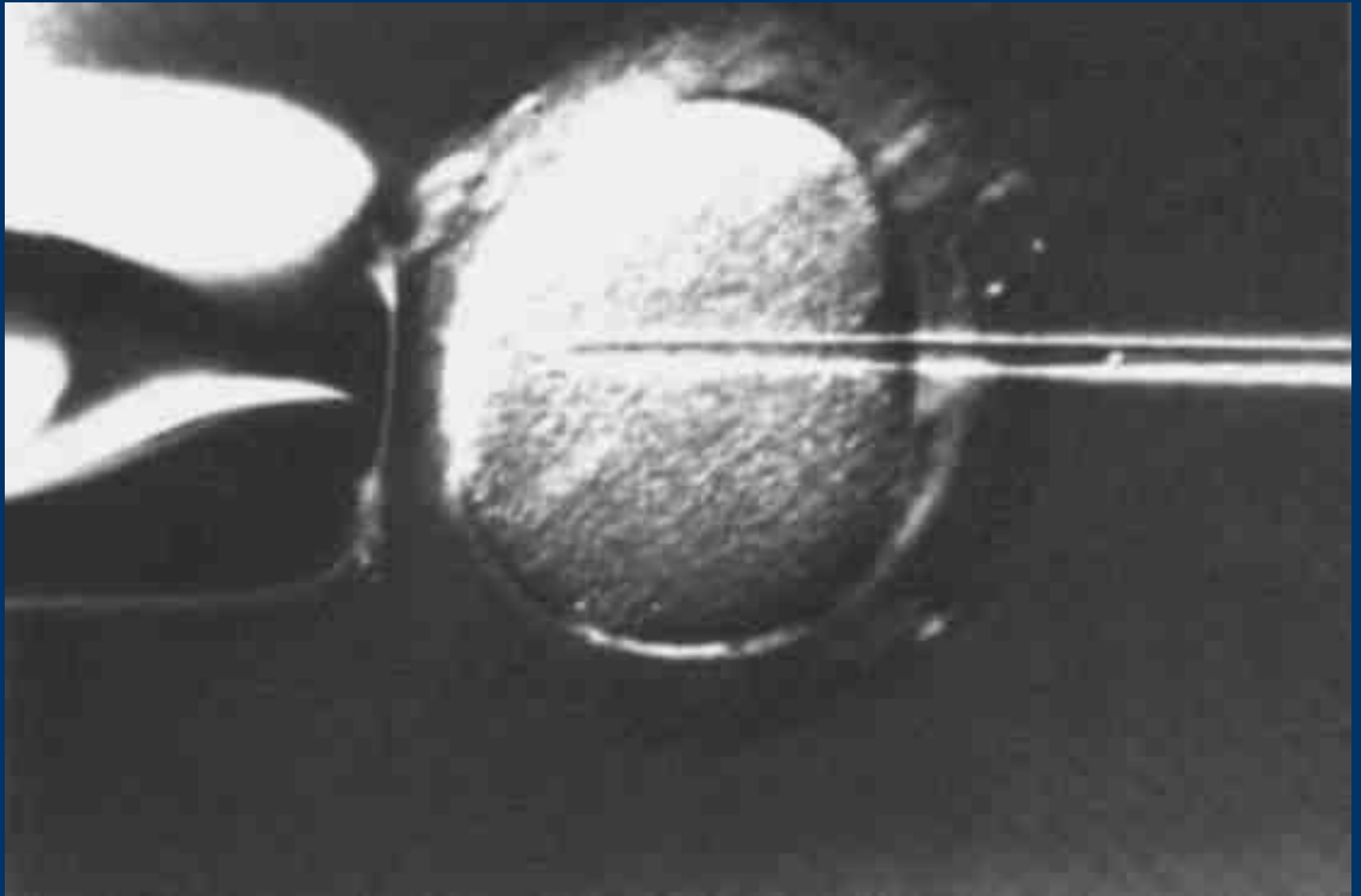
The old Alexandria medical school





The uterus (after Soranos of Ephesus)

Intracytoplasmic sperm injection (ICSI)



Results of ART in the USA in 2001

	IVF	GIFT	ZIFT
N of cycles	79,042	340	661
N of pregnancies	25,949	89	217
Pregnancy rate/retrieval	31.6%	21.9%	31%
Singleton delivery	64.1%	69.2%	72.8%
Rate of ectopic pregnancy	1.8%	1.8%	4.3%

SART, ASRM, Fertil Steril 87(6): 1253-66, 2007

Cumulative pregnancy rate after 3 IVF cycles

Study	CPR
De Mouzon et al, 1998	24.4%
Ubaldi et al, 2004 (>38 years)	42.8%
Check et al, 2002	44%
Shroder et al, 2004	53.3%
Engmann et al, 1999	57.8%
Shulman et al, 2002 (testicular sperm)	61.8%
Olivius et al, 2002	65.5%
Ubaldi et al, 2004 (<38 years)	74%
Shulman et al, 2002 (ejaculated sperm)	80.44%
Lurie et al, 2001	88%

Approaches to improve success in IVF and ICSI

- Refining stimulation protocols
 - Refining oocyte retrieval
- Refining laboratory techniques
 - Refining embryo selection
- Refining embryo transfer technique
- Improving endometrial receptivity
- Improving the implantation capacity of the embryo

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Refining the embryo transfer technique

1. Position during embryo transfer
 2. General anaesthesia
3. Gentle and atraumatic technique
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5. Intrauterine or intratubal transfer
 6. Ultrasound guidance
 7. Full bladder
8. Removing cervical mucus
9. Flushing the cervical canal
10. Avoiding the tenaculum

Refining the embryo transfer technique

11. Soft catheter
12. Air in the transfer catheter
13. Cleavage stage or blastocyst transfer
 14. Assisted hatching
 15. Site of embryo deposition
 16. Waiting 30 seconds
 17. Fibrin sealant
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 19. Routine antibiotics
20. Experience of the clinician

Evidence-based medicine

Level A – The recommendation based on good and consistent scientific evidence (RCT)

Level B – The recommendation is based on limited or inconsistent scientific evidence (CT, cohort, case control)

Level C – The recommendation is based primarily on consensus and expert opinion

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Position of the patient during embryo transfer (Englert et al, 1986 - CT)

	Dorsal (n=50)	Knee to chest (n=50)	P value
Failures	1	5	NS
Pregnancies	14/49	9/45	NS
Pregnancy rate	28.5%	20.0%	NS

Englert et al, J In Vitro Fert Embryo Transf, 3:243-6, 1986

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ET under general anaesthesia (van der Ven, 1988 - CT)

	General anaesthesia	No anaesthesia	P value
Pregnancies	151/795	127/603	NS
Pregnancy rate	19%	21%	NS

Van der Ven et al, Hum Reprod 3 (Suppl 2):81-3, 1988

Effect of acupuncture (RCT)

	Acupuncture (n = 80)	No acupuncture (n = 80)	P value
Pregnancy rate	42.5 %	26.3 %	<0.03

Paulus et al, Fertil Steril 77: 721, 2002

Effect of acupuncture (RCT)

	Acupuncture (n = 95)	No acupuncture (n = 87)	P value
Clinical pregnancy rate	39 %	26 %	<0.05
Ongoing pregnancy rate	36 %	22 %	<0.05

Westergaard et al, Fertil Steril 85: 1341, 2006

Effect of acupuncture (RCT)

	Acupuncture (n = 114)	No acupuncture (n = 114)	P value
Clinical pregnancy rate	31 %	23 %	<0.05
Ongoing pregnancy rate	28 %	18 %	NS

Smith et al, Fertil Steril, April 2006, [Epub ahead of print]

Refining the embryo transfer technique

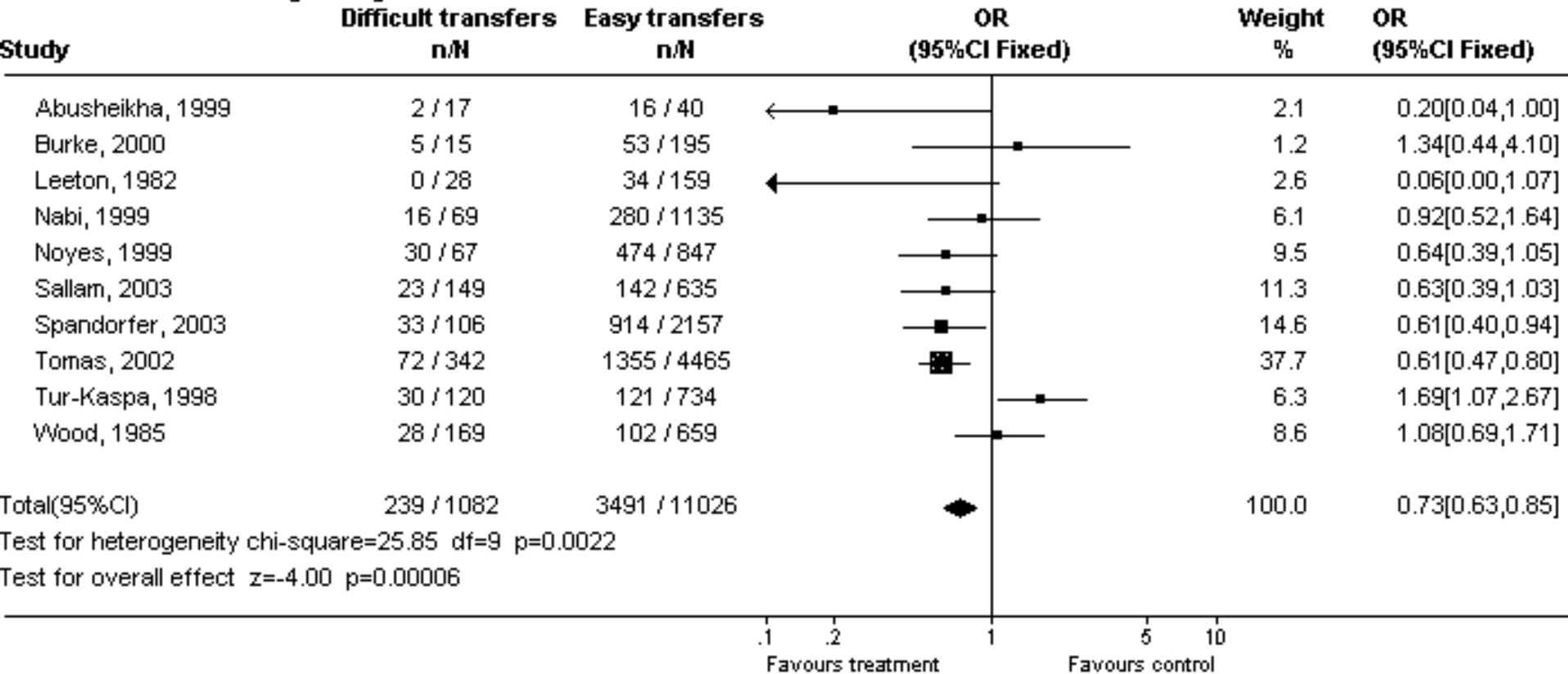
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Pregnancy rates with difficult transfers

(Sallam et al, 2004)

Comparison: 01 Difficult versus easy transfers

Outcome: 01 Pregnancy rate

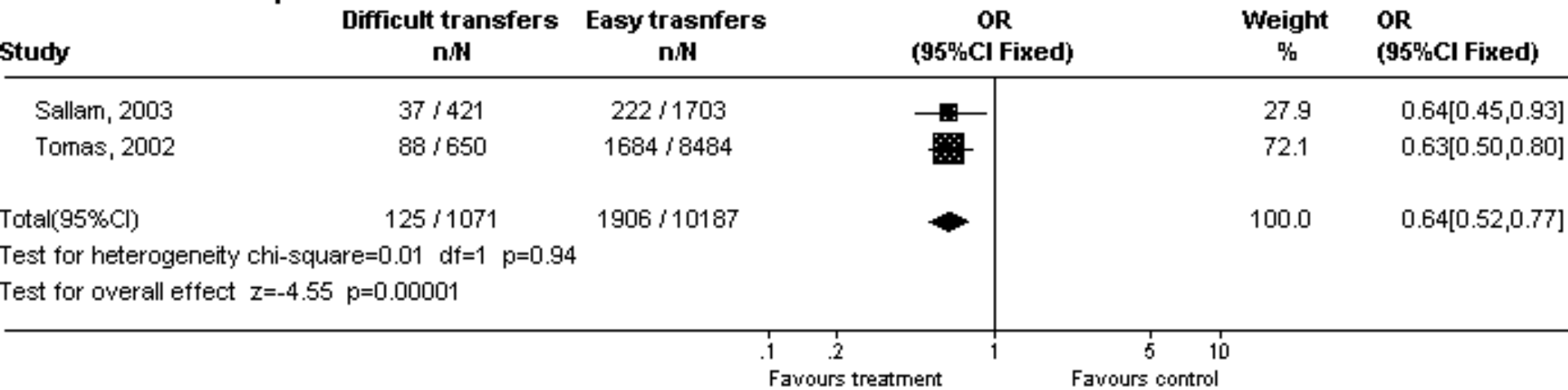


Sallam et al, Fertil Steril, 81 (Supplement 3): 22, 2004

Implantation rates with difficult transfers (Sallam et al, 2004)

Comparison: 01 Difficult versus easy transfers

Outcome: 02 Implantation rate



Sallam et al, Fertil Steril, 81 (Supplement 3): 22, 2004

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Dummy (trial) embryo transfer

Study	n	Pregnancy rate	Implantation rate
Sharif et al, 1995 (CT)	113	45.1 %	20.6 %
Mansour et al, 1990 (RCT)	167	22.8 %	7.2 %

Dummy (trial) embryo transfer (Mansour et al, 1990 - RCT)

	Dummy transfer (n= 167)	Control group (n= 168)	P
Pregnancy rate	22.8 %	13.1%	<0.05
Implantatio n rate	7.2 %	4.3%	<0.05

Mansour et al, Fertil Steril, 54: 678-81, 1990

Uterine position at mock ET

(Henne and Milki, 2004 (OS))

Uterine position at mock ET	AV at actual ET	RV at actual ET
AV 623	608 (98%)	15 (2%)
RV 213	118 (55%)	95 (45%)

Henne and Milki, Hum Reprod 19: 570-2, 2004

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Intrauterine versus intratubal ET (Habana and Palter, 2001 - Meta-analysis)

	ZIFT	IVF-ET	OR (95% CI)
Pregnancy/ retrieval	42/212	48/220	0.88 (0.55-1.40)
Pregnancy/ transfer	53/162	60/186	0.99 (0.62-1.57)
Implantation rate	72/481	63/523	1.25 (0.87-1.80)
Ongoing preg/transfers	39/132	30/150	1.61 (0.93-2.78)

Habana and Palter, Fertil Steril, 76: 286-93, 2001

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Ultrasound-guided embryo transfer (Strickler et al, 1985)



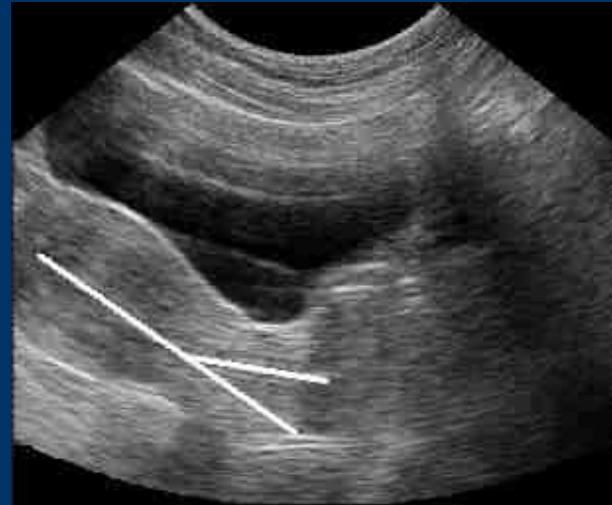
Strickler et al, Fertil Steril 43: 54-61, 1985

