



# **Treatment of endometriosis- associated infertility**

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# Background

- aetiology:
  - retrograde menstruation implant
  - metaplasia of coelomic cells
  - haematogenous/lymphatic spread
  - immunologic
- prevalence: 20% - 40% (Mahmood 1991)
- revised American Fertility Society classification (1985)

# Treatment options

- Medical (drug induced ovarian suppression)
- Surgical (laparoscopy, laparotomy)
- In vitro fertilisation

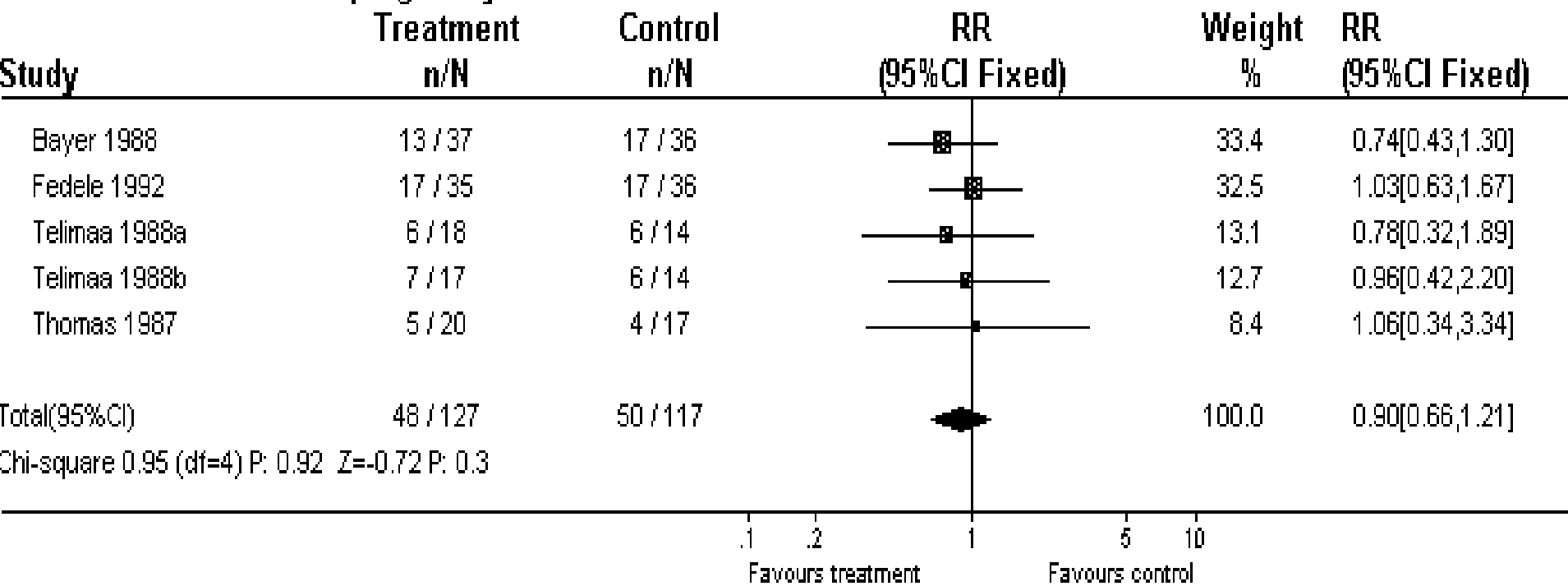
# Ovulation suppression

- danazol, MPA, gestrinone, COC, GnRHa versus placebo/no (4 RCTs)
- any ovulation suppression versus danazol (8 RCTs)

