Is the fallopian tube better than the uterus?

Evidence on intrauterine insemination vs fallopian sperm perfusion

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Porsgrunn

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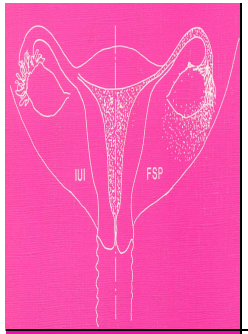
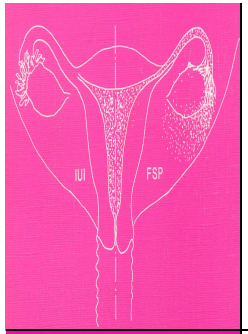
Thanks to my friend and colleague Jarl Kahn



Thanks to my friend and colleague Jarl Kahn

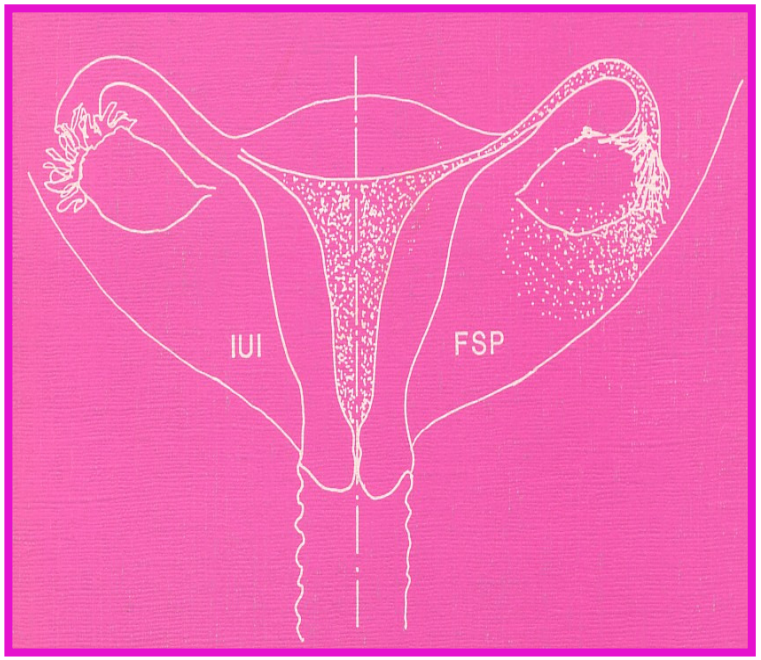
I want to flush the tubes with sperm This will increase the chance that the egg and the sperm meets..!!

Ok..?

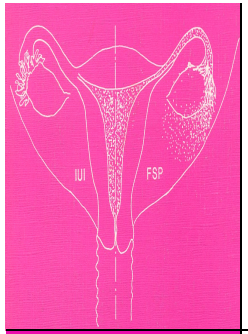


Fallopian tube perfusion - FSP

- End of the 80'ties
  - "We want to flush the tubes with sperm"
- Volumetric study on volunteers to be sterilised.
  - The uterus perfused with using an IV-pump set at 0,5ml/min
  - Fluid passed out of the distal end of the tubes after 0,5-1,8ml was perfused.
- "let's use 4ml inseminate.."



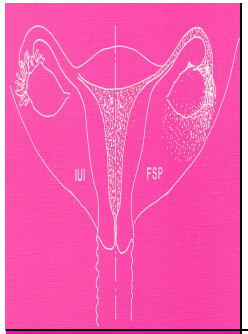
Kahn et al Human Reprod. 7 (suppl 1), 19-24, 1992



FSP – first results

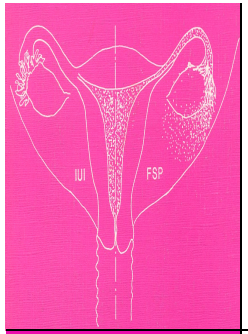
- Tested on patients with different infertility diagnosis
  - 139 couples, 239 cycles,
  - 32 pregnancies (23% /13,4%)
  - “Seems good in Unexplained infertility
    - (49% / 27%)”
  - “Not good result where the semen quality is reduced (5,2%/3,0%)

