

## **To inseminate or not: that's the question!**

The evidence for insemination versus intercourse or IVF

# There are believers and non-believers

Human Reproduction, Vol.24, No.10 pp. 2523–2530, 2009  
Advanced Access publication on July 14, 2009 doi:10.1093/humrep/dep239

human  
reproduction

ORIGINAL ARTICLE *Infertility*

## Individual versus standard dose of rFSH in a mild stimulation protocol for intrauterine insemination: a randomized study

N. la Cour Freiesleben<sup>1,5</sup>, K. Lossl<sup>1</sup>, J. Bogstad<sup>2</sup>, H.E. Bredkjær<sup>3</sup>,  
B. Toft<sup>4</sup>, M. Rosendahl<sup>1</sup>, A. Loft<sup>1</sup>, S. Bangsboll<sup>1</sup>, A. Pinborg<sup>1</sup>,  
and A. Nyboe Andersen<sup>1</sup>

Human Reproduction Update, Vol.15, No.3 pp. 265–277, 2009  
Advanced Access publication on February 23, 2009 doi:10.1093/humupd/dmp003

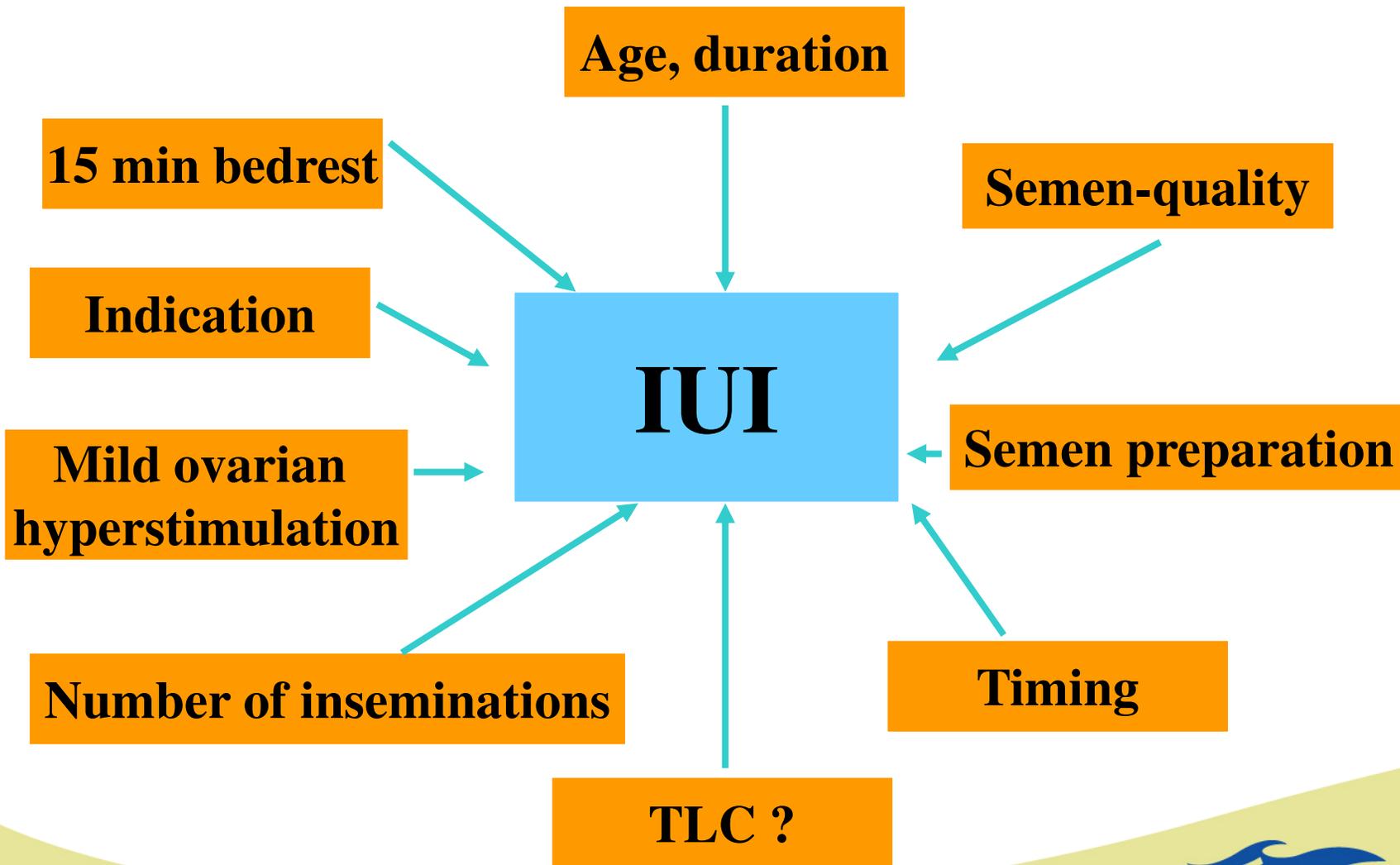