*Hughes E. et al. (Cochrane systematic review) In: The Cochrane Library*

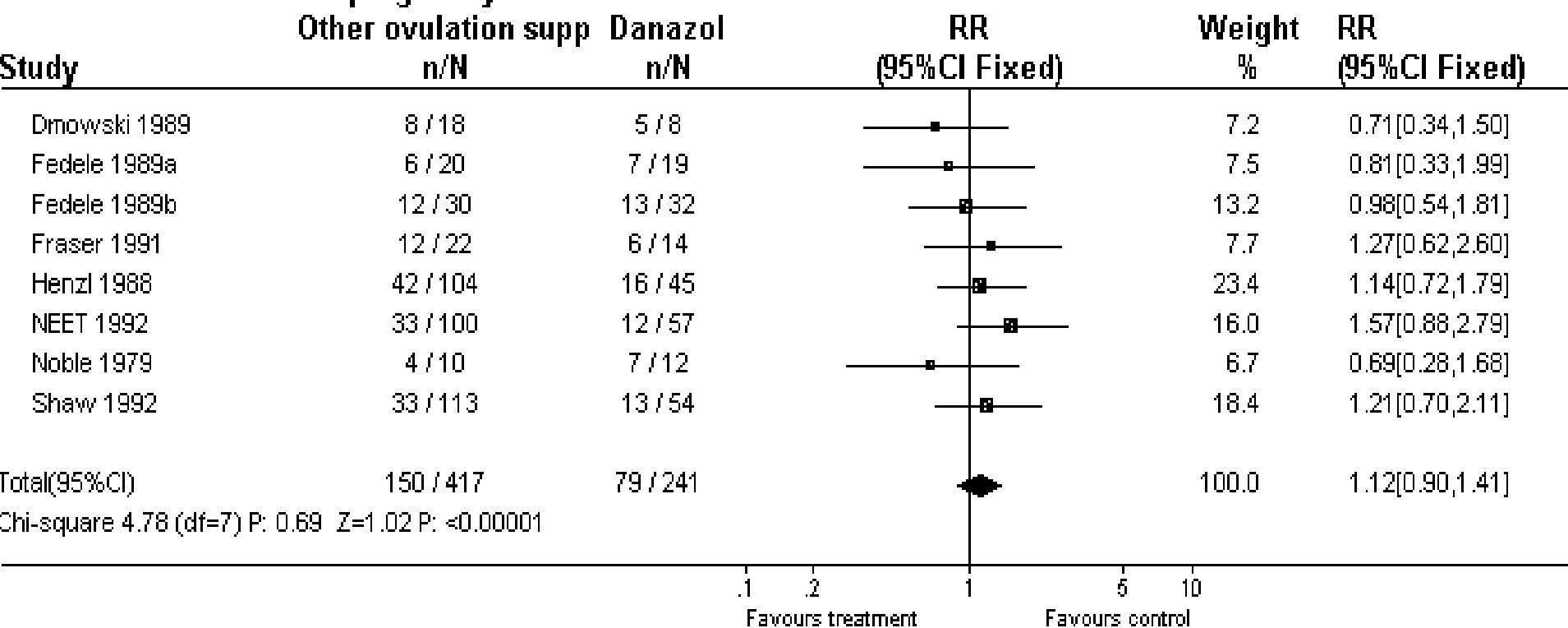
**Comparison: 01 Ovulation suppression vs placebo**

**Outcome: 01 Clinical pregnancy**



**Comparison: 02 Other ovulation suppression vs danazol**

**Outcome: 01 Clinical pregnancy**



# Pentoxifylline

- Pilot study, RCT (n=60)
- rAFS I, II
- Pentoxifylline 800mg/d vs placebo (12months)
- pregnancy rates: 31% (Pe) vs 18.5% (PI)

*Balasch J. Hum Reprod 1997*

# Surgical treatment

- laparoscopy/ laparotomy versus medical treatment/no treatment

2 meta-analyses, 22 cohort studies

*Hughes E. Fertil Steril, 1993;59:963,*

*Adamson G. Am J Obstet Gynecol 1994;171:1488*



# Surgical treatment

- RCT, laparoscopy: resection/ablation versus diagnostic  
341 infertile women with minimal or mild endometriosis

*Marcoux S. NEJM 1997; 337:217*

# Fecundity rates and cumulative probabilities of pregnancy

(Marcoux 1997)