Measuring the uterocervical angle prior to ET

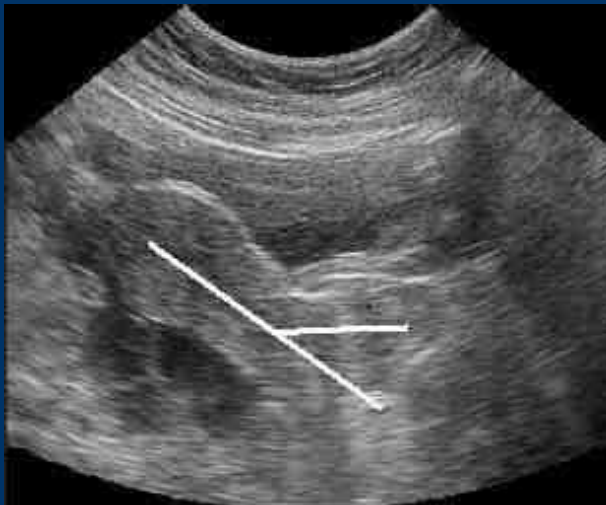
12.2 %



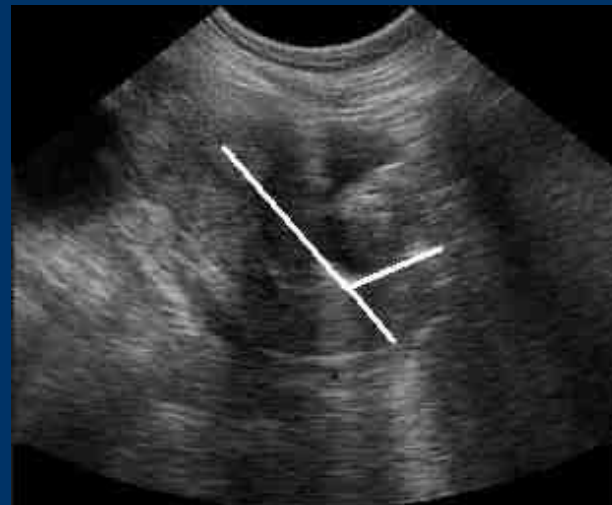
10 %



37.2 %



40.6 %



Sallam et al, Hum Reprod, 17: 1767-72, 2002

Ultrasound-guided embryo transfer

Study	Trial	n	No U/S	U/S	P
Kojima et al, 2001	CT	846	28.9%	13.1%	<0.01
Prapas et al, 2001	CT	1069	47%	36%	<0.001
Coroleu et al, 2000	RCT	362	50%	33.7%	<0.002
Wood et al, 2000	CT	518	38%	25%	<0.002
Lindheim et al, 1999	CT	137	63.1%	36.1%	<0.05

Ultrasound-guided embryo transfer

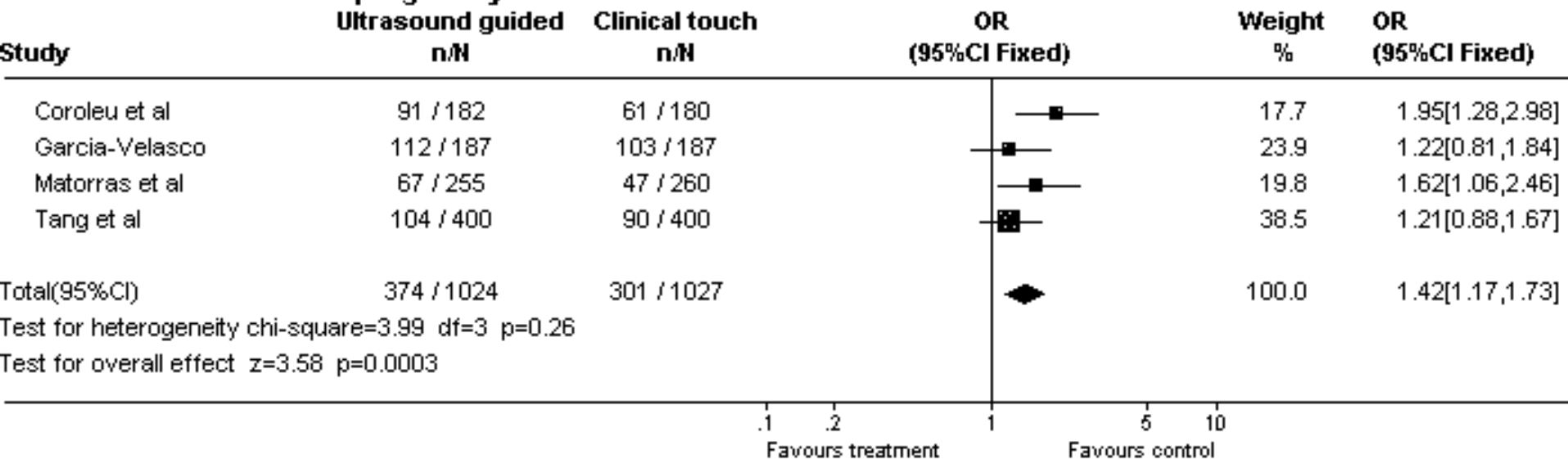
Study	Trial	n	U/S	No U/S	P
Kan et al, 1999	CT	187	37.8%	28.9%	NS
Prapas et al, 1995	RCT	132	36.1%	22.6%	NS
Al-Shawaf et al, 1993	CT	178	30.3%	29.0%	NS
Hurley et al, 1991	RCT	340	20.2%	17.5%	NS
Tang et al, 2001	RCT	800	26.0%	22.5%	NS

Ultrasound-guided embryo transfer

Clinical pregnancy rate (Meta-analysis)

Comparison: 01 Ultrasound versus clinical touch

Outcome: 01 Clinical pregnancy rate

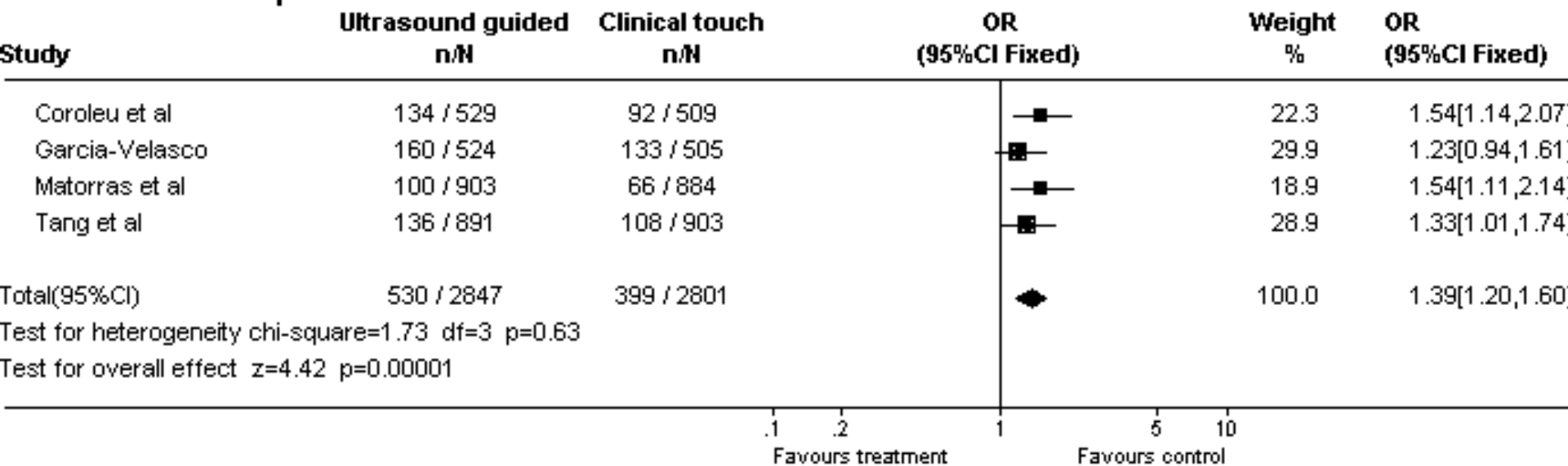


Sallam and Sadek, Fertil Steril, 80: 1042-6, 2003

Ultrasound-guided embryo transfer Implantation rate (Meta-analysis)

Comparison: 01 Ultrasound versus clinical touch

Outcome: 02 Implantation rate

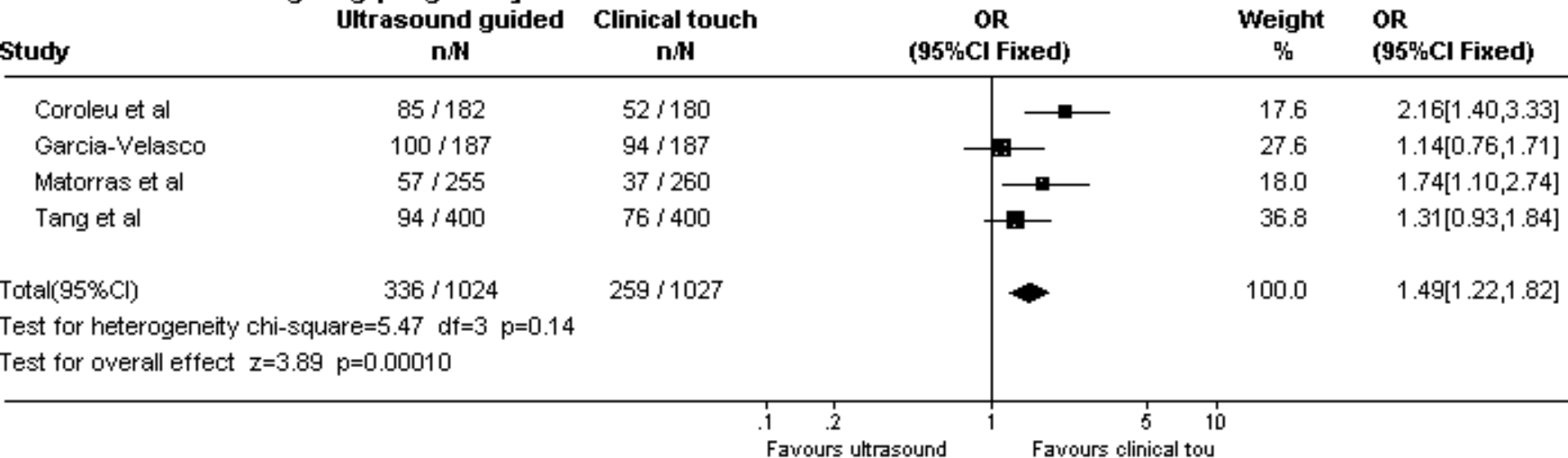


Sallam and Sadek, Fertil Steril, 80: 1042-6, 2003

Ultrasound-guided embryo transfer

Ongoing pregnancy rate (Meta-analysis)

Comparison: 01 Ultrasound versus clinical touch
 Outcome: 03 On-going pregnancy rate



Sallam and Sadek, Fertil Steril, 80: 1042-6, 2003

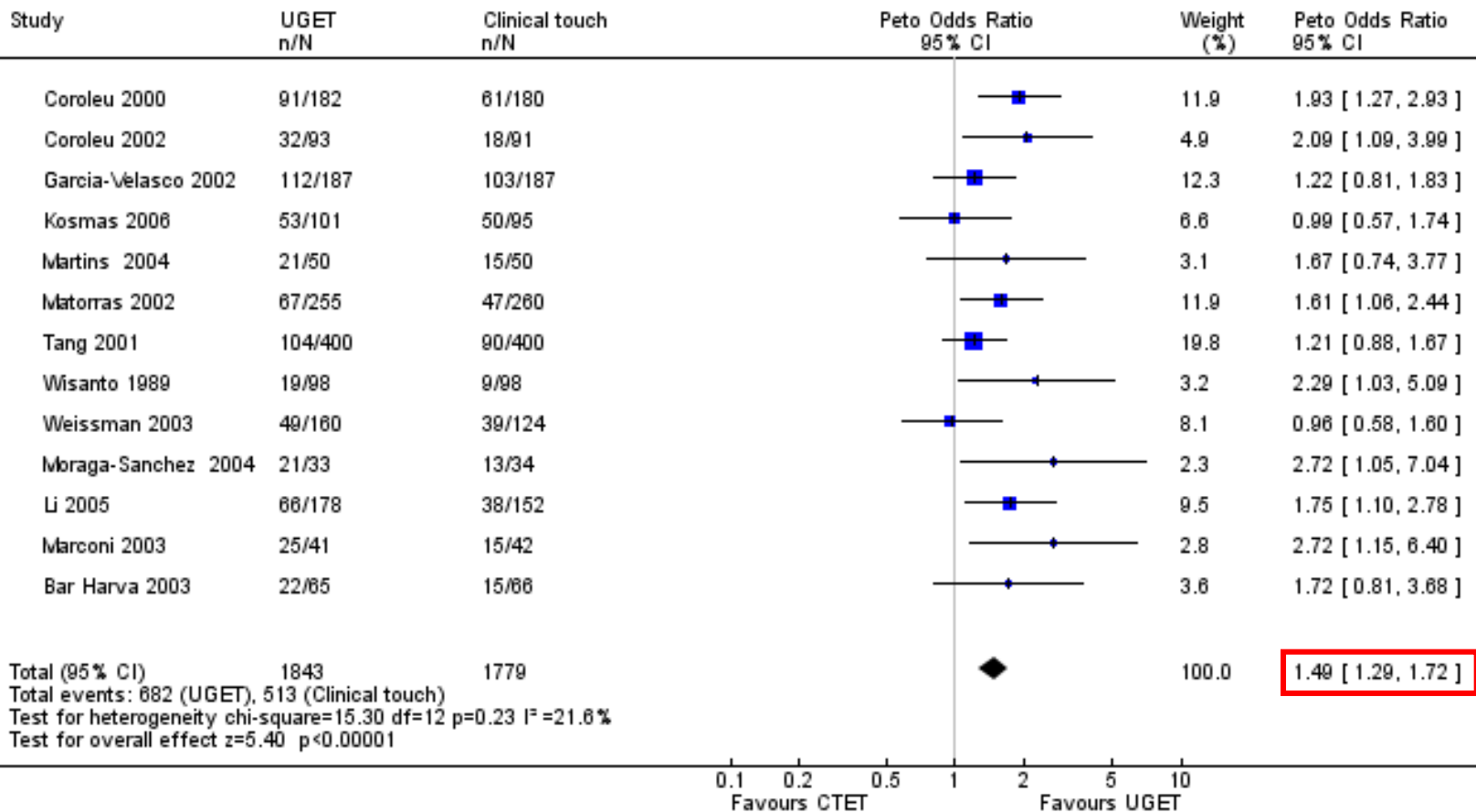
Ultrasound-guided embryo transfer (Buckett, 2003 - meta-analysis)

Outcome measure	CI (95% CI)
Clinical pregnancy rate	1.44 (1.18 – 1.74)
Implantation rate	1.38 (1.20 – 1.60)

Buckett, Fertil Steril, 80: 1037-41, 2003

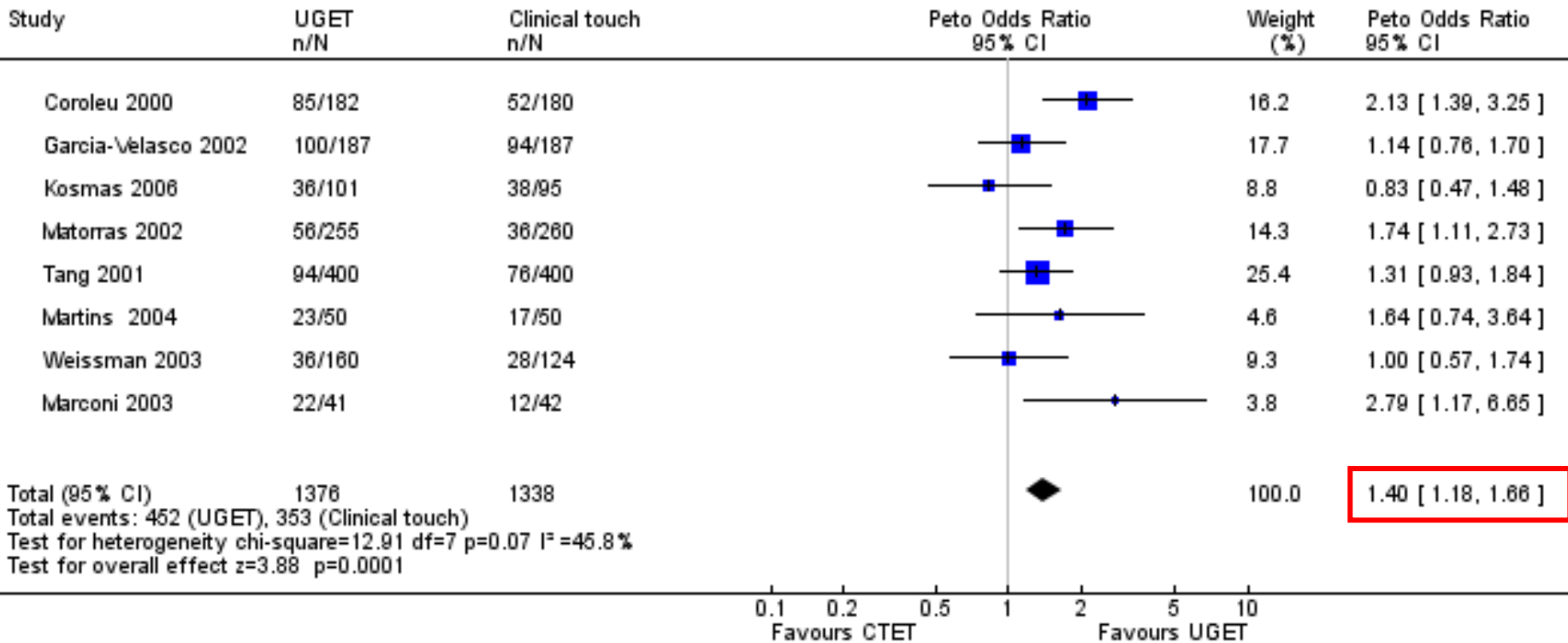
Cochrane review, CPR (Brown et al, 2007)