human  
reproduction  
update

## Intrauterine insemination

The ESHRE Capri Workshop Group<sup>1</sup>

Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility  
Cantineau, AEP, Cohlen,BJ; Cochrane database

# Many confounders: ground for discussion



# In general: don't start too early!

Intrauterine insemination with controlled ovarian hyperstimulation versus expectant management for couples with unexplained subfertility and an intermediate prognosis: a randomised clinical trial. [Steures P](#), et al. Lancet. 2006 Jul 15;368(9531):216-21

6 months expectative management: 27% ongoing PR

6 months MOH/IUI

23% ongoing PR

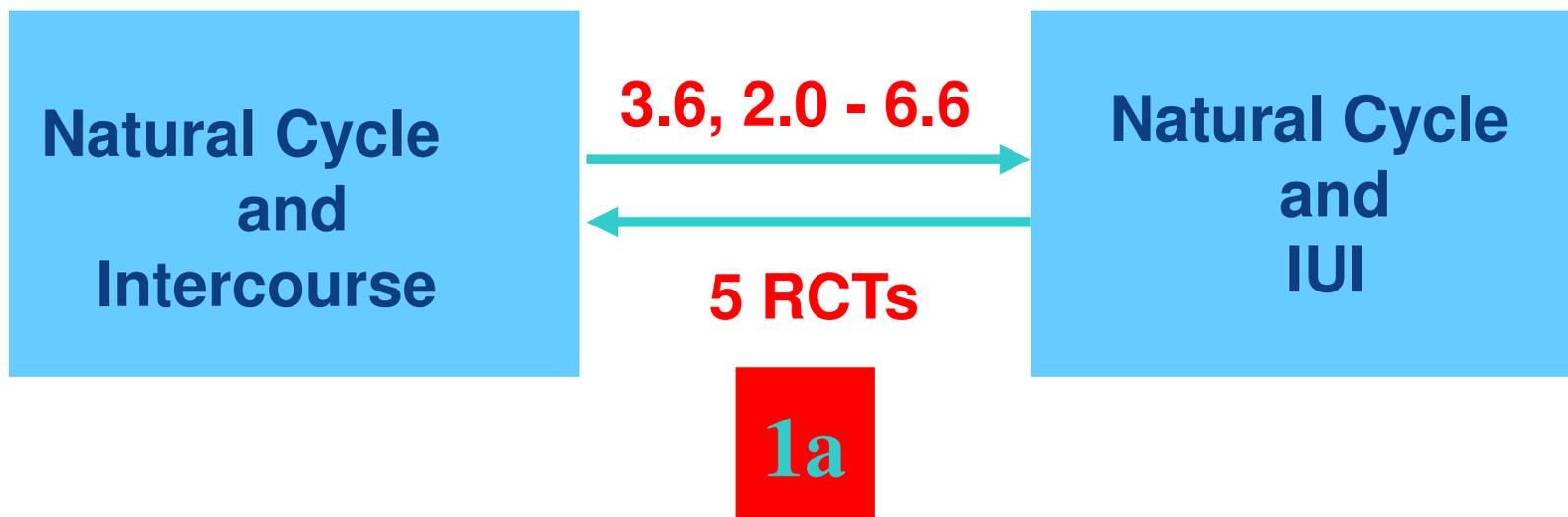
relative risk 0.85, 95% CI 0.63-1.1

# Focus on indication

## Three classical groups:

- ❖ **Cervical hostility**
- ❖ **Male subfertility**
- ❖ **Unexplained subfertility including mild endometriosis**