Kahn et al Human Reprod. 7 (suppl 1), 19-24, 1992

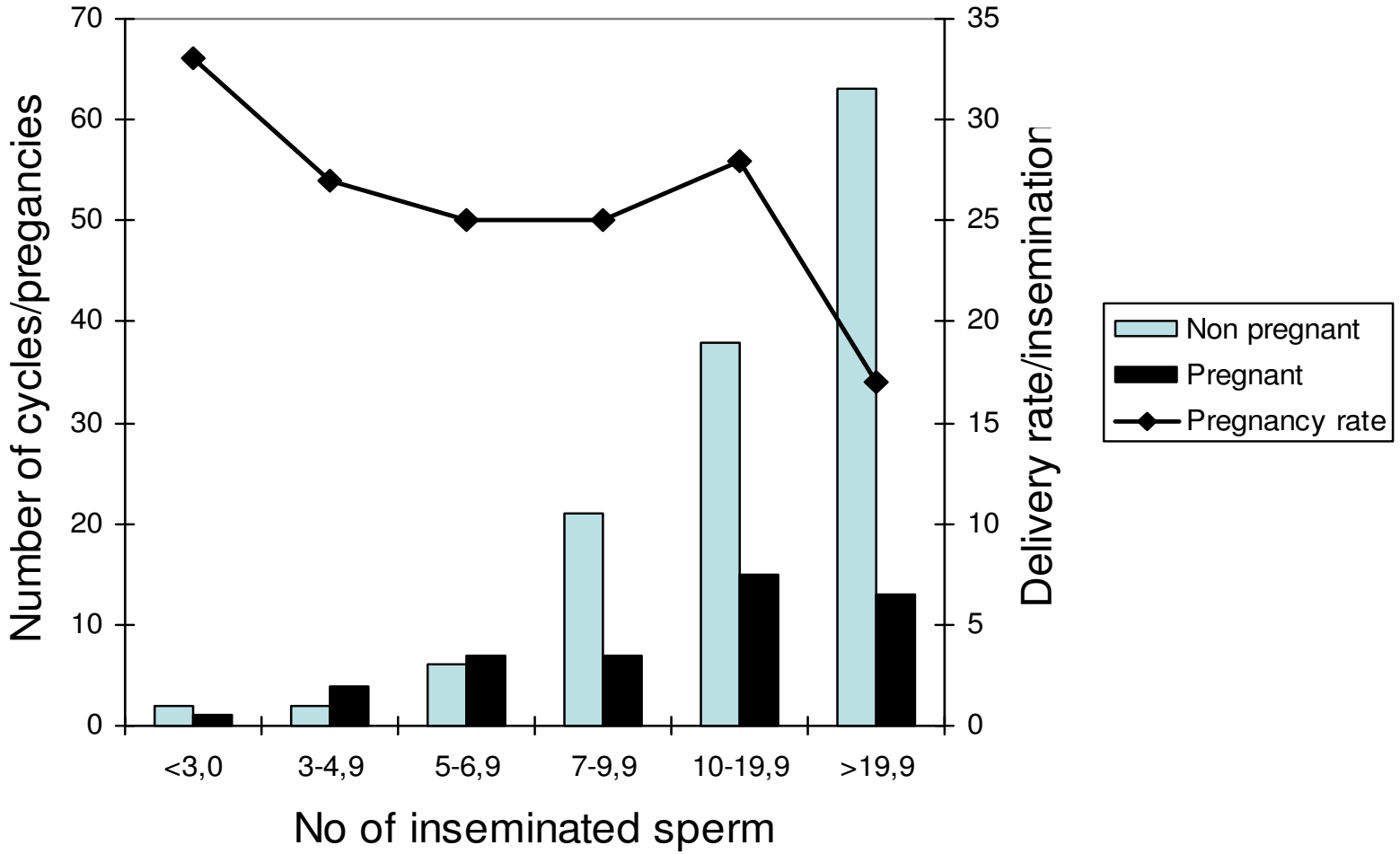


FSP – first results

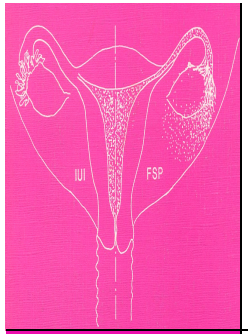
- ”Not do good with reduced semen quality”
- The sperm was (is) prepared with direct swim-up or just centrifugation and wash
- We aim(ed) at 10 million motile sperm in the inseminate