Review: Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women
 Comparison: 01 Pregnancy
 Outcome: 02 Clinical pregnancies (per woman randomised)



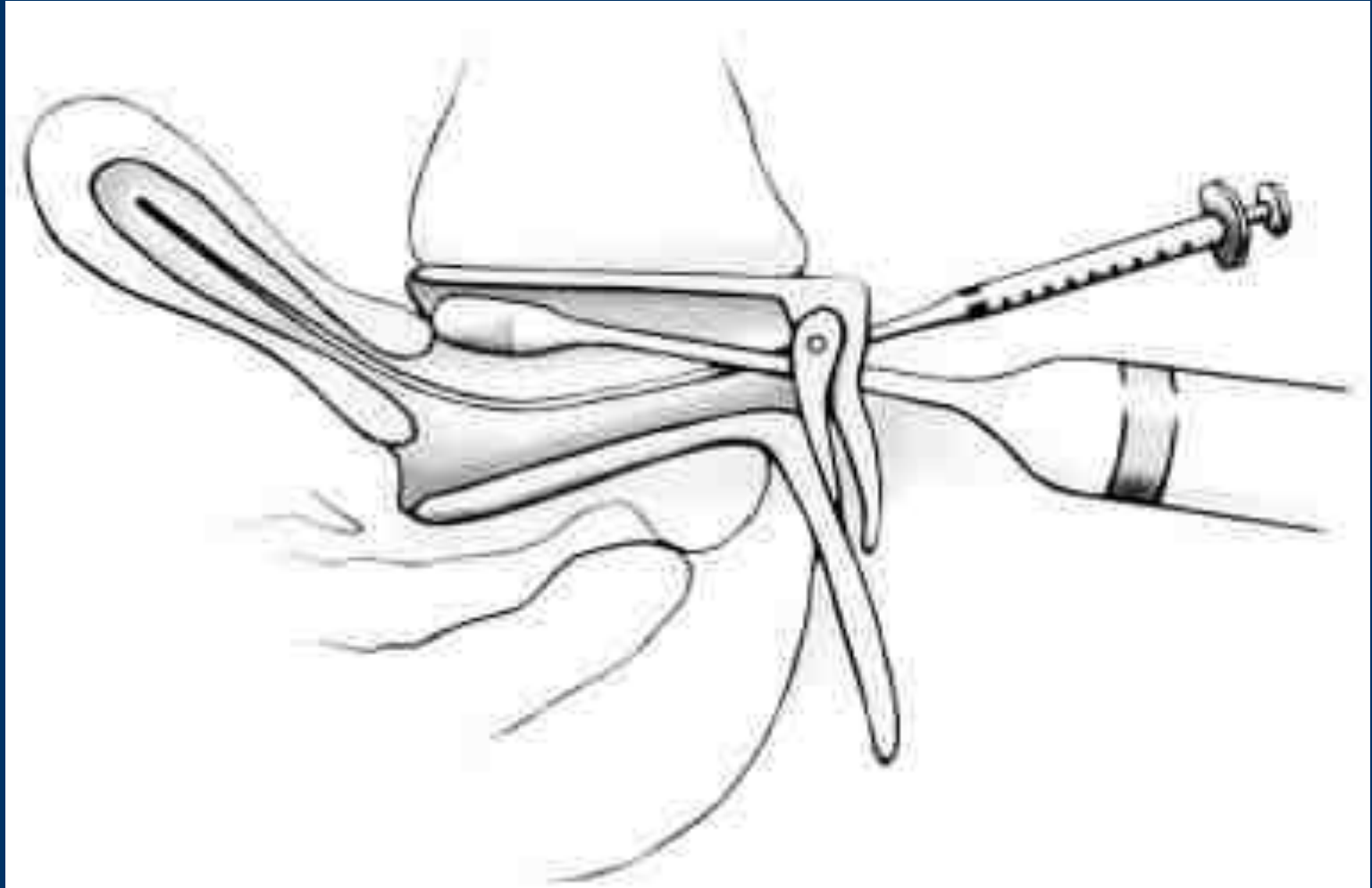
Cochrane review, LBR (Brown et al, 2007)

Review: Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women
 Comparison: 01 Pregnancy
 Outcome: 01 Live births versus ongoing pregnancies (per woman randomised)



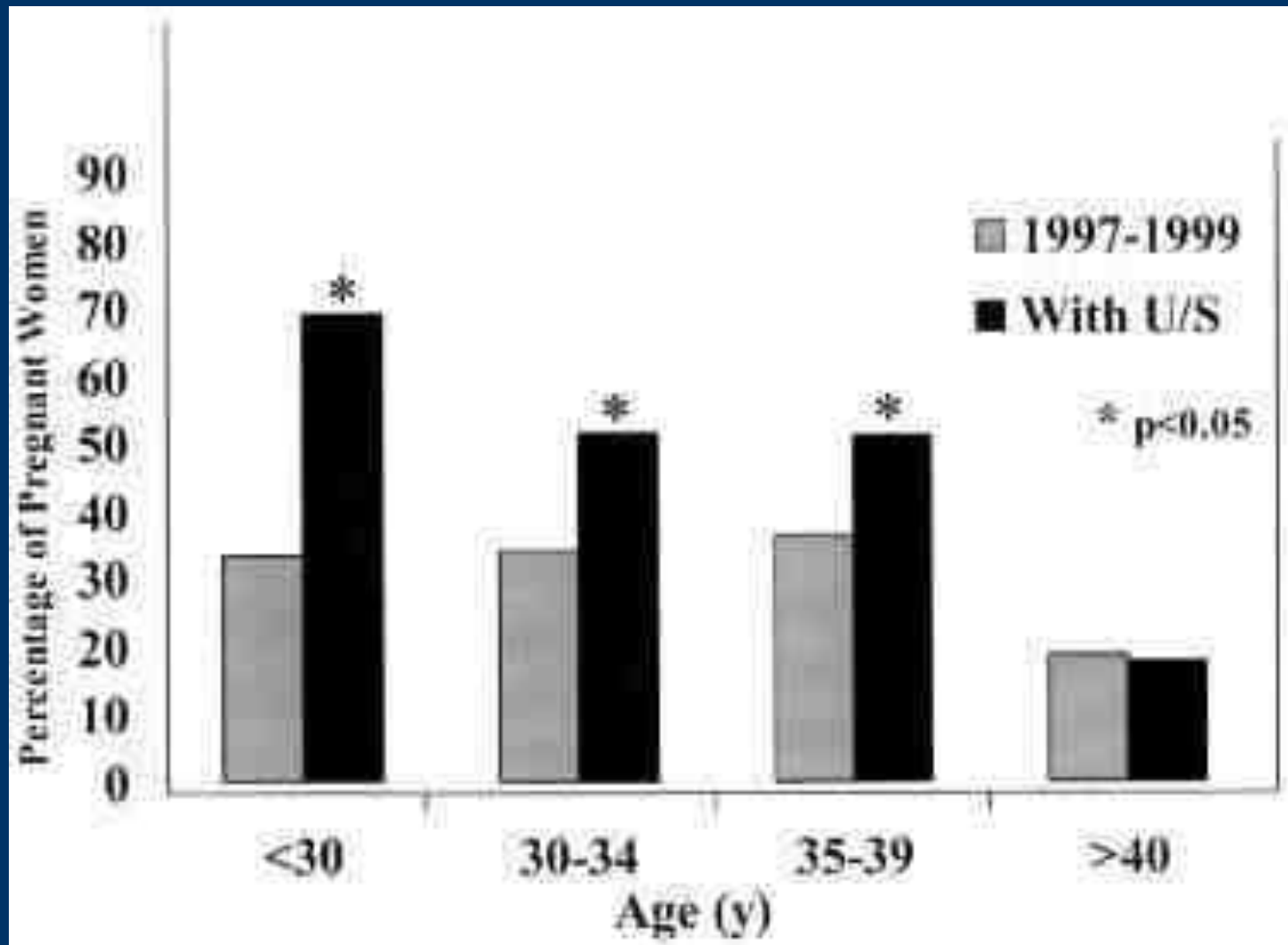
Brown et al, Cochrane Database 1:CD006107, 2007

Transvaginal ultrasound-directed ET



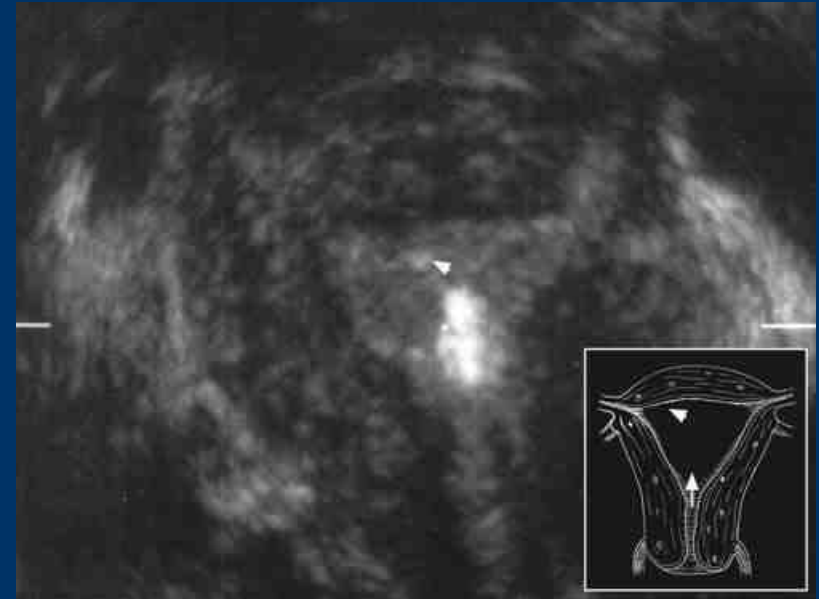
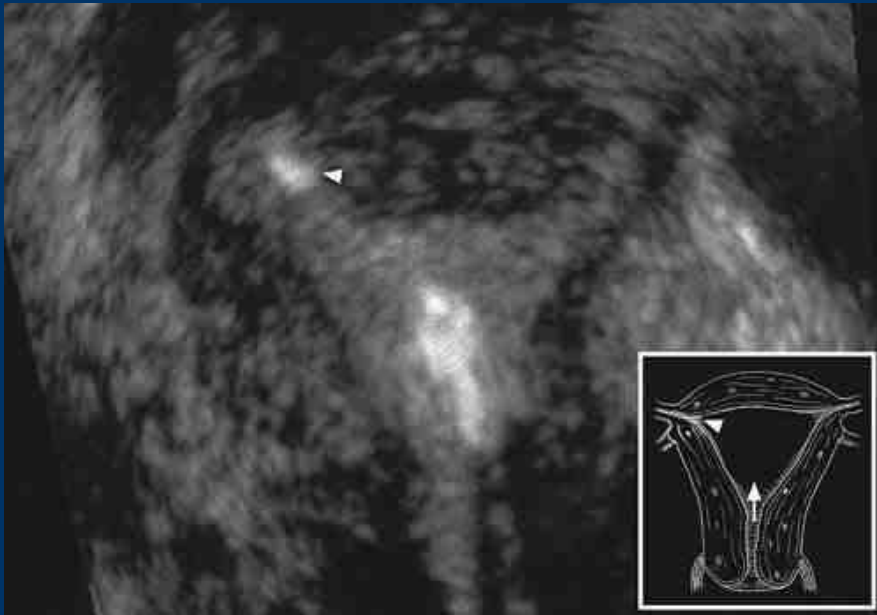
Anderson et al, Fertil Steril 77 (4): 769, 2002

Vaginal ultrasound-directed ET (CCT)



Anderson et al, Fertil Steril 77 (4): 769, 2002

Three-dimensional ultrasound-guided embryo transfer



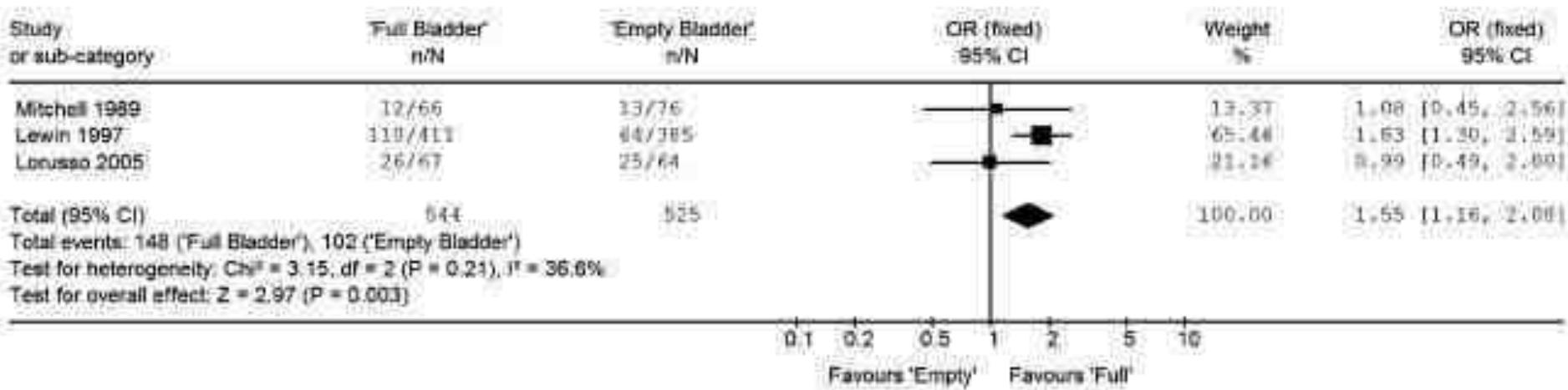
Letterie, Am J Obstet Gynecol 192: 1983, 2005

Refining the embryo transfer technique

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Embryo transfer with a full bladder

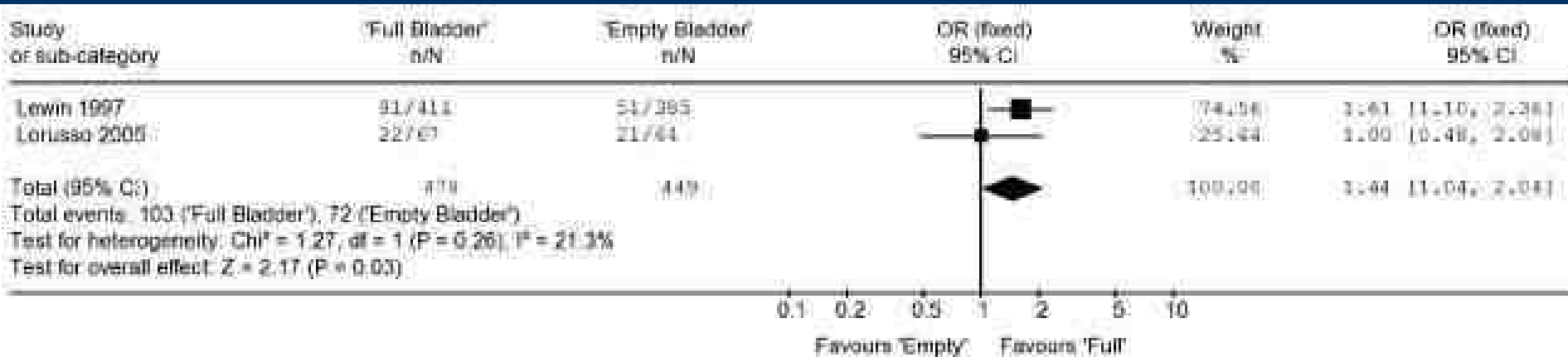
Clinical pregnancy rate



Abou-Setta. Acta Obstet Gynecol Scand 86(5):516-22, 2007

Embryo transfer with a full bladder

Live birth rate



Abou-Setta. Acta Obstet Gynecol Scand 86(5):516-22, 2007

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Removing cervical mucus prior to embryo transfer

Study	End point	Mucus not aspirated	Mucus aspirated	P value
Mansour et al, 1994 (CT)	Expulsion of dye	57%	23%	0.01
Nabi et al, 1997 (CT)	Retention of embryos	17.8%	3.3%	0.000001