<b>Outcome</b>	<b>Laparoscopic surgery (n=172)</b>	<b>Diagnostic laparoscopy (n=169)</b>	<b>RR (95% CI)</b>
Pregnancies carried beyond 20 weeks (No)	50	29	1.69 (1.13-2.54)
Fecundity rate/100 person months	4.7	2.4	1.9(1.2-3.1)
36-weeks cumulative probability (%)	30.7	17.7	1.7(1.2-2.6)
Recognised pregnancies (No)	63	37	
Fecundity rate/100 person months	6.1	3.2	1.9(1.3-2.9)

# IVF

- retrospective
- 140 patients /182 cycles with EM
- GnRH nasal 1.5mg/14 days
- HMG
- Progesterone 200mg/d for 10 days after embryo transfer

*Geber S. Hum Reprod 1995;10(6):1507*

## Pregnancy outcome and implantation rate after IVF using GnRH analogues (Geber S. Hum Reprod 1995)

<b>Groups</b>	<b>No of cycles</b>	<b>Implantation rate</b>	<b>Pregnancy rate/transfer</b>	<b>Miscarriage rate</b>
1) Male factor	45	23.4%	39%(9/23)	0
2) Unexplained	196	27.6%	48%(76/159)	3.9%(3)
3) Tubal factor	1136	23.4%	45%(465/1039)	3.4%(16)
4) Endometriosis	129	21.8%	40%(44/110)	0

Implantation rate and pregnancy outcome after IVF using GnRH analogues according to the stage of endometriosis (Geber S. Hum Reprod 1995)

<b>AFS stage</b>	<b>No of cycles</b>	<b>Implantation rate</b>	<b>Pregnancy rate/transfer</b>	<b>Miscarriage rate</b>
I-II	100	19%	35.0% (29/83)	0
III-IV	29	28%	55.5% (15/27)	0

The difference between the pregnancy rates/transfer was 20.5% (95%CI: -0.8 to42)

# IVF

- retrospective
- objective: impact of endometriosis stage on IVF outcome
- endometriosis vs tubal infertility

*Oliviennes F. Fertil Steril 1995;64:392*

All endometriosis patients and tubal controls (Oliviennes F Fertil Steril 1995)

<b>Outcome</b>	<b>Endometriosis (n=214, cycles =360)</b>	<b>Tubal factor (n=111, cycles=160)</b>
Clinical pregnancies/transfer	35.9% (104/290)	41.9%(57/136)
Deliveries/transfer	30.0% (87/290)	37.5% (51/136)
Miscarriage	16.4% (17/104)	10.5% (6/57)

## Pregnancy outcomes according to subgroups

Outcome	Endometriosis only (cycle n=236)	Endometriosis and tubal factor (cycle n=63)	Endometriosis and male factor (cycle n=61)	Mechanical factor (cycle n=160)
Clinical pregnancy /transfer	80/204 (39.2%)	8/44 (18.2%)	16/42 (38.1%)	57/136 (41.9%)
Deliveries/ transfer	72/204 (35.3%)	5/44 (11.4%)	10/42 (23.8%)	51/136 (37.5%)
Miscarriage	8/80 (10%)	3/8 (37.5%)	6/16 (37.5%)	6/57 (10.5%)



# Intrauterine insemination

- RCT: superovulation (FSH) and intrauterine insemination
- 103 couples with minimal / mild endometriosis

*Tummon S. Fertil Steril 1997;68:8-12*

# Intrauterine insemination

- Live births
- superovulation /IUI:
  - 14/127 (11%)
- no treatment:
  - 4/184 (2%)

# Conclusion 1

- Ovulation suppression
  - lack of evidence to support ovulation suppression for treatment of em-associated infertility
  - disadvantages: side effects, loss of time, cost
- Pentoxifyllin
  - cannot be recommended at this stage

# Conclusion 2

- Surgical treatment (laparoscopy/laparotomy)
  - limited evidence to suggest surgery might be better than no treatment

# Conclusion 3

- IVF:
  - similar rates of pregnancy in women with endometriosis and other causes of infertility (retrospective data)
  - no comparison between IVF and other treatments have been made
- Superovulation and intrauterine insemination
  - could be beneficial, more evidence needed