# Cervical factor: IUI more effective



# The Cochrane changed:

2000



2007

Completed cycles

Started cycles

Drop-outs excluded

Intention-to-treat

(ongoing) pregnancy

Live birth rate

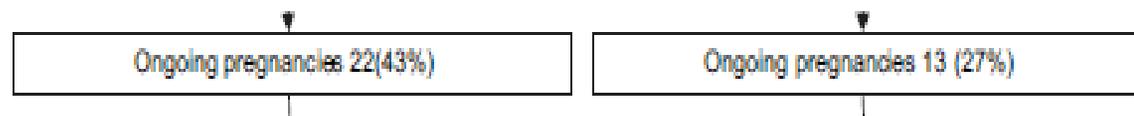
Results per cycle

Results per couple

# Modern evidence: NNT 6

1b

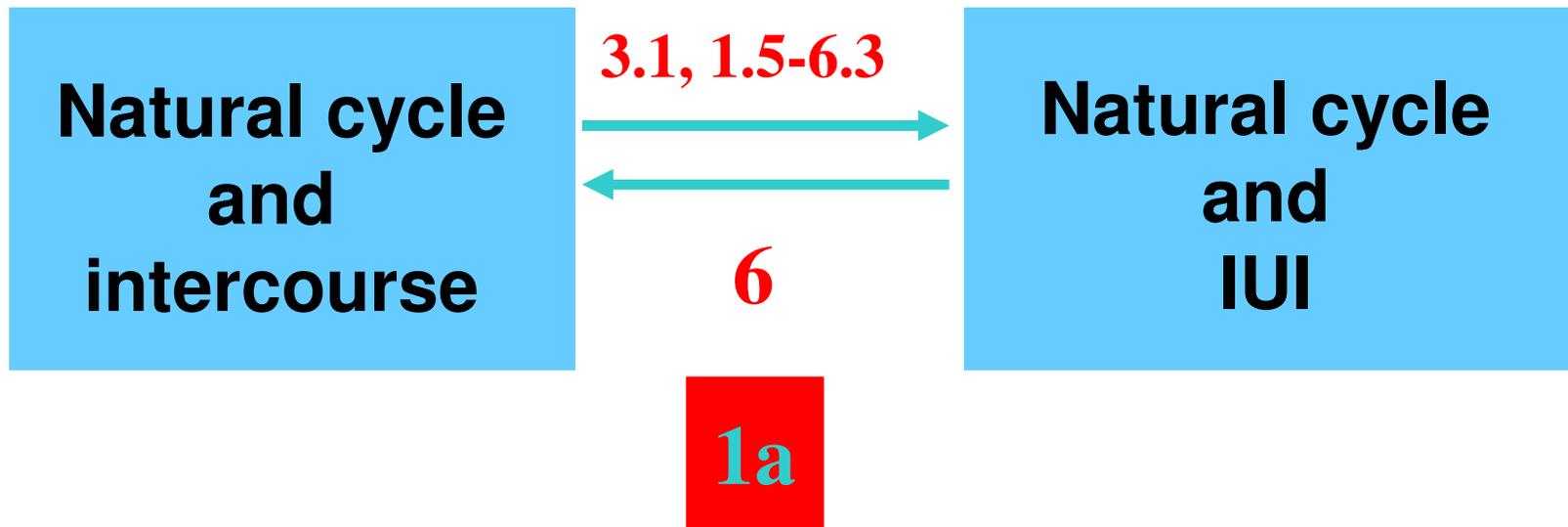
## Effectiveness of intrauterine insemination in subfertile couples with an isolated cervical factor: a randomized clinical trial