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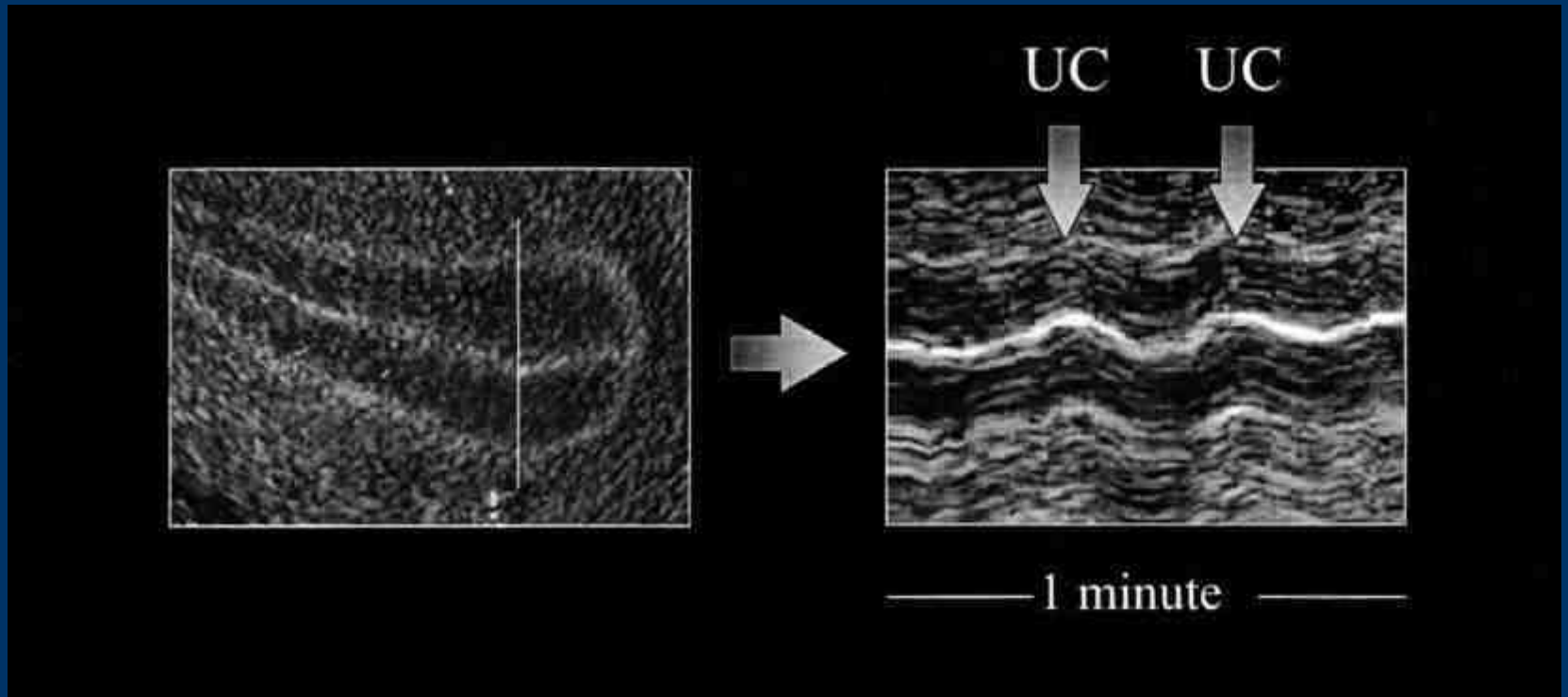
Flushing the cervical canal with culture medium prior to ET

	Flushing	No flushing	P
MacNamee et al (1999) (CT) (148/145)	36.2 %	25.3 %	<0.05
Sallam et al (2000) (RCT) (99/99)	27.52 %	22.15 %	0.2834

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Uterine contractions during embryo transfer (Fanchin et al, 1998)



Fanchin et al, Hum Reprod 13: 1968-74, 1998

Avoiding the use of a tenaculum

(Lesny et al, 1999 – OS-) (n=20)

Junctional zone	Before tenaculum	After tenaculum	P value
contractions			
Cervico-fundal	4	34	0.005
Fundo-cervical	0	9	NS
Random	24	45	0.001
contractions			
Opposing	35	58	0.07
contractions			
Total	63	146	0.0003

Lesny et al, Hum Reprod 14: 2367-70, 1999

Sexual intercourse after embryo transfer (RCT - Tremellen et al, 2000)

	Intercourse	No intercourse	P
Pregnancy rate	23.6 %	21.2 %	NS
Implantation rate	11.01 %	7.69 %	0.036

Tremellen et al, Hum Reprod 15: 2653-8, 2000

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14. Assisted hatching

15. Site of embryo deposition

16. Waiting 30 seconds

17. Fibrin sealant

18. Bed rest after transfer

19. Routine antibiotics

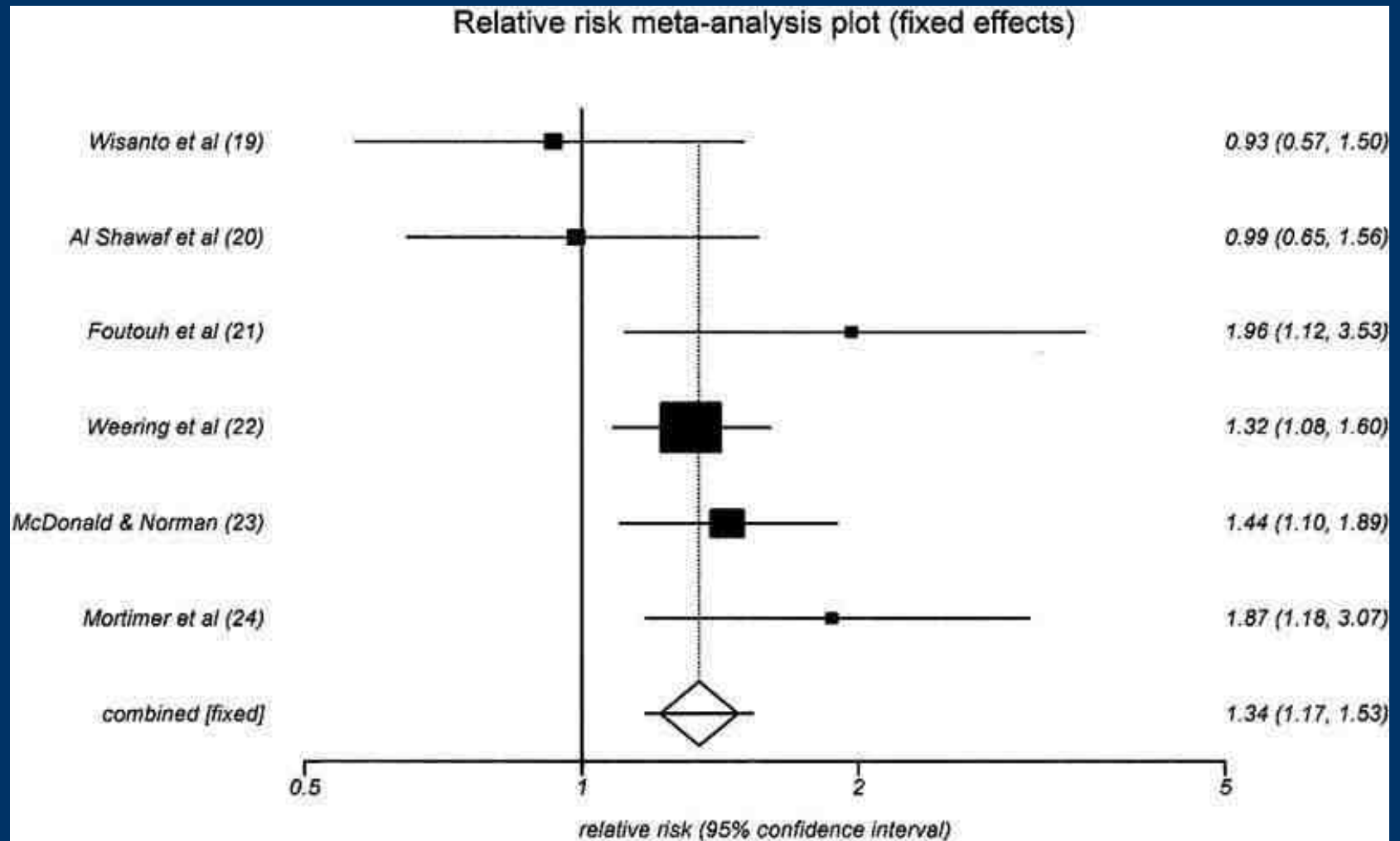
20. Experience of the clinician

Soft catheters versus rigid catheters

Soft catheters	Rigid catheters
<ul style="list-style-type: none">• Cook• Wallace	<ul style="list-style-type: none">• TDT• Frydman• Tomcat• Rocket

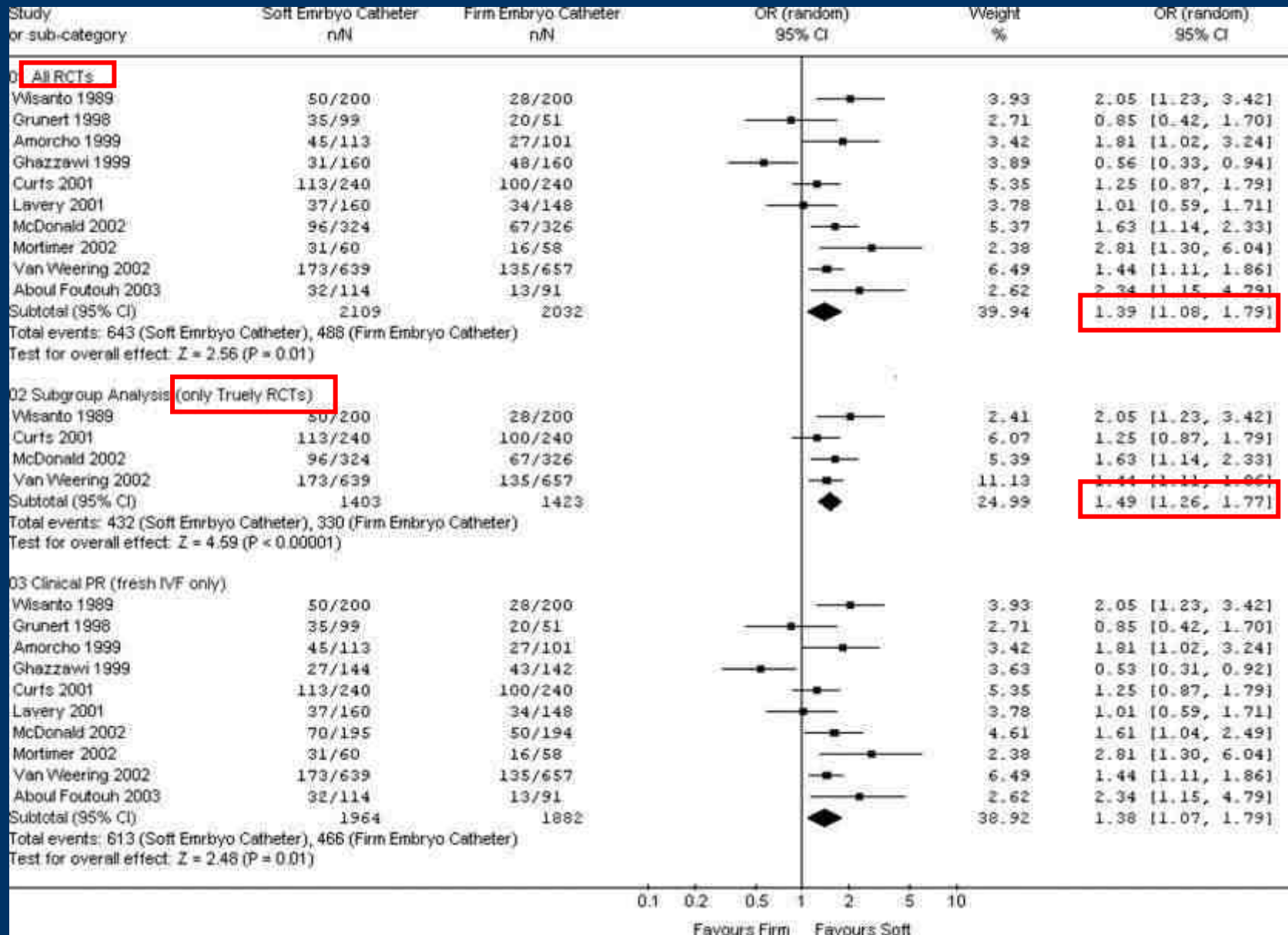
Buckett, Fertil Steril 85: 728, 2006

Soft catheters versus rigid catheters (CPR)



Buckett, Fertil Steril 85: 728, 2006

Soft versus firm ET catheters (CPR)



Soft versus firm catheters under ultrasound guidance (Meta-analysis)

Outcome measure	Soft catheters	Firm catheters	P value
Clinical pregnancy rate	44.6%	34.6%	NS
Implantation rate	23.2%	18.9%	NS
Ongoing pregnancy rate	38.5%	27.7%	NS

Aboufotouh et al, Fertil Steril 17 July 2007 [Epub ahead of print]

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Air in the transfer catheter

(Moreno et al, 2004 RCT)

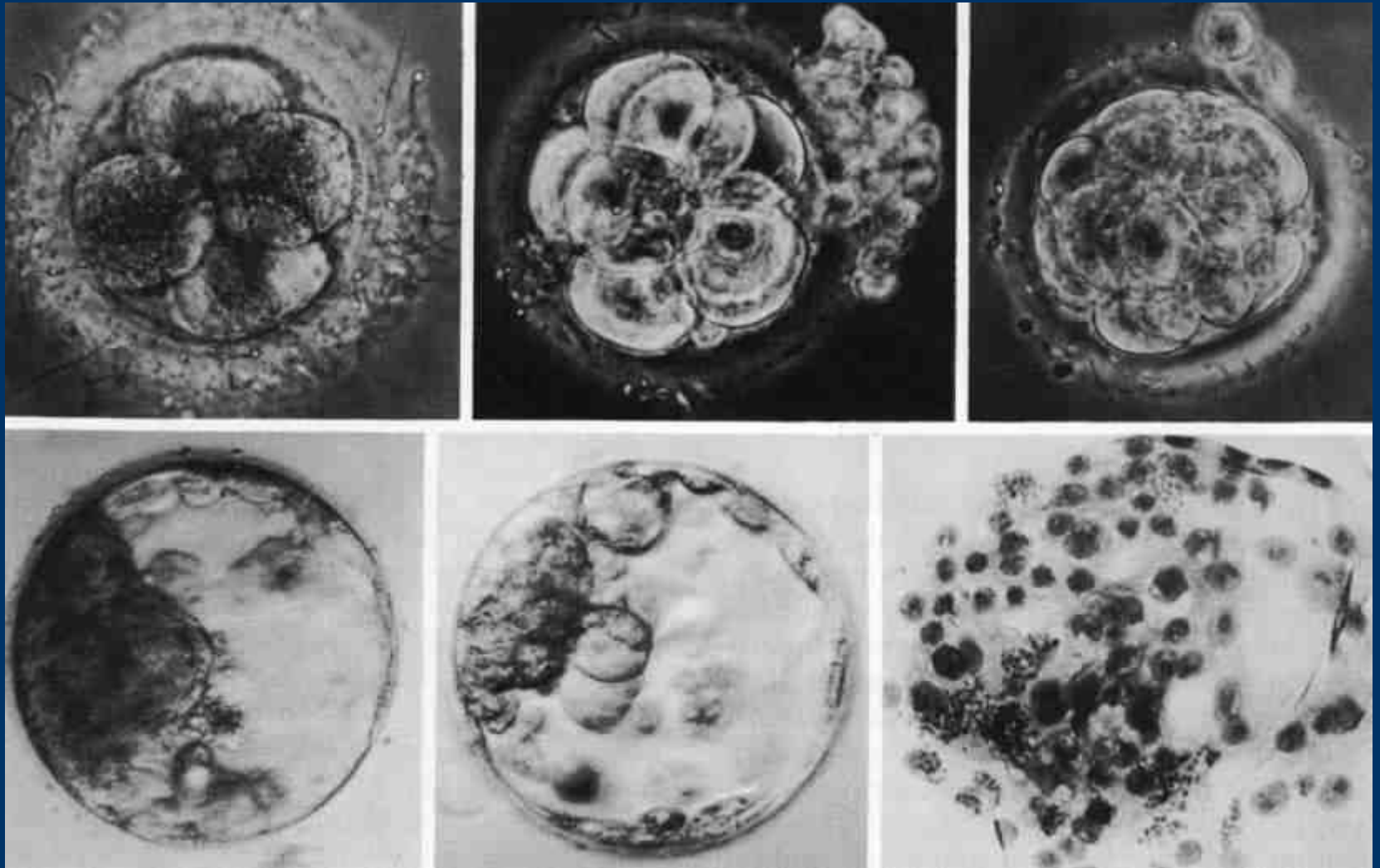
	Air in catheter (n = 52)	No air in catheter (n= 50)	P value
Pregnancy rate	42.3%	34%	NS
Implantation rate	24.4%	18.8%	NS

Moreno et al, Fertil Steril 81: 1366-70, 2004

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Stages of embryo development (Edwards and Brody, 1996)



Day 3 versus day 2

(Oatway et al, 2004 - Cochrane review)

Outcome measure	OR (95% CI)
Clinical pregnancy rate	1.26 (1.06 - 1.51) *
On-going pregnancy rate	1.05 (0.83 - 1.32)
Live birth rate	1.07 (0.84 - 1.37)

