Inseminate to perfection

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Introduction

The result of intrauterine insemination (IUI) depends on variable factors

- semen quality
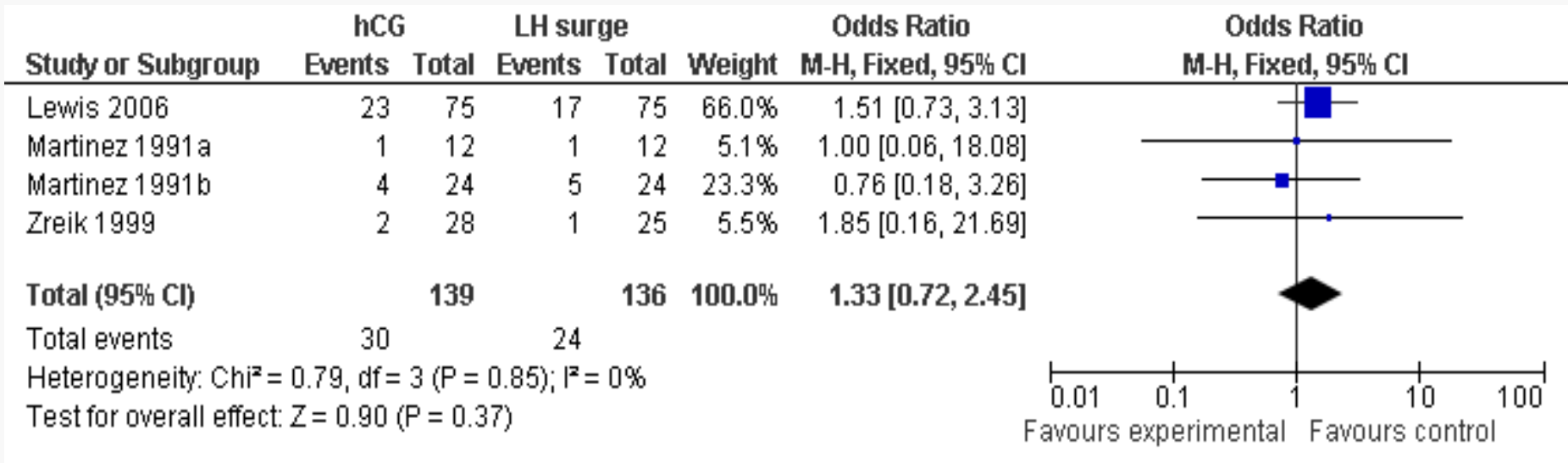- age of the patients
- timing of insemination

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Isis

The live giving qualities of an Egypt goddess

Methods of timing

- hCG
- LH detection
- GnRH analogs
- Recombinant LH
- Ultrasound detection alone

hCG versus LH surge detection

Study or Subgroup	hCG Events	Total	LH surge Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Lewis 2006	23	75	17	75	66.0%	1.51 [0.73, 3.13]	
Martinez 1991a	1	12	1	12	5.1%	1.00 [0.06, 18.08]	
Martinez 1991b	4	24	5	24	23.3%	0.76 [0.18, 3.26]	
Zreik 1999	2	28	1	25	5.5%	1.85 [0.16, 21.69]	
Total (95% CI)		139		136	100.0%	1.33 [0.72, 2.45]	
Total events	30		24				

Heterogeneity: Chi² = 0.79, df = 3 (P = 0.85); I² = 0%
Test for overall effect: Z = 0.90 (P = 0.37)

Favours experimental   Favours control

Cantineau et al Cochrane database submitted

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hCG versus LH

	applying hCG	**LH surge detection**
advantages	clinical predictability	cheap non-invasive
disadvantages	spontaneous LH surge	false negative results high drop-out

Spontaneous LH surges using hCG

49% of the cycles: spontaneous LH surges

Premature LH and Progesterone rise in intrauterine insemination cycles: analysis of related factors. *Cunha-Filho et al 2003*