FSP vs. semen quality

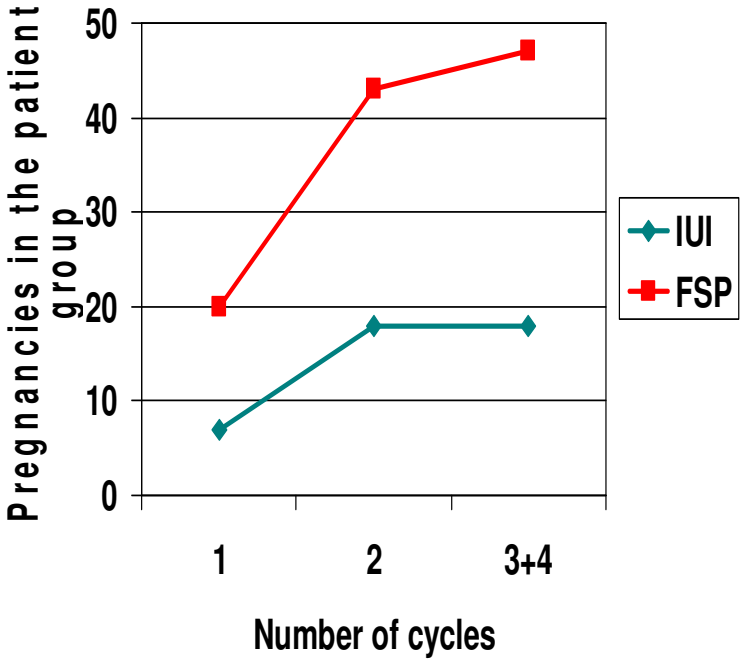


Strandell et al., Acta Obstet Gynecol Scand, 82,1023-1029, 2003

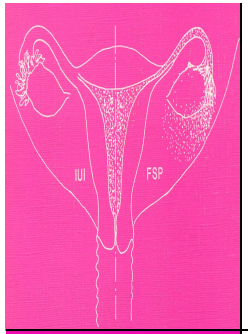


FSP better than IUI?

- A Prospective randomised multi-centre study
  - 60 couples randomised
  - FSP group 30 women, 52 cycles
  - IUI group 28 women, 51 cycles

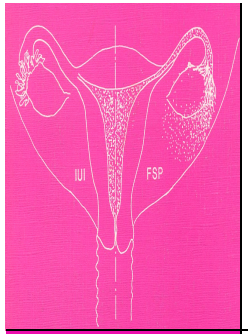


Kahn et al. Human Reprod., 8, 890-894,1993



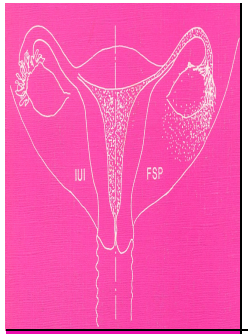
FSP – how to do it?

- **Fanchin et al.**
  - A new system for fallopian tube sperm perfusion leads to pregnancy rates twice as high as standard intrauterine insemination
  - Fertil Steril. 64, 505-510, 1995
  - **A special device ”The FAST System ©”**
- **Mamas , L**
  - Higher pregnancy rates with a simple method for fallopian tube sperm perfusion, using the cervical clamp double nut bivalve speculum in the treatment of unexplained infertility: a prospective randomised study,
  - Human Reprod. 11, 2618-2622, 1995
  - **”The DNB-Speculum©”**
- **Ricci et al**
  - A simple method for fallopian tube sperm perfusion using a blocking device in the treatment of unexplained infertility.
  - Fertil Steril, 76, 1242-1248, 2001
  - **Cervix adaptor, bivalve speculum, forceps**



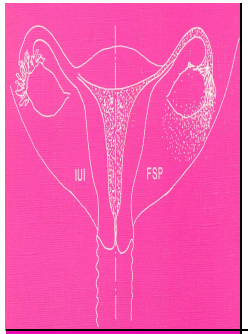
FSP – how to do it?