Oatway et al, Cochrane Database Syst Rev, CD004378, 2004

Blastocyst versus cleavage stage

(Blake et al, 2005 - Cochrane review)

Outcome measure	OR (95% CI)
Clinical pregnancy rate	1.05 (0.88 to 1.26)
Live birth rate	1.16 (0.74 to 1.44)
Multiple pregnancy rate	0.85 (0.63 to 1.13)

Blake et al, Cochrane Database, 19;(4):CD002118, 2005

Single blastocyst versus single cleavage stage transfer (RCT)

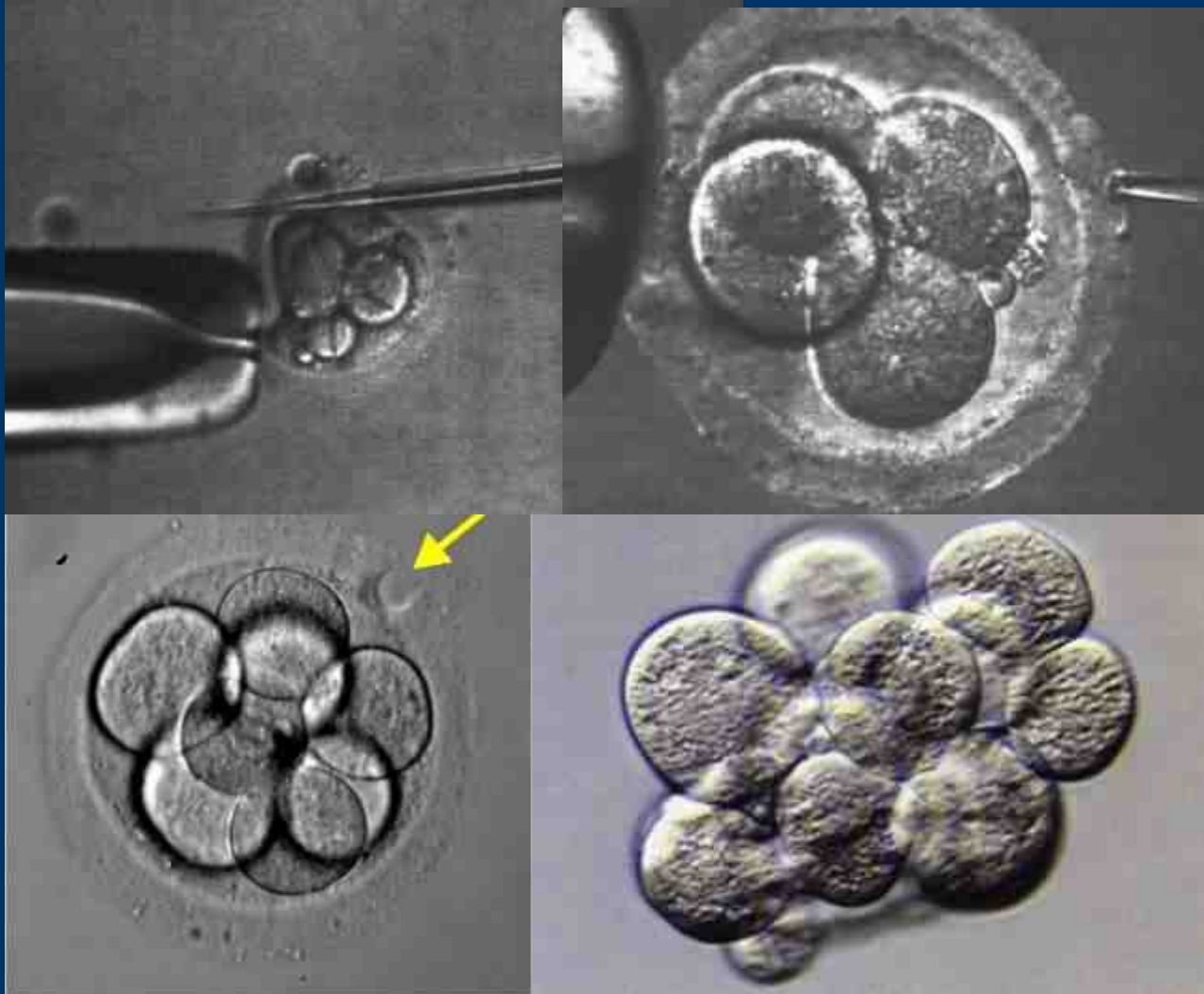
	Single blastocyst (n= 175)	Single cleavage stage ET (n = 176)	P value
Clinical pregnancy rate	23.1 %	23.3 %	0.04
Ongoing pregnancy rate	33.1 %	21.6 %	0.02
Delivery rate	32.0 %	21.6 %	0.03

Papanikolaou et al, N Eng J Med 354: 1139, 2006

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Assisted hatching

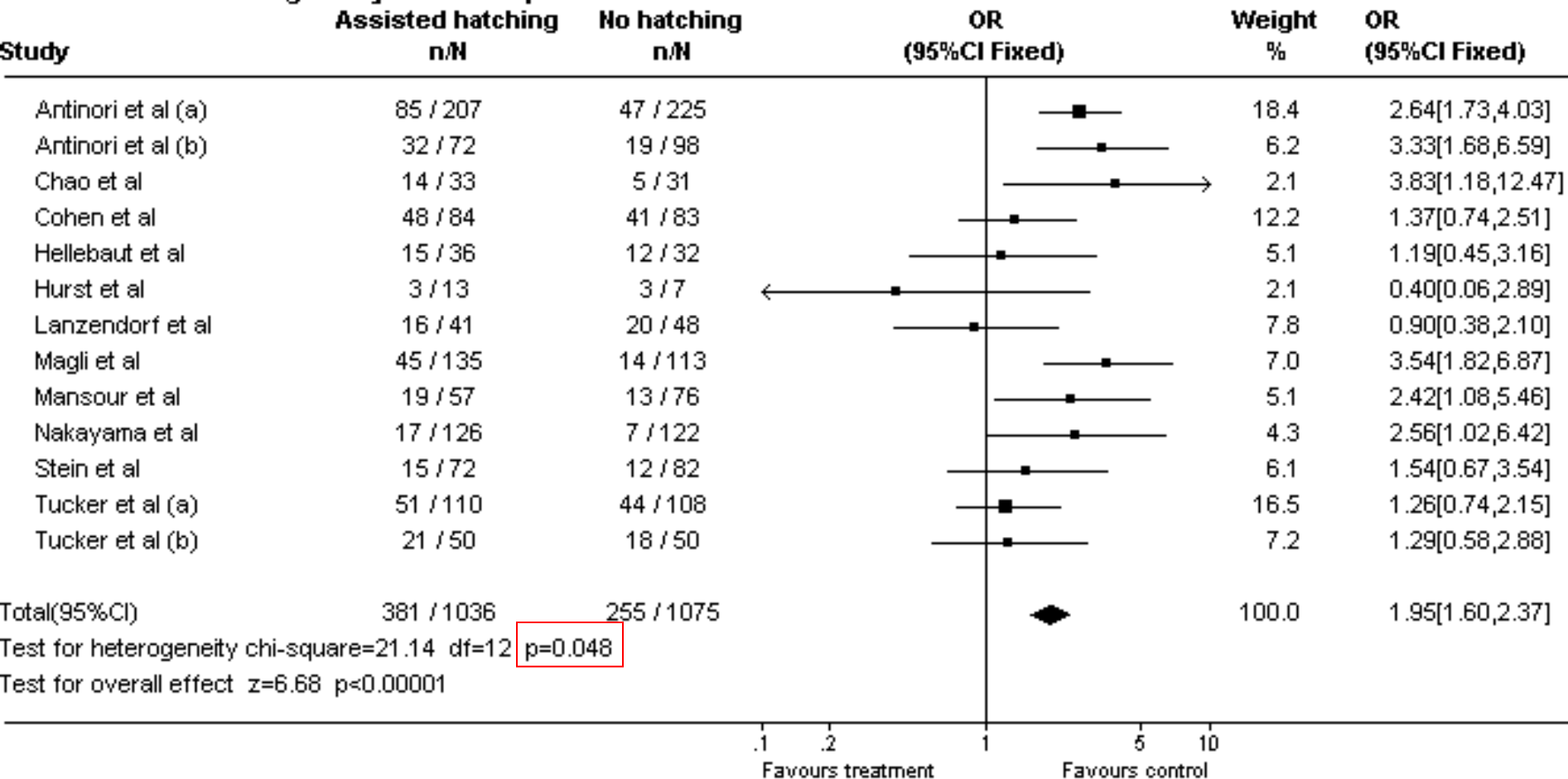


Assisted hatching v/s no hatching

Pregnancy rate - all patients (Sallam et al, 2003)

Comparison: 01 Assisted hatching versus no assisted hatching

Outcome: 01 Pregnancy rate - all patients



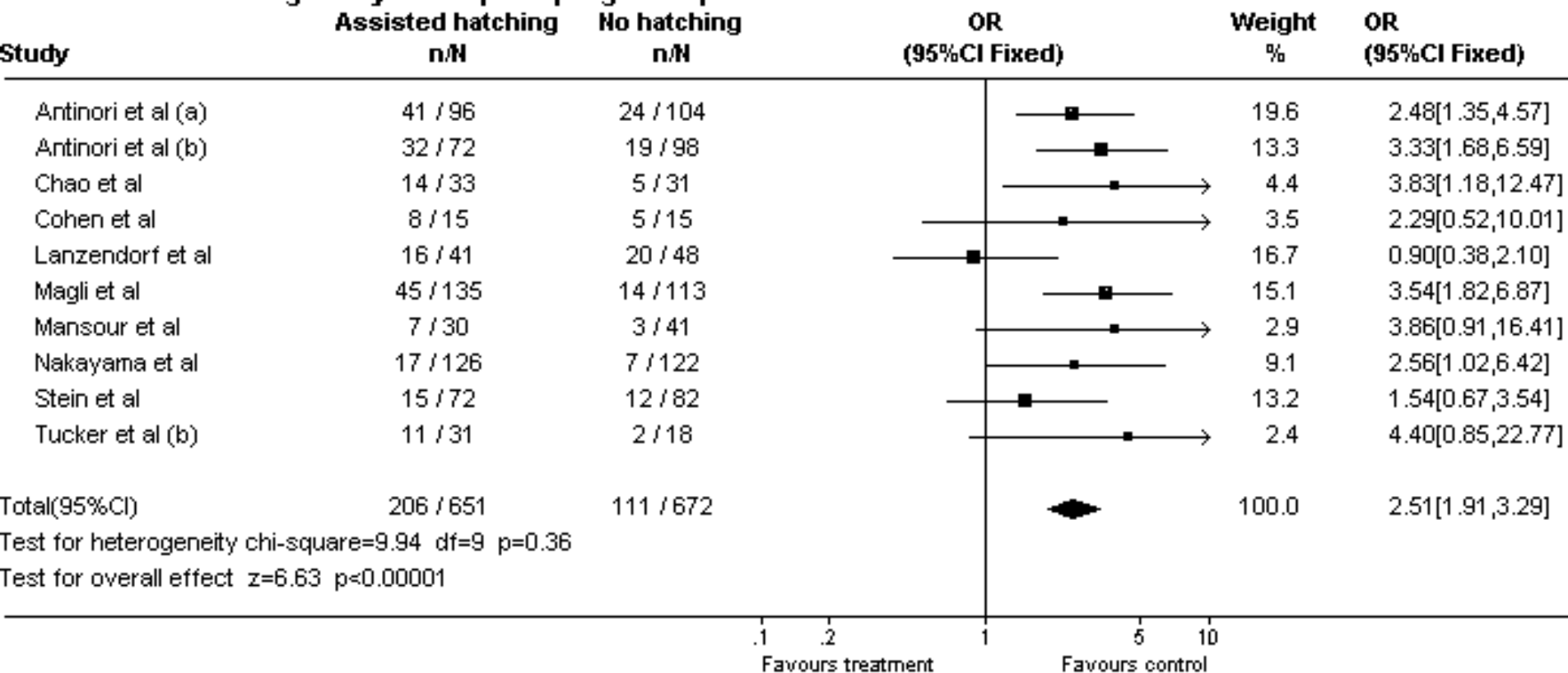
Sallam et al, J Assist Reprod Genet, 20: 332-42, 2003

Assisted hatching v/s no hatching

CPR - poor prognosis patients (Sallam et al, 2003)

Comparison: 01 Assisted hatching versus no assisted hatching

Outcome: 04 Pregnancy rate - poor prognosis patients



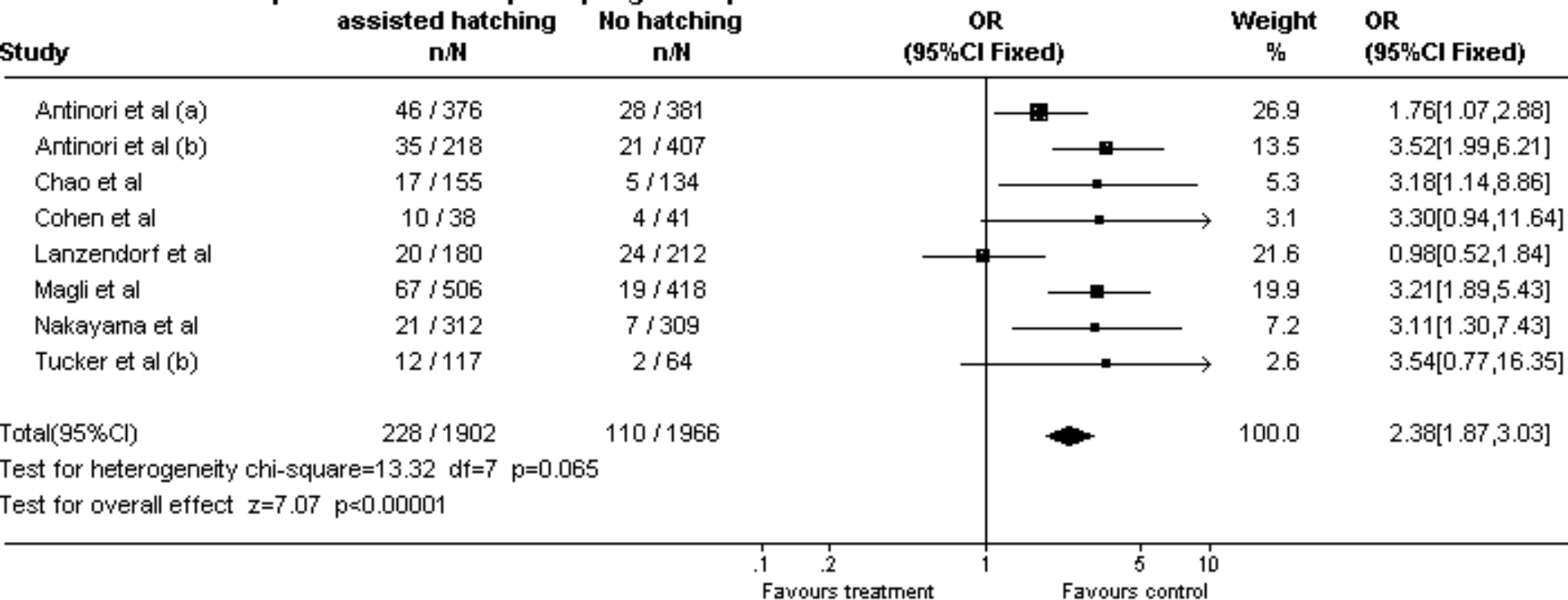
Sallam et al, J Assist Reprod Genet, 20: 332-42, 2003

Assisted hatching v/s no hatching

IR - poor prognosis patients (Sallam et al, 2003)