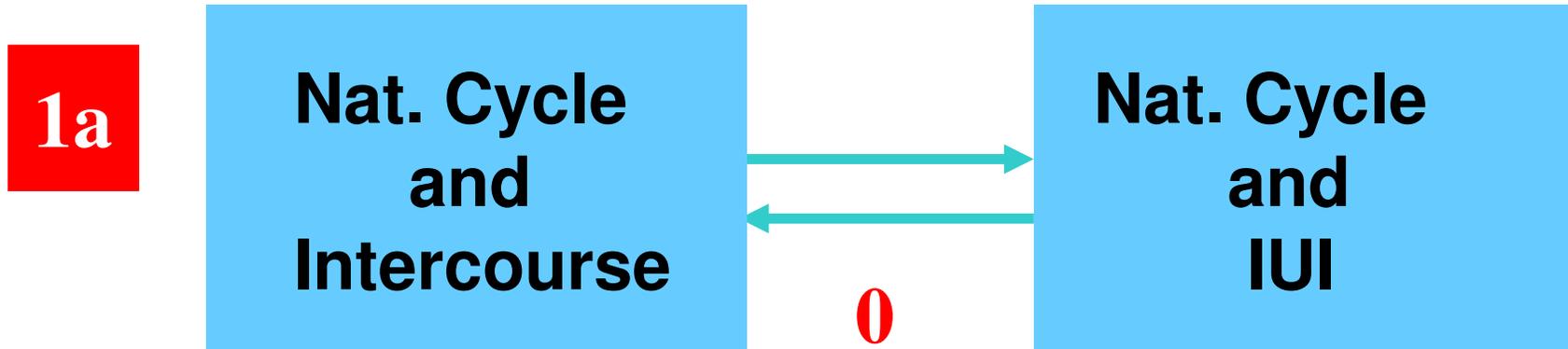
Pietermel Steures, M.D.<sup>a,b,c</sup>  
Jan Willem van der Steeg, M.D.<sup>a,b,c</sup>  
Peter G. A. Hompes, M.D., Ph.D.<sup>a</sup>  
Patrick M. M. Bossuyt, Ph.D.<sup>d</sup>  
J. Dik F. Habbema, Ph.D.<sup>c</sup>  
Marinus J. C. Eijkemans, Ph.D.<sup>c</sup>  
Willem A. Schöls, M.D.<sup>e</sup>  
Jan M. Burggraaff, M.D.<sup>f</sup>  
Fulco van der Veen, M.D., Ph.D.<sup>b</sup>  
Ben W. J. Mol, M.D., Ph.D.<sup>b,g</sup> For CECERM