- The different variants of FSP might well generate different results
- This is unknown and untested
- May contribute to the variations in results obtained



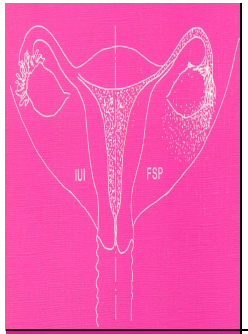
FSP – our results

- FSP in ”Unexplained infertility”
- Donor insemination with frozen semen (Cryos,Denmark)



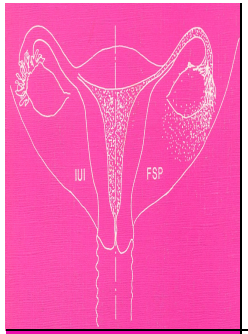
FSP with husbands semen All indications

- Our data from 1988 to 2002
- 1340 started cycles
  - 221 cancelled cycles
    - 95 cycles to IVF (doing good)
- 1005 inseminations
- 142 pregnancies (14,1%)
- 112 deliveries (11,1%)
  - 5 sets of twins (4,5%)
  - 1 set of triplets (0,9%)



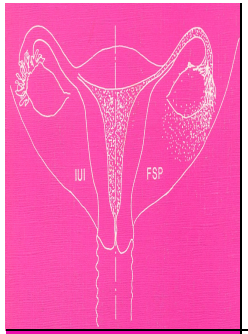
FSP with frozen donor semen

- Our data from 1990 to 2002
- 1316 started cycles
  - 116 cancelled cycles
    - Donor IVF not allowed
- 1200 inseminations
- 333 pregnancies (27,8%)
- 226 deliveries (18,8%)
  - 36 sets of twins (15,9%)



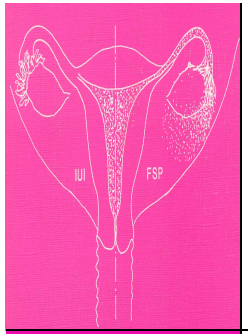
FSP – how many cycles?

- In our hands
  - the pregancy rate drops after 3-4 cycles both in Unexplained infertility and in Donor insemination
  - We advocate not more than 3 cycles in Unexplained infertility



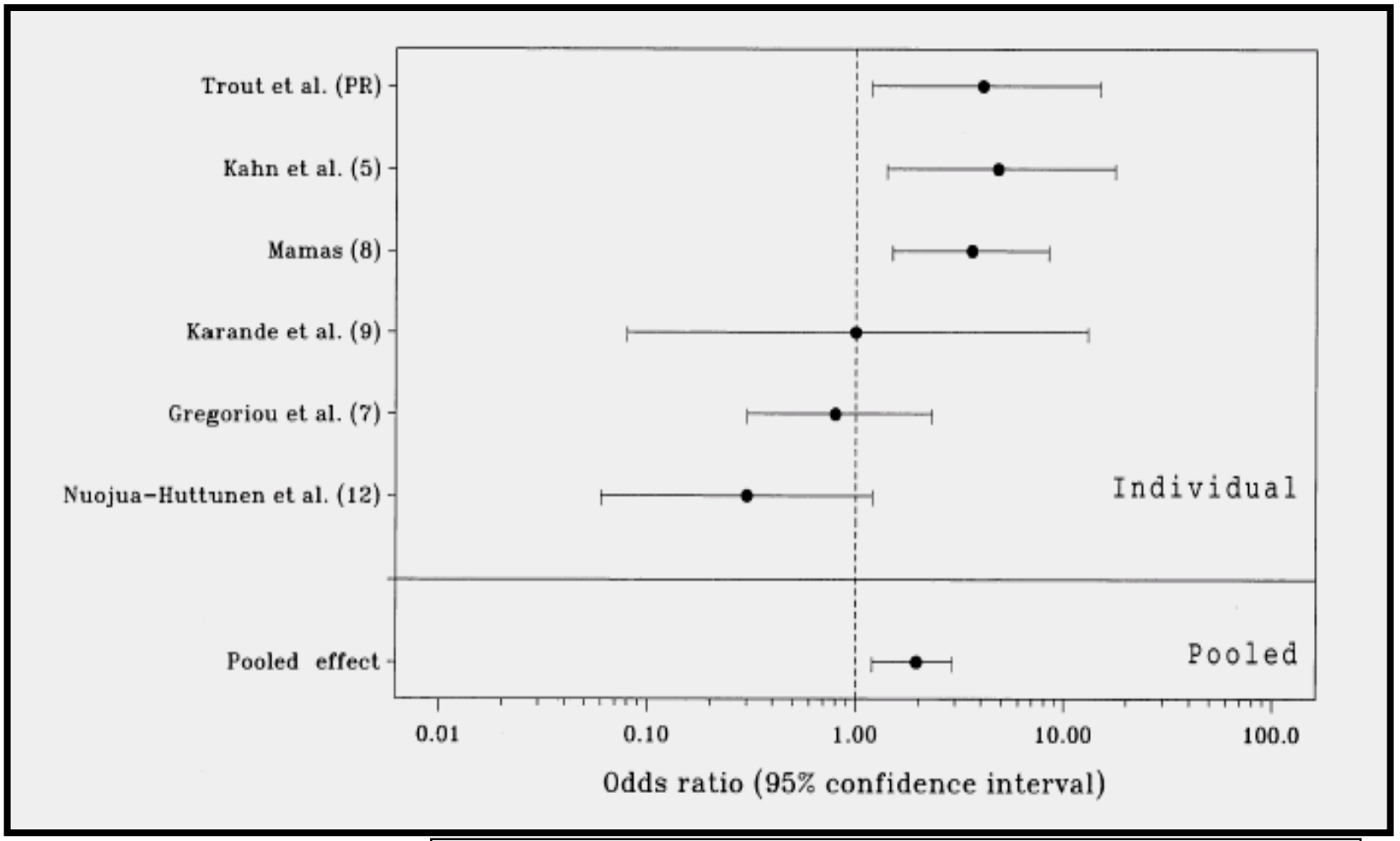
FSP vs. IUI
What's best ?