Comparison: 01 Assisted hatching versus no assisted hatching

Outcome: 05 Implantation rate - poor prognosis patients



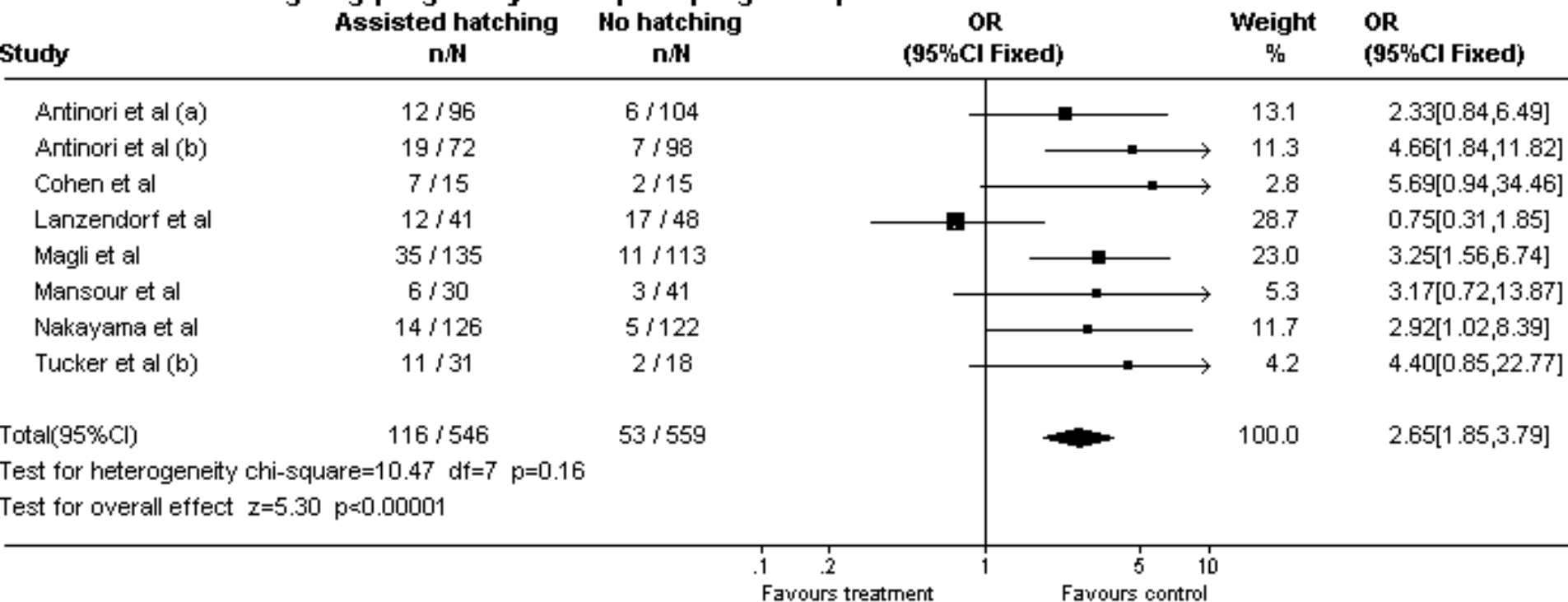
Sallam et al, J Assist Reprod Genet, 20: 332-42, 2003

Assisted hatching v/s no hatching

Ongoing pregnancy rate - poor prognosis patients

Comparison: 01 Assisted hatching versus no assisted hatching

Outcome: 06 On-going pregnancy rate - poor prognosis patients



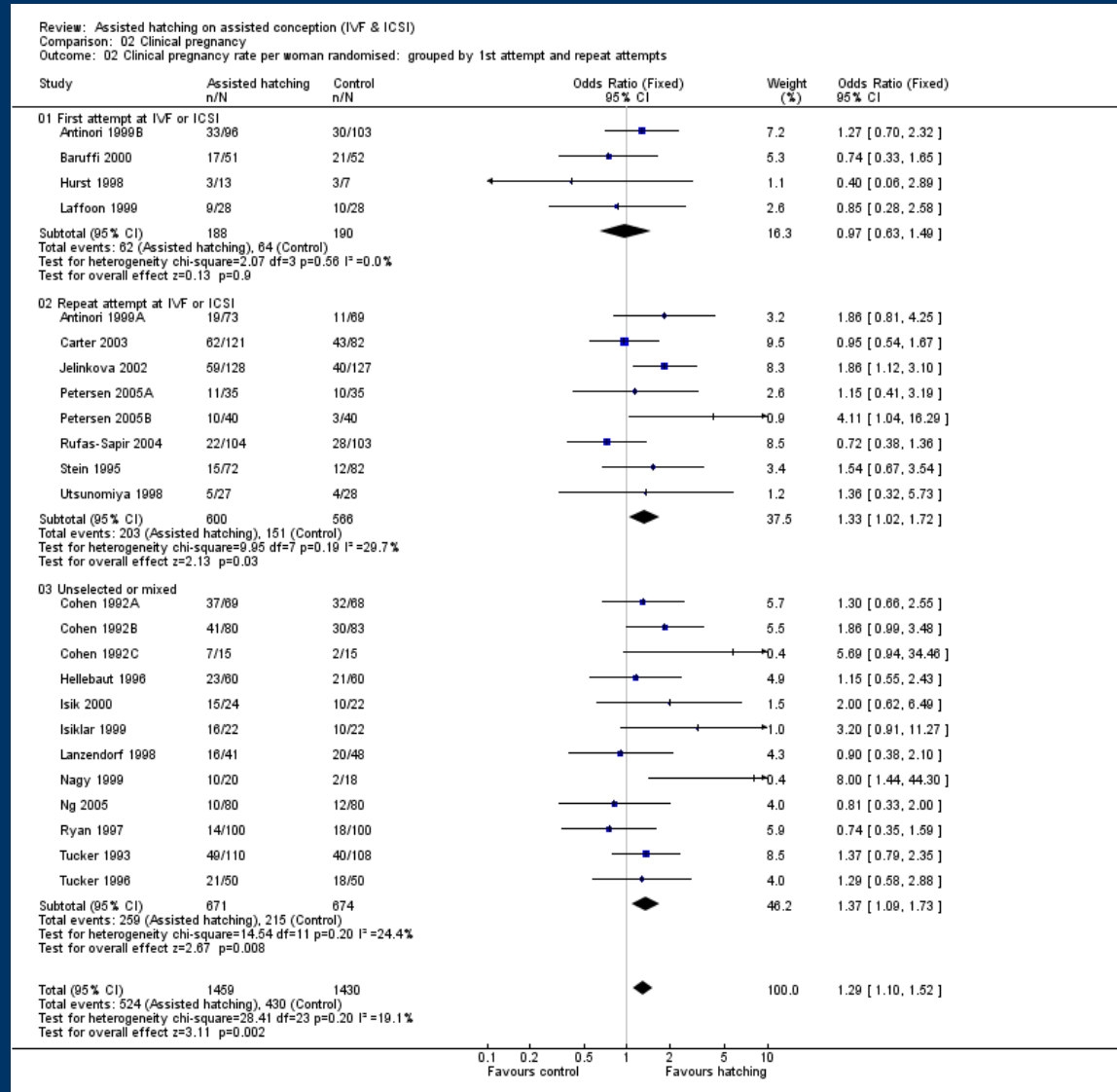
Sallam et al, J Assist Reprod Genet, 20: 332-42, 2003

Clinical pregnancy rate per woman

First attempt

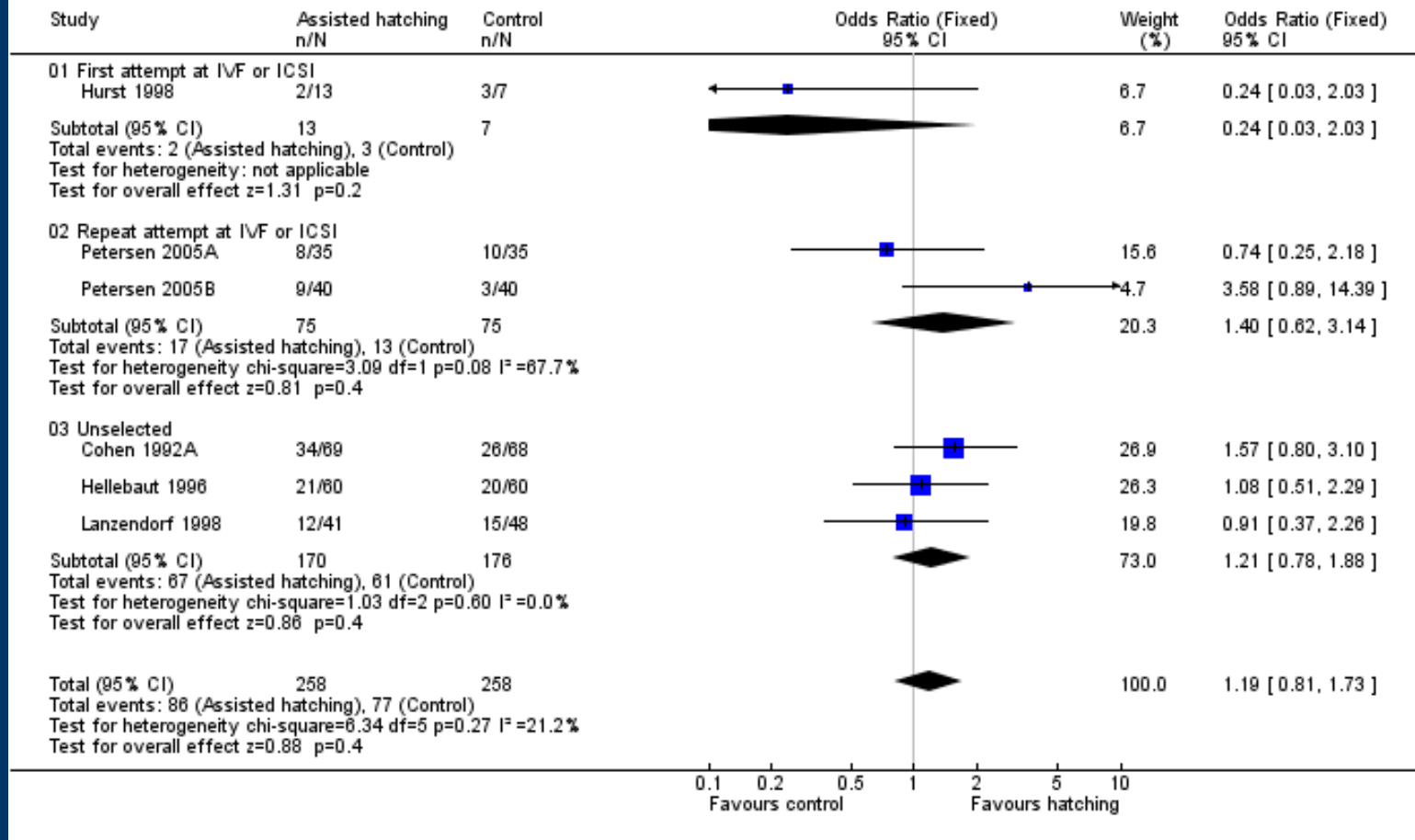
Repeated attempts

Mixed



Live birth rate per woman randomized

Review: Assisted hatching on assisted conception (IVF & ICSI)
 Comparison: 01 Live birth rate
 Outcome: 02 Live birth rate per women randomised: grouped by 1st attempt and repeat attempts



First attempt

Repeated attempts

Mixed

Refining the embryo transfer technique

11. Soft catheter
12. Air in the transfer catheter
13. Cleavage stage or blastocyst transfer
14. Assisted hatching
15. Site of embryo deposition
16. Waiting 30 seconds
17. Fibrin sealant
18. Bed rest after transfer
19. Routine antibiotics
20. Experience of the clinician

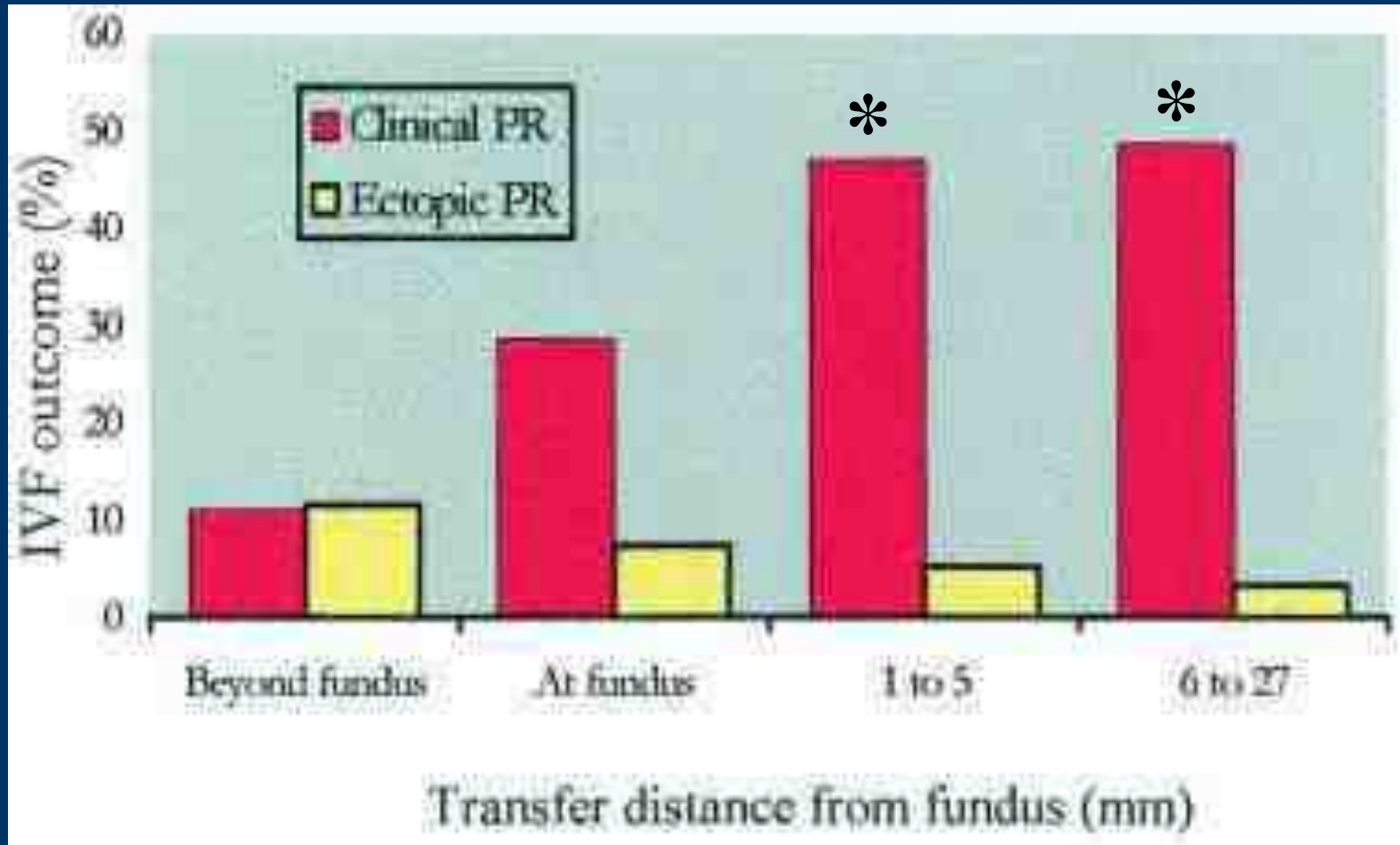
Site of embryo deposition (Coroleu et al, 2002 - RCT)

	Distance from fundus (mm)	Implantation rate
Group I	10.2 +/- 0.9	20.6%
Group II	14.6 +/- 0.7	31.3%*
Group III	19.3 +/- 0.8	33.3%*

* = statistically significant from group I

Coroleu et al, Hum Reprod 17: 341-6, 2002

Site of embryo deposition (Pope et al, 2004 - OS)



Pope et al, Fertil Steril 81: 51-8, 2004

Site of embryo deposition (Pope et al, 2004)

Regression analysis showed that for every additional millimeter embryos are deposited away from the fundus, the odds of clinical pregnancy increased by 11%.