# Male Subfertility: old evidence: per cycle

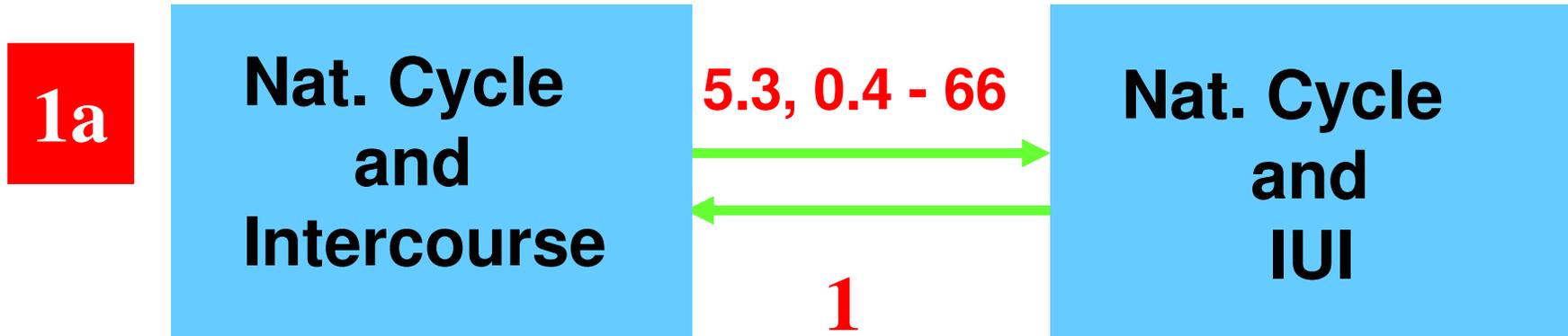


# Male subfertility: live birth rates/couple



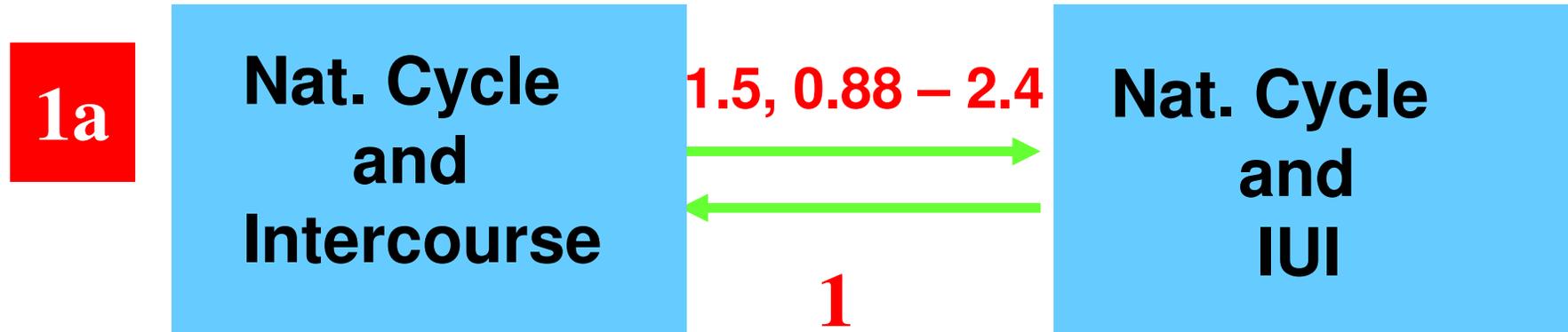
Bensdorp et al. 2007  
Cochrane collaboration

# Male subfertility: Pregnancy rates/couple



Bensdorp et al. 2007  
Cochrane collaboration

# Unexplained subf.: live birth rates/couple



BMJ

RESEARCH

Clomifene citrate or unstimulated intrauterine insemination compared with expectant management for unexplained infertility: pragmatic randomised controlled trial

S Bhattacharya, professor of reproductive medicine,<sup>1</sup> K Harrild, medical statistician,<sup>1</sup> J Mollison, senior medical statistician,<sup>2</sup> S Wordworth, senior research officer,<sup>3</sup> C Tay, consultant gynaecologist,<sup>4</sup> A Harrold, consultant gynaecologist,<sup>2</sup> D McQueen, consultant gynaecologist,<sup>5</sup> H Lyall, consultant gynaecologist,<sup>7</sup> L Johnston, research nurse,<sup>1</sup> J Durrage, research nurse,<sup>6</sup> S Grossett, research nurse,<sup>5</sup> I I Walton, research nurse,<sup>7</sup> J Lynch, research nurse,<sup>7</sup> A Johnstone, research nurse,<sup>4</sup> S Kini, clinical research fellow,<sup>4</sup> A Raja, clinical research fellow,<sup>4</sup> A Templeton, professor of obstetrics and gynaecology<sup>1</sup>

# Conclusion

## IUI in natural cycles:

- ❖ has been proven effective in cervical hostility
- ❖ might be effective in male subfertility
- ❖ is ineffective in unexplained subfertility

# IUI or IVF?

Why the "OR" and why not the "AND" ?



# We do need an adequate number of motile sperm

Fertil Steril. 2004 Sep;82(3):612-20.

**Performance of the postwash total motile sperm count as a predictor of pregnancy at the time of intrauterine insemination: a meta-analysis.**

**van Weert JM, et al.**

RESULT(S): We detected 16 studies that reported on postwash TMC at insemination and IUI outcome. Summary receiver operating characteristics (ROC) curves indicated a reasonable predictive performance toward IUI outcome, and, at cut-off levels between 0.8 to 5 million motile spermatozoa, the postwash TMC provided a substantial discriminative performance. At these cut-off levels, the specificity of the postwash TMC, defined as the ability to predict failure to become pregnant, was as high as 100%; the sensitivity of the test, defined as the ability to predict pregnancy, was limited.

# (MOH)/IUI versus IVF

1b



**\$ 5,000**



**\$ 13,000**

Goverde et al. Lancet 2000

# MOH/IUI versus IVF

1b



**\$ 10,000**



**\$ 43,000**

Van Voorhis et al. Fertil Steril 1998

# IUI versus ICSI, moderate male SF

2b



*Philips et al. Hum Reprod 2000*

# IUI or IVF: Dutch prizes 2009

	<b>MOH/IUI</b>	<b>IVF/ICSI</b>
Treatment cycle	€ 410	€ 1717
Drugs (rec FSH)	€ 372	€ 980
<b>Total:</b>	<b>€ 782</b>	<b>€ 2697</b>
Visits: on average	4-5 times	5-7 times