- Meta-analysis
  - –An exercise on its own..
  - –..☺

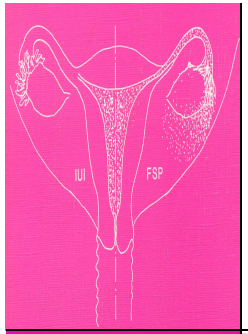


FSP – meta-analysis
The first one…

1999



Trout & Kemmann. Fertil Steril. 71, 881-885, 1999



2004

Cantineau AEP, Cohlen BJ, Al-Inany H, HeinemanMJ.

Intrauterine insemination versus fallopian tube sperm perfusion for non tubal infertility

Analysis 01.02. Comparison 01 Intrauterine insemination versus fallopian tube sperm perfusion, Outcome 02 pregnancy rate per couple for non tubal subfertility

Review: Intrauterine insemination versus fallopian tube sperm perfusion for non tubal infertility

Comparison: 01 Intrauterine insemination versus fallopian tube sperm perfusion

Outcome: 02 pregnancy rate per couple for non tubal subfertility

Study	FSP n/N	IUI n/N	Odds Ratio (Fixed) 95% CI	Weight (%)	Odds Ratio (Fixed) 95% CI
El Sadek 1998	9/48	8/48		19.3	1.15 [0.40, 3.30]
Gregoriou 1995	11/30	12/30		22.6	0.87 [0.31, 2.46]
Kahn 1993	14/30	5/28		8.2	4.03 [1.21, 13.42]
Nuojua-Huttunen 1997	4/50	10/50		27.4	0.35 [0.10, 1.20]
Prietl 1999	33/46	17/49		13.8	4.78 [2.00, 11.41]
Ricci 2001	14/33	5/32		8.7	3.98 [1.23, 12.92]
Total (95% CI)	237	237		100.0	1.85 [1.23, 2.79]

Total events: 85 (FSP), 57 (IUI)

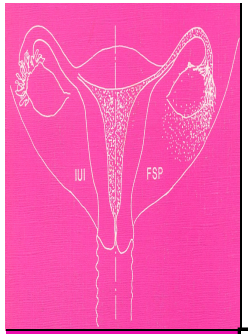
Test for heterogeneity chi-square=17.63 df=5 p=0.003 I^2 =71.6%

Test for overall effect z=2.94 p=0.003

0.1 0.2 0.5 1 2 5 10

Favours IUI Favours FSP

Cochrane Database of Systematic Reviews 2004



2004

Cantineau AEP, Cohlen BJ, Al-Inany H, HeinemanMJ.
Intrauterine insemination versus fallopian tube sperm perfusion for non tubal infertility

Analysis 01.03. Comparison 01 Intrauterine insemination versus fallopian tube sperm perfusion, Outcome 03 Subgroup: pregnancy rate per couple for unexplained subfertility