Pope et al, Fertil Steril 81: 51-8, 2004

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Waiting 30 seconds after ET

(RCT - Martinez et al, 2001)

	No wait	30 sec wait	P value
No. of patients	51	49	
Pregnancy rate	60.8%	69.4%	NS

Martinez et al, Hum Reprod 16: 871-4, 2001

Time between loading and discharging the embryos (Matorras et al, 2004) (OS)

	<30 sec	31-60 sec	61- 120 sec	>120 sec	P value
n	113	214	76	47	
Pregnancy rate	38.9%	33.2%	31.6%	19.1%	<0.05
Implantation rate	21.2%	15.4%	15.9%	9.4%	<0.01

Matorras et al, Hum Reprod 19: 2027-30, 2004

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The use of a fibrin sealant (Clinical pregnancy rates)

Study	No fibrin	Fibrin sealant	P value
Feichtinger et al (1992) (RCT)	17.0 %	18.9 %	NS
Bar-Hava et al (1999) (CT)	14.9 %	25.3%	<0.05

EmbryoGlue (Valojerdi et al, 2006) (QRT)

	EmbryoGlue (n = 417)	Controls (n = 398)	P value
Pregnancy rate	31.2%	29.1%	NS
Implantation rate	15%	13%	NS
Multiple pregnancy rate	30.8%	25.9%	NS

Valojerdi et al, J Assist Reprod Genet 23(5):207-12 , 2006

Refining the embryo transfer technique

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17. Fibrin sealant
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19. Routine antibiotics
20. Experience of the clinician

Bed rest after embryo transfer

Study	Trial	n	Bed rest	No rest	P
Sharif et al, 1998	Cohort	1019	18.6 %	23.5 %	NS
Botta et al, 1997	RCT	182	24.1 %	23.6 %	NS
Bar-Hava et al, 2005	RCT	406	21.3%	24.6%	NS

Refining the embryo transfer technique

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Infection and embryo transfer (Pregnancy rates)

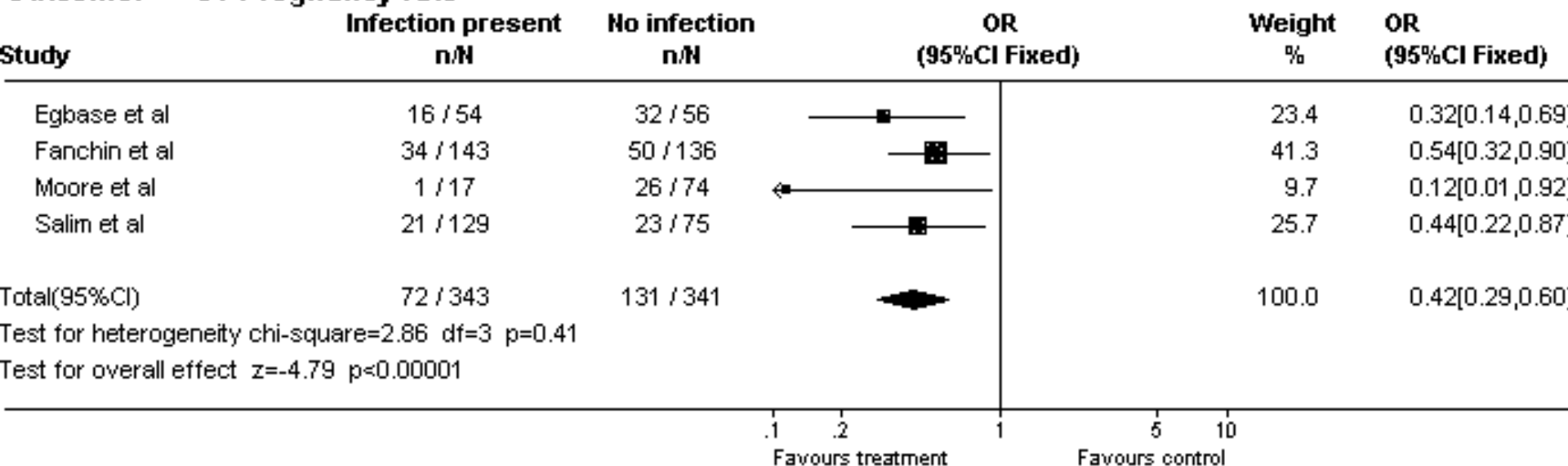
Study	n	No infection	Infection	P
Egbase et al, 1996 (OS)	110	57.1%	29.6%	<0.005
Fanchin et al, 1998 (OS)	279	37%	24%	<0.02
Moore et al, 2002 (OS)	91	35%	6%	<0.05
Salim et al, 2002 (OS)	204	30.7%	16.3%	<0.002

Effect of infection on the pregnancy rate

(Sallam et al, 2003 - Meta-analysis)

Comparison: 01 Infection versus no infection

Outcome: 01 Pregnancy rate



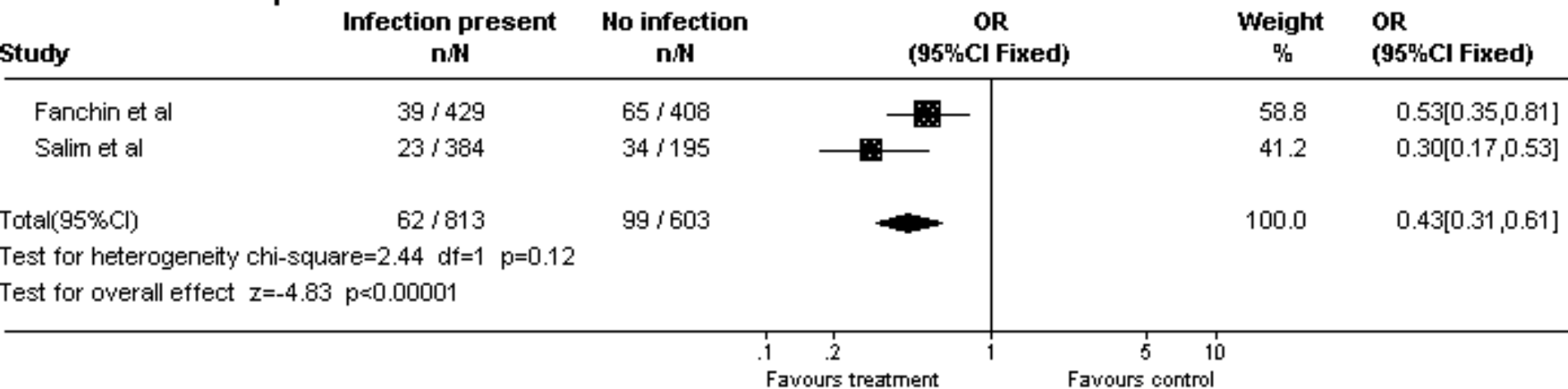
Sallam et al, Fertility and Sterility, 80 (Suppl 3): 110, 2003

Effect of infection on the implantation rate

(Sallam et al, 2003 - Meta-analysis)

Comparison: 01 Infection versus no infection

Outcome: 02 Implantation rate



Sallam et al, Fertility and Sterility, 80 (Suppl 3): 110, 2003

Prophylactic antibiotics prior to embryo transfer (CT - Egbase et al, 1999)

	No antibiotics	Antibiotics	P
Implantation rate	9.3 %	21.6 %	<0.001
Pregnancy rate	18.7 %	41.3 %	<0.01

Egbase et al, Lancet 354(9179): 651-2, 1999

Amoxicillin + clavulanic acid before embryo transfer (RCT)

	Antibiotics	No antibiotics	P value
No. of patients	48	53	
Implantation rate	36.9 %	36.5 %	NS
Miscarriage rate	33.3% (16/48)	20.8% (11/53)	NS

Refining the embryo transfer technique

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20. Experience of the clinician

Experience of the clinician (Hearns-Stokes et al, 2000 - OS)

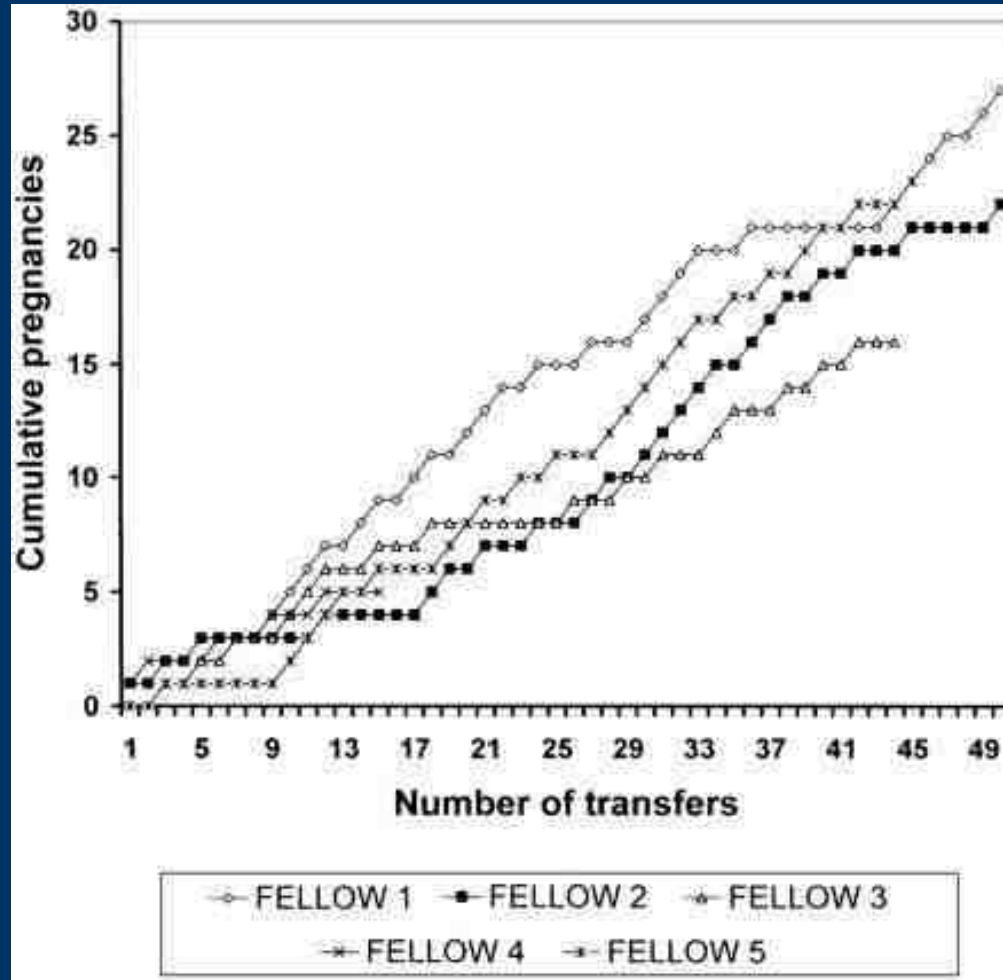
	Clinician A	Clinician B	P value
Pregnancies	8/47	31/57	
Pregnancy rate	17%	54.7%	<0.05

Hearns-Stokes, Fertil Steril 74: 80-6, 2000

Embryo transfer by nurses/midwives

	ET by midwives	ET by gynaecologists	P value
Barber et al, 1996 (CT)	246/679 (36%)	20/68 (29%)	NS
Bjuresten et al, 2004 (RCT)	16/51 (31%)	15/51 (29%)	NS

Minimal number of ETs for proficiency = 50



Papageorgiou et al, Hum Reprod 16: 1415, 2001

Conclusions 1

The following procedures have been shown
(by RCTs) to improve pregnancy rates:

1. Ultrasound guidance
2. Dummy embryo transfer
3. Mid-fundal deposition
4. Assisted hatching for repeated failures

Conclusions 2

Meta-analysis show that the following factors significantly diminish the pregnancy and implantation rates:

1. Difficult transfers
2. Cervical infection

Conclusions 3

The following procedures have been shown
(by RCTs) NOT to affect pregnancy rates:

1. Bed rest after embryo transfer
2. Waiting 30 seconds after ET
3. The use of a fibrin sealant
4. Sexual intercourse
5. Embryo stage at the time of transfer
6. Presence of air in the ET catheter

Conclusions 4

The following factors are still being evaluated:

1. Position of the patient during ET
2. Performing ET under general anaesthesia
3. Performing ET with a full bladder
 4. Removal of cervical mucus
 5. Flushing the cervical canal
6. Avoiding the use of a tenaculum
 7. Soft v/s rigid catheters
 8. Routine use of antibiotics

Bibliotheca Alexandrina





Euclid of Alexandria, Father of geometry, c. 300 BC



Plato

Socrates

Aristotle

Zoroaster

Rafaello

Zeno

Ptolemy

Averroes

Phythagoras

Epicurus

Heraclitus

Euclid



7th annual congress of the Mediterranean Society for Reproductive Medicine, Hammamet, Tunisia, 15-18 May 2008



Drugs to induce uterine relaxation

Fanchin R, Righini C, de Ziegler D, et al. Effects of vaginal progesterone administration on uterine contractility at the time of embryo transfer. *Fertil Steril*. 2001; 75:1136-1140.

Baruffi R, Mauri AL, Petersen CG, et al. Effects of vaginal progesterone administration starting on the day of oocyte retrieval on pregnancy rates. *J Assist Reprod Genet* 2003; 20:517-520.

Shaker AG, Fleming R, Jamieson ME, Yates RW, Coutts JR. Assessments of embryo transfer after in-vitro fertilization: effects of glyceryl trinitrate. *Hum Reprod*. 1993 Sep;8(9):1426-8.

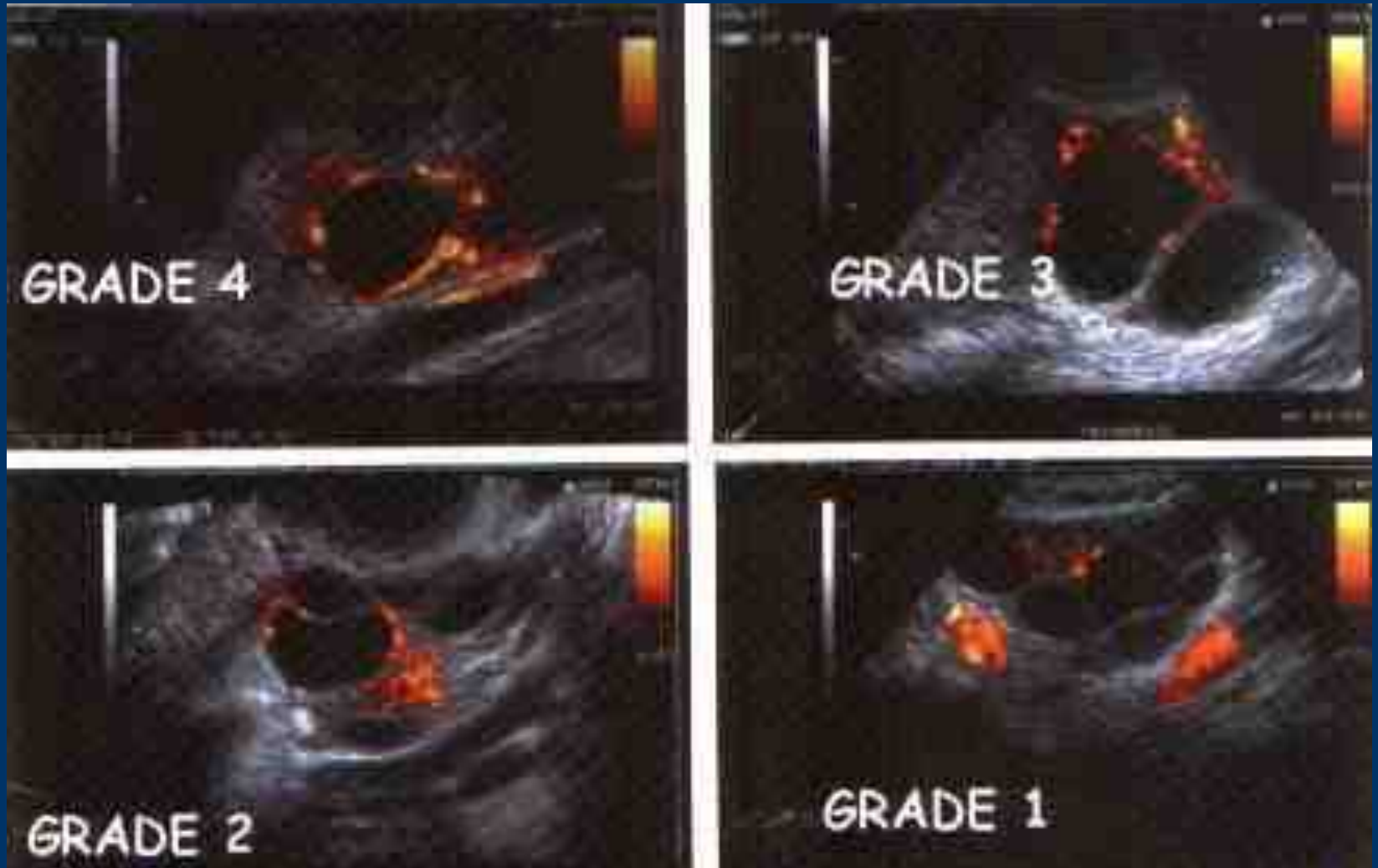
Moon HS, Park SH, Lee JO, Kim KS, Joo BS. *Fertil Steril*. 2004 Oct;82(4):816-20. Treatment with piroxicam before embryo transfer increases the pregnancy rate after in vitro fertilization and embryo transfer.