**Direct costs: 3-4 cycles MOH/IUI equal 1 cycle IVF/ICSI**

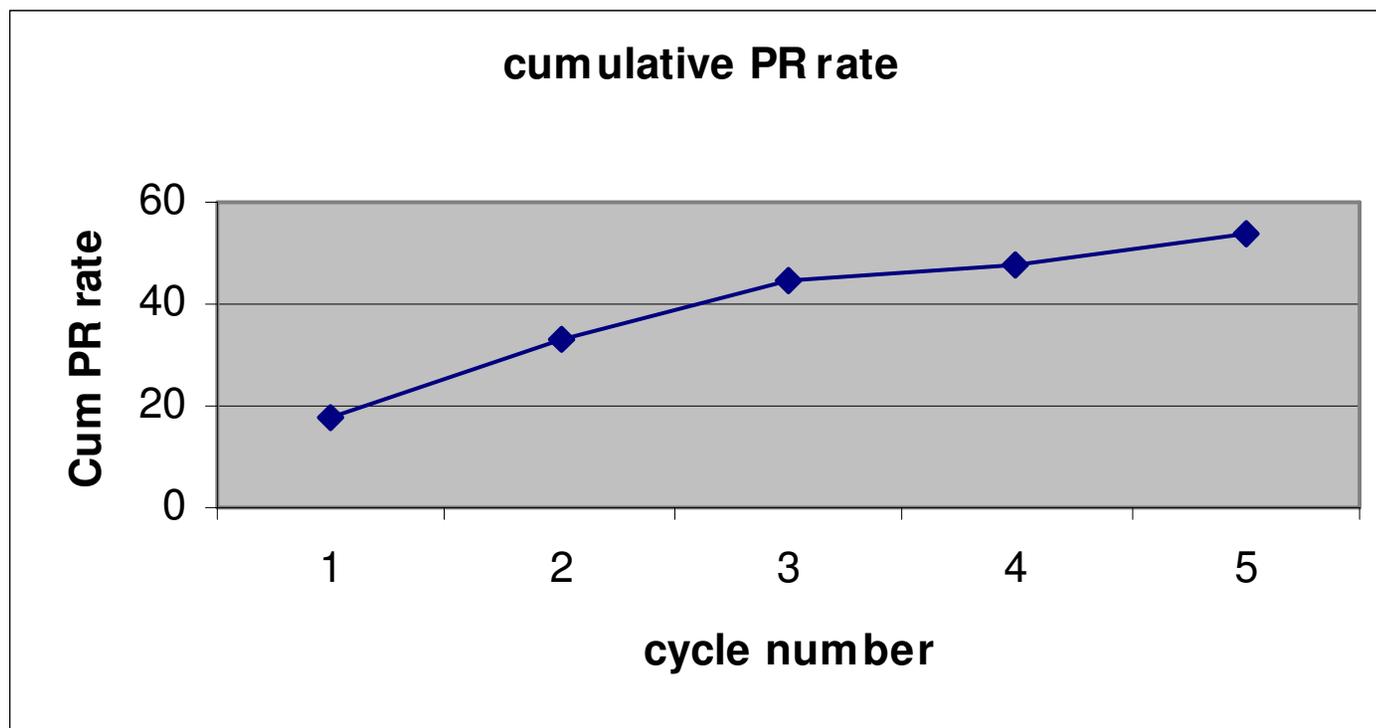
Statement: IUI /MOH seems cost-effective only when the percentage of multiple pregnancies is kept to a minimum

# And this seems possible.....

2 ½ year IUI in Zwolle: pregnancies per started cycle

Natural cycle IUI:	44/496 (8.9%)	(1 twin: 2%)
MOH/IUI:	206/1510 (13.6%)	(14 twins: 6.8% 1 triplet: 0.5%)

# Cohort MOH/IUI started in 2008



# Conclusion

## IUI in natural cycles:

- ❖ has been proven effective in cervical hostility
- ❖ might be effective in male subfertility
- ❖ is ineffective in unexplained subfertility

# Conclusion

- Why the “or” question instead of “and”.
- No level 1 evidence comparing IUI in natural cycles with IVF/ICSI
- Three cycles of MOH/IUI equal one cycle of IVF regarding direct costs and cumulative live births rates might be higher.
- Research question should therefore be:

Do three cycles of MOH/IUI equal one cycle of IVF regarding cost-effectiveness including perinatal costs and long-term follow up?

Multicenter Dutch trial: INEZ TRIAL (see next speaker)