Review: Intrauterine insemination versus fallopian tube sperm perfusion for non tubal infertility

Comparison: 01 Intrauterine insemination versus fallopian tube sperm perfusion

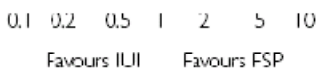
Outcome: 03 Subgroup: pregnancy rate per couple for unexplained subfertility

Study	FSP n/N	IUI n/N	Odds Ratio (Fixed) 95% CI	Weight (%)	Odds Ratio (Fixed) 95% CI
Gregoriou 1995	11/30	12/30		42.4	0.87 [0.31, 2.46]
Kahn 1993	14/30	5/28		15.4	4.03 [1.21, 13.42]
Prietl 1999	33/46	17/49		25.9	4.78 [2.00, 11.41]
Ricci 2001	14/33	5/32		16.3	3.98 [1.23, 12.92]
Total (95% CI)	139	139		100.0	2.88 [1.73, 4.78]

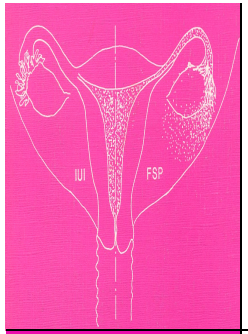
Total events: 72 (FSP), 39 (IUI)

Test for heterogeneity chi-square=6.97 df=3 p=0.07 I^2 =57.0%

Test for overall effect z=4.08 p=0.00005



Cochrane Database of Systematic Reviews 2004

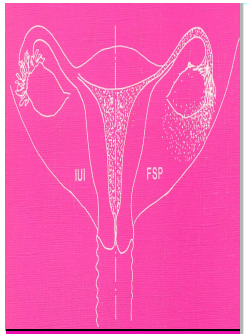


Cantineau AEP, Cohlen BJ, Al-Inany H, HeinemanMJ.

Intrauterine insemination versus fallopian tube sperm perfusion for non tubal infertility.

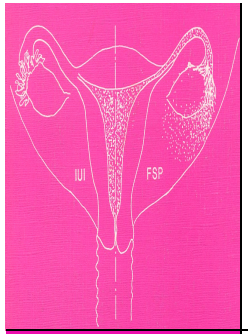
- "There is some evidence from subgroup analysis that FSP gives rise to higher pregnancy rates in couples with unexplained subfertility."

Cochrane Database of Systematic Reviews 2004



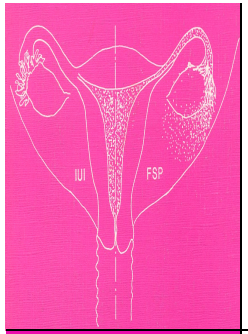
Clinical Guideline February 2004
Guidelines for the NHS by NICE

- "A meta-analysis of five RCTs (number of patients in trials uncertain, 610 cycles) comparing fallopian sperm perfusion to IUI in women with various causes of infertility found that **fallopian sperm perfusion improved pregnancy rates only in women with unexplained infertility** who underwent controlled ovarian stimulation with gonadotrophin/insemination protocols (OR 1.9, 95% CI 1.2 to 3).397 [Evidence level 1a]"



Meta - analysis

- Recent Cohrane Review 2009



2009

Cantineau AEP, Cohlen BJ, Heineman MJ.

'Intra-uterine insemination versus fallopian tube sperm perfusion for non-tubal infertility.

Analysis 1.2. Comparison 1 Intrauterine insemination versus fallopian tube sperm perfusion, Outcome 2 pregnancy rate per couple for non tubal subfertility.

Review: Intra-uterine insemination versus fallopian tube sperm perfusion for non-tubal infertility

Comparison: 1 Intrauterine insemination versus fallopian tube sperm perfusion

Outcome: 2 pregnancy rate per couple for non tubal subfertility

Study or subgroup	FSP n/N	IUI n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Biacchiardi 2004	1/22	8/34		12.5 %	0.15 [0.02, 1.34]
El Sadek 1998	9/48	8/48		13.6 %	1.15 [0.40, 3.30]
Gregoriou 1995	11/30	12/30		15.9 %	0.87 [0.31, 2.46]
Kahn 1993	14/30	5/28		5.8 %	4.03 [1.21, 13.42]
Ng 2003	17/30	11/30		10.0 %	2.26 [0.80, 6.36]
Nuojua-Huttunen 1997	4/50	10/50		19.2 %	0.35 [0.10, 1.20]
Papier 1998	5/50	9/50		16.9 %	0.51 [0.16, 1.63]
Ricci 2001	14/33	5/32		6.1 %	3.98 [1.23, 12.92]
Total (95% CI)	**293**	**302**		**100.0 %**	**1.17 [0.79, 1.71]**