24% of the cycles: spontaneous LH surges

Controlled ovarian hyperstimulation and intrauterine insemination for treating male subfertility: a controlled study. *Cohlen et al. 1998*
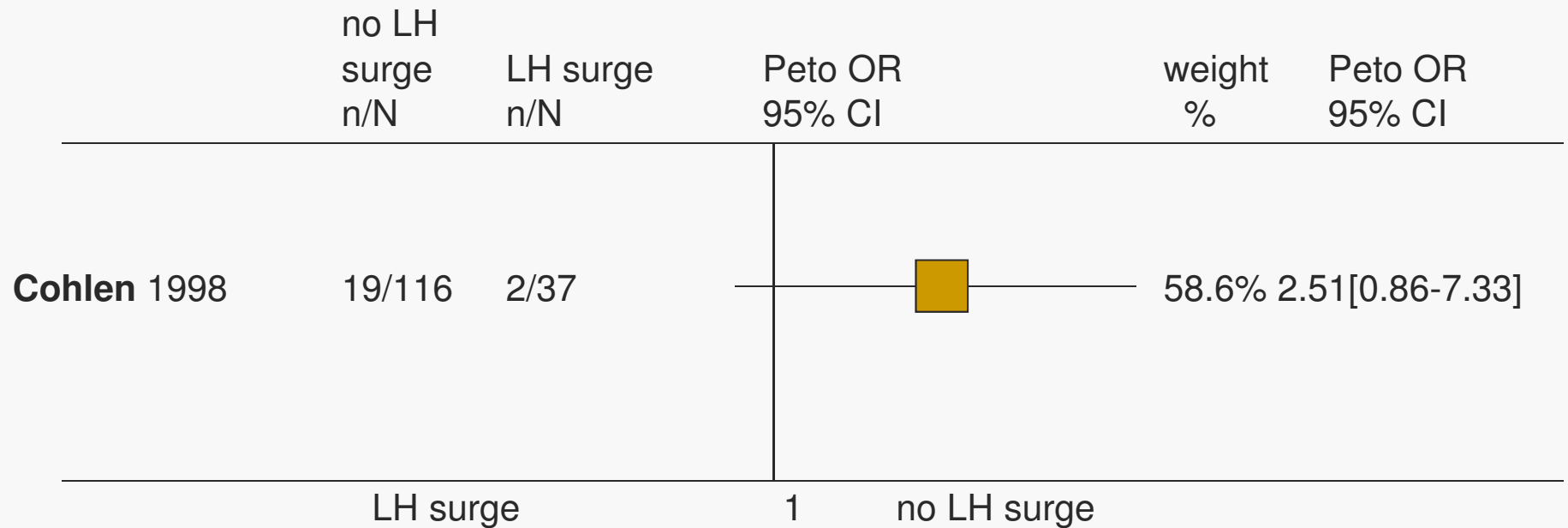
36% of the cycles: spontaneous LH surges

The prevalence and influence of luteinizing hormone surges in stimulated cycles combined with intrauterine insemination during a prospective cohort study. *Cantineau et al. 2007*