Ultrasound-guided echogenic catheter (RCT)

	Echogenic catheter (n = 98)	Non-echogenic catheter (n = 95)	P value
Clinical pregnancy rate	54.1 %	41 %	NS
Implantation rate	37.1 %	23.2 %	<0.05

Coroleu et al, Hum Reprod, March 2006 [Epub ahead of print]

Perifollicular blood flow



NUMBERS NEEDED TO STUDY

For 5% improvement in pregnancy rate
(e.g. from 25 % to 30 %)

At $P=0.05$

80% probability of detecting a true difference

NNS = 636

Implantation is an immunological paradox whereby the semi-allograft human conceptus, immunologically foreign to the mother, evades immune rejection (Medawar, 1953)

Position of the patient during embryo transfer (Englert et al, 1986 - CT)

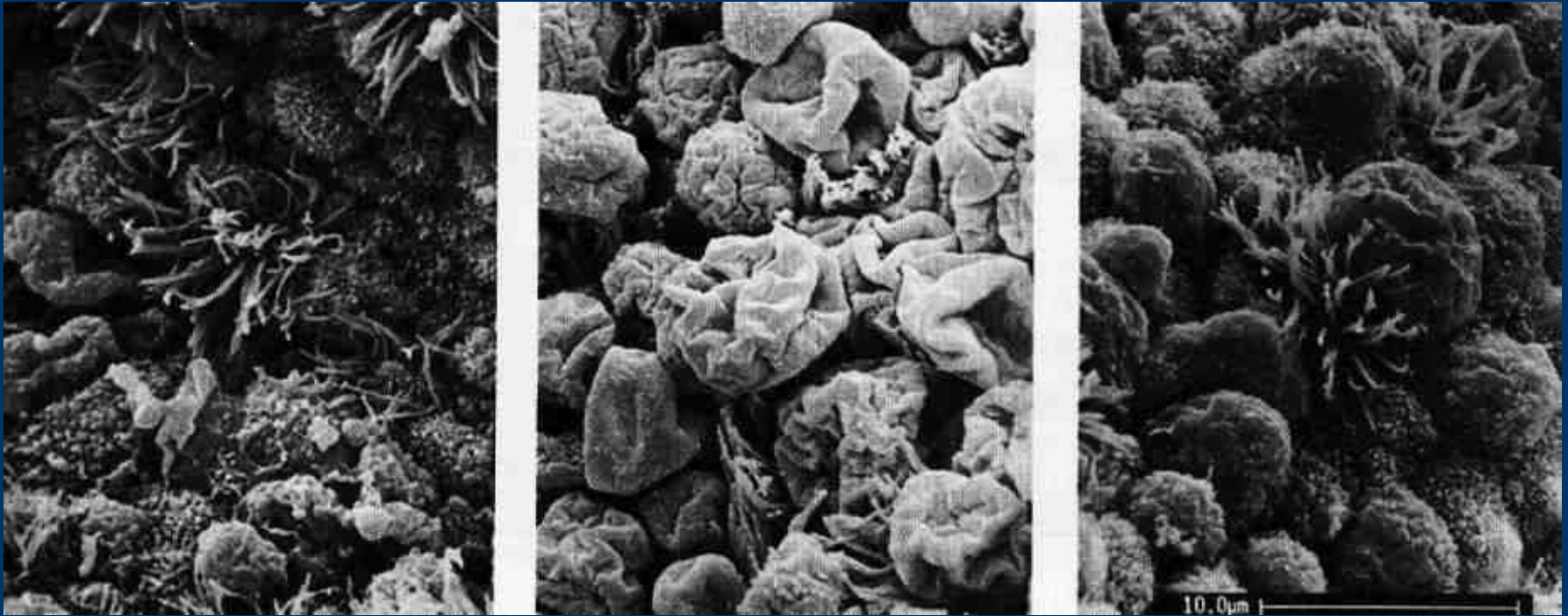
Position	Number of cycles	Failures	Pregnancies (%)
Dorsal	50	1	14/49 (28.5%)
Knee to chest	50	5	9/45 (20.0%)

Englert et al, J In Vitro Fert Embryo Transf, 3:243-6, 1986

Implantation window

- LH+7 to LH+10 (Bergh and Novat, 1992)
- Day POD+5 to POD+7 (Psychoyos, 1993)
 - Day 20 to 24 (Anderson, 1990)

Pinopods



Developing

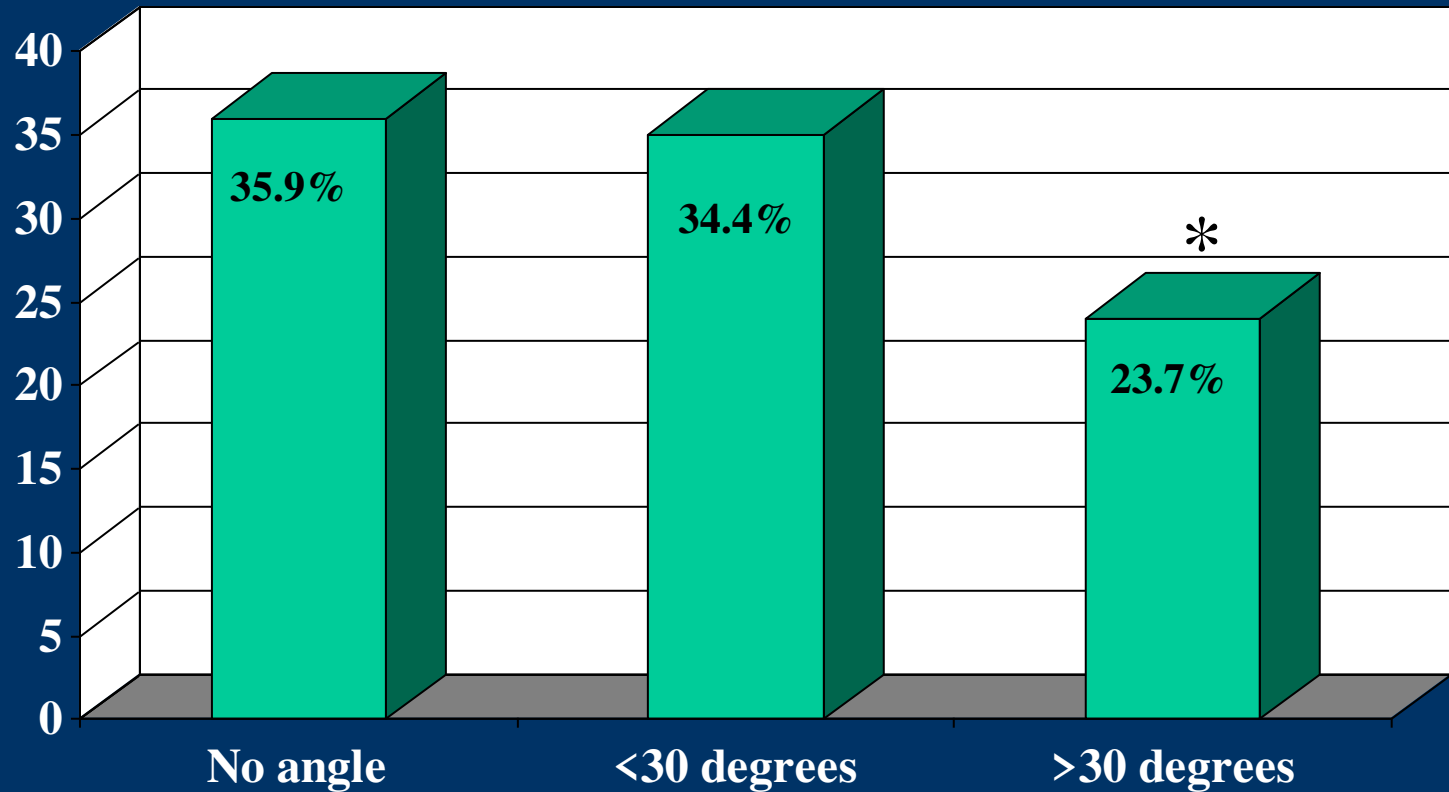
Fully developed

Regressing

Molecular factors implicated in implantation

1. Adhesion molecules (integrins, mucins, trophinins, tastins)
2. Proteases (serine proteases, MMPs)
3. Cytokines (ILs, TNFs, CSF, LIF)

Relationship between the utero-cervical angle and clinical pregnancy rate (%)



Sallam et al, Hum Reprod, 17: 1767-72, 2002

Ultrasound measurement of the utero-cervical angle (QCT)

	Ultrasound (n= 320)	No ultrasound (n= 320)	P value
Clinical pregnancy rate	26.25%	18.43%	<0.02
Implantation rate	13.78%	9.82%	<0.01
Ectopic pregnancy	1	3	NS

Sallam et al, Hum Reprod, 17: 1767-72, 2002

Embryo transfer using a soft catheter (CPR)

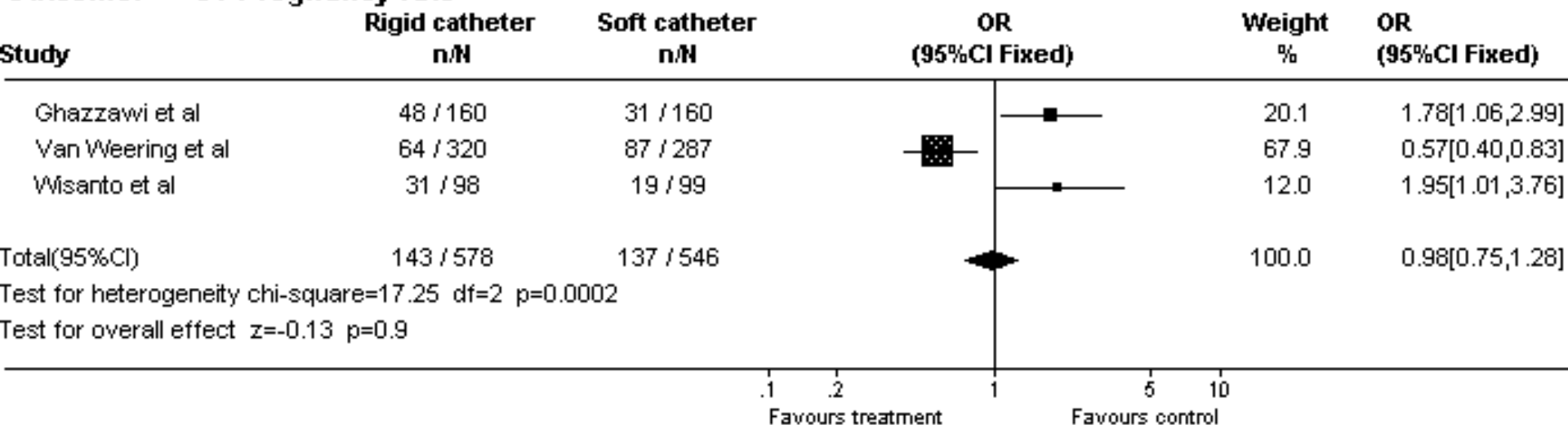
Study	N	Soft catheter	Rigid catheter	P
Wisanto et al, 1989 (RCT)	400	19.2%	32.3%	<0.05
Al-Shawaf et al, 1993 (CT)	178	30.3%	30.7%	NS
Urman et al, 2000 (CT)	428	41.6%	36.0%	NS
Wood et al, 2000 (CT)	518	36%	17%	<0.000
Ghazawi et al, 2000 (RCT)	320	19%	30%	NS
van Weering et al, 2002 (RCT)	2059	27.1%	20.5%	<0.01

Soft catheters versus rigid catheters

Sallam et al, 2005 (Meta-analysis)

Comparison: 01 Soft versus rigid catheter

Outcome: 01 Pregnancy rate



Blastocyst versus cleavage stage

(Blake et al, 2004 - Cochrane review)

Outcome measure	OR (95% CI)
Pregnancy rate	0.91 (0.71- 1.17)
Live birth rate	0.83 (0.48 - 1.42)
Multiple pregnancy rate	0.77 (0.52 - 1.13)

Blake et al, Hum Reprod, 19: 795-807, 2004

Bed rest after embryo transfer

Study	Trial	n	Bed rest	No rest	P
Sharif et al, 1998	Cohort	1019	18.6 %	23.5 %	NS
Botta et al, 1997	RCT	182	24.1 %	23.6 %	NS

Embryo transfer with a full bladder (Lewin et al, 1997 - CT)

	Empty bladder	Full bladder	P value
Pregnancies	64/385	110/411	
Pregnancy rate	16.6%	26.8%	<0.01

Lewin et al, J Assist Reprod Genet 14: 32-4, 1997

Embryo transfer with a full bladder

(Lorusso et al, 2005 - RCT)

	Empty bladder (n=64)	Full bladder (n=67)	P value
Implantation rate	15.4 %	16.1 %	NS
Clinical pregnancy rate	38.7 %	39 %	NS

Lorusso et al, Fertil Steril 84: 1046, 2005

Cochrane Database Syst Rev. 2005
Jul 20;(3):CD004829. Links

Conscious sedation and analgesia for
oocyte retrieval during in vitro
fertilisation procedures.

Kwan I, Bhattacharya S, Knox F,
McNeil A.

Stener-Victorin E, Waldenström U, Nilsson L, Wikland M and Janson PO (1999) A prospective randomized study of electro-acupuncture versus alfentanil as anaesthesia during oocyte aspiration in in-vitro fertilization. *Hum Reprod* **14**,2480–2484.[\[Abstract/Free Full Text\]](#)

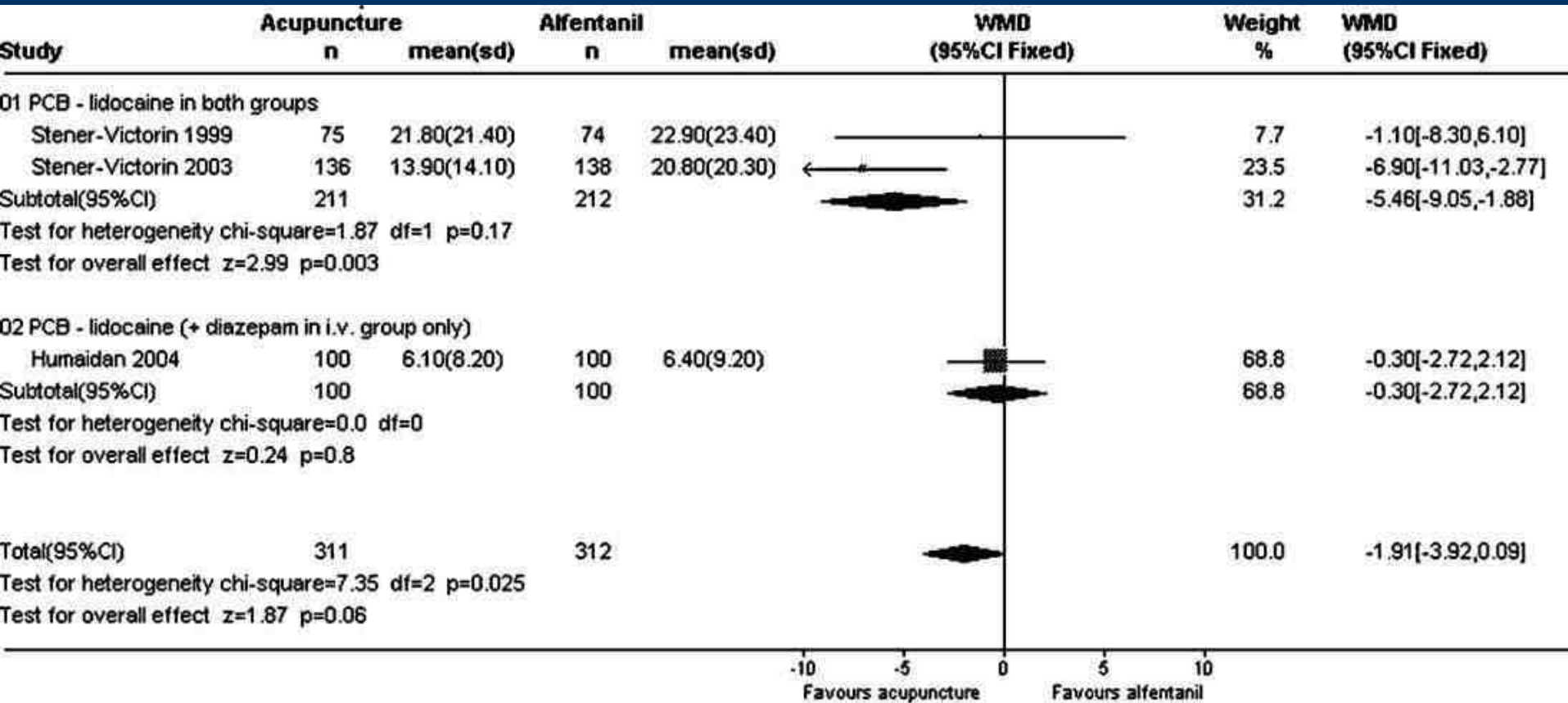
Stener-Victorin E, Waldenström U, Wikland M, Nilsson L, Hägglund L and Lundeberg T (2003) Electro-acupuncture as a per-operative analgesic method and its effects on implantation rate and neuropeptide Y concentrations in follicular fluid. *Hum Reprod* **18**, 1454–1460.[\[Abstract/Free Full Text\]](#)

Trout SW, Hazard Vallerand AH and Kemmann E (1998) Conscious sedation for in vitro fertilization. *Fertil Steril* **69**,799–808.[\[CrossRef\]](#)[\[ISI\]](#)[\[Medline\]](#)

Electric acupuncture for oocyte retrieval (RCT)

	Electro- acupuncture	Conventional medical analgesia	P value
No. of patients	100	100	
Maximum pain during oocyte retrieval (SD)	4.6 (2.5)	3.2 (2.3)	<0.001
Mean pain during oocyte retrieval (SD)	2.6 (1.8)	1.8 (1.7)	<0.001
Pain directly after oocyte retrieval (SD)	1.9 (1.9)	1.5 (1.9)	<0.01

Maximal pain, assessed with a visual analogue scale (VAS), during oocyte retrieval



Stener-Victorin, Hum Reprod 20: 339, 2005

Implantation failure

In normal fertile women, 78 to 83 % of embryos fail to implant (Wilcox et al, 1988; Elish et al, 1996)

In infertile women, 85 % of embryos fail to implant (Edwards et al, 1995)