Total events: 75 (FSP), 68 (IUI)

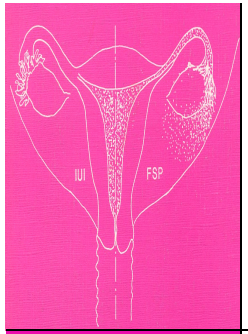
Heterogeneity: Chi^2 = 19.11, df = 7 (P = 0.01); I^2 =63%

Test for overall effect: Z = 0.79 (P = 0.43)

0.01 0.1 1 10 100

Favours IUI Favours FSP

Cochrane Database of Systematic Reviews 2009



2009

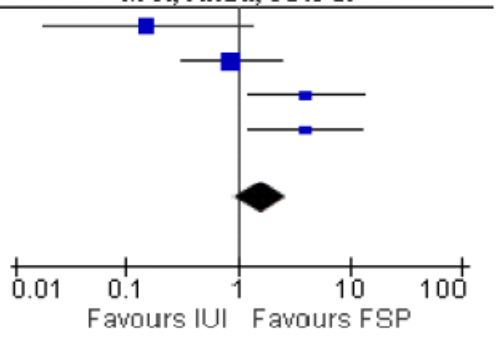
Cantineau AEP, Cohlen BJ, Heineman MJ.

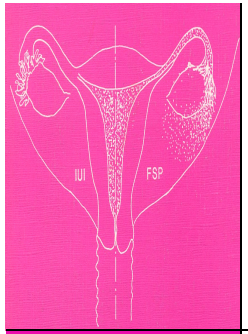
Intra-uterine insemination versus fallopian tube sperm perfusion for non-tubal infertility.

Figure 4. Forest plot of comparison: 1 Intrauterine insemination versus fallopian tube sperm perfusion, outcome: 1.3 Subgroup: pregnancy rate per couple for unexplained subfertility.

Study or Subgroup	FSP Events	FSP Total	IUI Events	IUI Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Biacchiardi 2004	1	22	8	34	31.1%	0.15 [0.02, 1.34]
Gregoriou 1995	11	30	12	30	39.4%	0.87 [0.31, 2.46]
Kahn 1993	14	30	5	28	14.3%	4.03 [1.21, 13.42]
Ricci 2001	14	33	5	32	15.2%	3.98 [1.23, 12.92]
Total (95% CI)		**115**		**124**	**100.0%**	**1.57 [0.89, 2.76]**
Total events	40		30			

Heterogeneity: Chi² = 10.42, df = 3 (P = 0.02); I² = 71%
Test for overall effect: Z = 1.57 (P = 0.12)



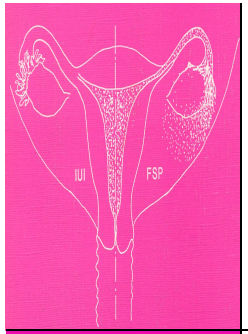


Cantineau AEP, Cohlen BJ, Heineman MJ.
Intra-uterine insemination versus fallopian tubesperm perfusion for non-tubal infertility.
Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD001502. DOI:

- **"Implications for practice**

- There is no evidence that FSP results in higher pregnancy rates in couples suffering from non-tubal subfertility than with IUI.

- This conclusion is based on eight studies involving a total of 595 couples. As a result no advice can be given, based on the meta analysis on the optimal treatment of non-tubal subfertility. **We advise, therefore, familiarity with one procedure since knowledge and routine use of one technique is possibly of more importance than the technique itself."**



FSP or IUI ?

- **Currently there is not sufficient evidence to suggests that FSP is better than IUI.**

- Indication:
  - √ **Unexplained infertility**
  - ? Reduced semen quality
    - The Gothenburg data
  - ? Endometriosis,
  - ? Cervical,
  - ? Ovulation disorders

- There might be an effect of the way FSP is practically done
  - Catheters, speculums, forceps….
  - Unknown which variant is the best…and if a certain variant consistently will give better results tat traditional IUI