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What to do with premature LH surges?
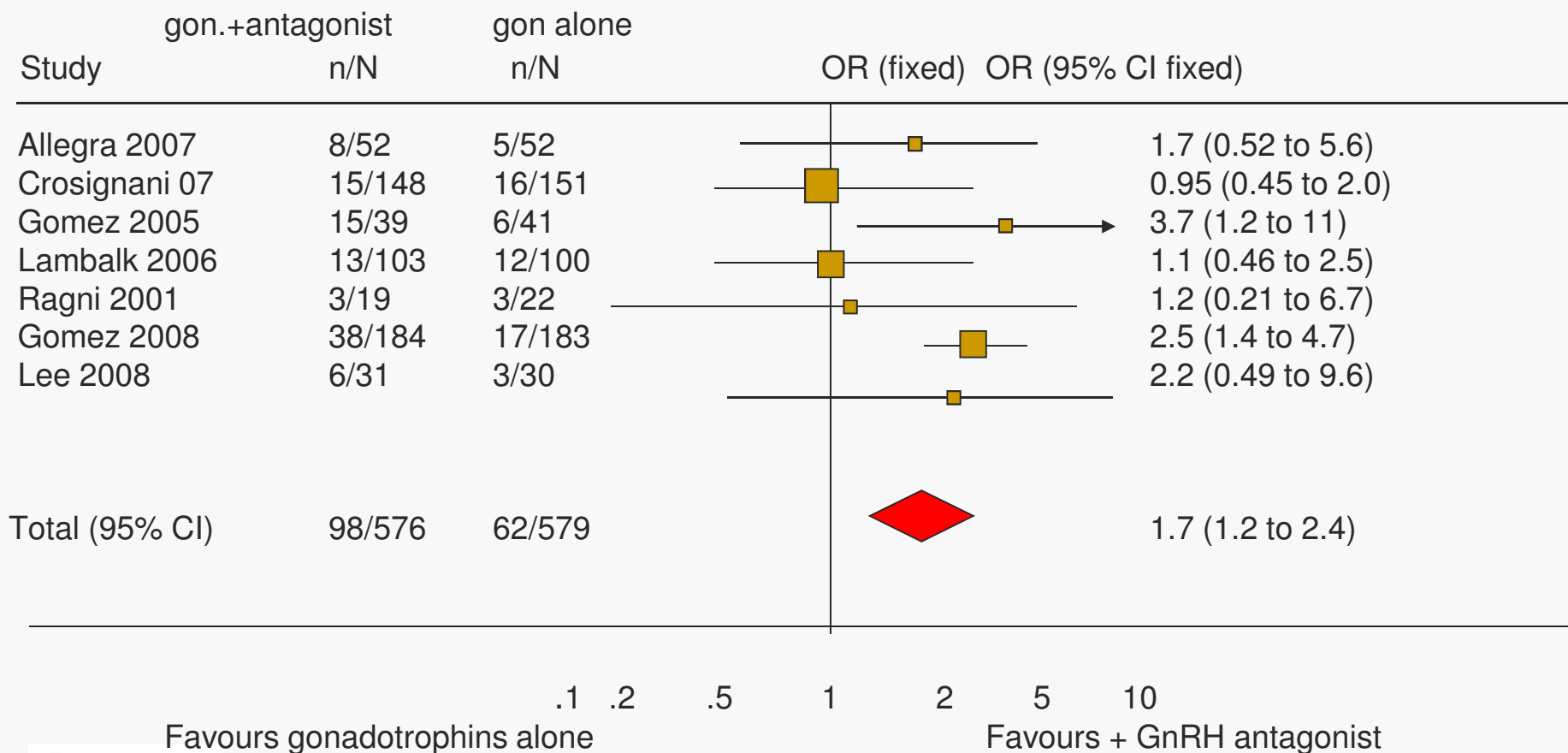
- Adjust timing when premature LH surge is detected

- Prevent spontaneous LH surges by administrating a GnRH antagonist

Adjust timing

	no LH surge n/N	LH surge n/N	Peto OR 95% CI		weight %	Peto OR 95% CI
Cohlen 1998	19/116	2/37			58.6%	2.51[0.86-7.33]

LH surge 1 no LH surge

Cohlen et al 1998 Hum Reprod

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Add GnRH antagonist

Ongoing pregnancy rate per couple

Study	gon.+antagonist n/N	gon alone n/N	OR (fixed)	OR (95% CI fixed)
Allegra 2007	8/52	5/52		1.7 (0.52 to 5.6)
Crosignani 07	15/148	16/151		0.95 (0.45 to 2.0)
Gomez 2005	15/39	6/41		3.7 (1.2 to 11)
Lambalk 2006	13/103	12/100		1.1 (0.46 to 2.5)
Ragni 2001	3/19	3/22		1.2 (0.21 to 6.7)
Gomez 2008	38/184	17/183		2.5 (1.4 to 4.7)
Lee 2008	6/31	3/30		2.2 (0.49 to 9.6)
Total (95% CI)	98/576	62/579		1.7 (1.2 to 2.4)

.1 .2   .5   1   2   5   10

Favours gonadotrophins alone   Favours + GnRH antagonist

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Timing

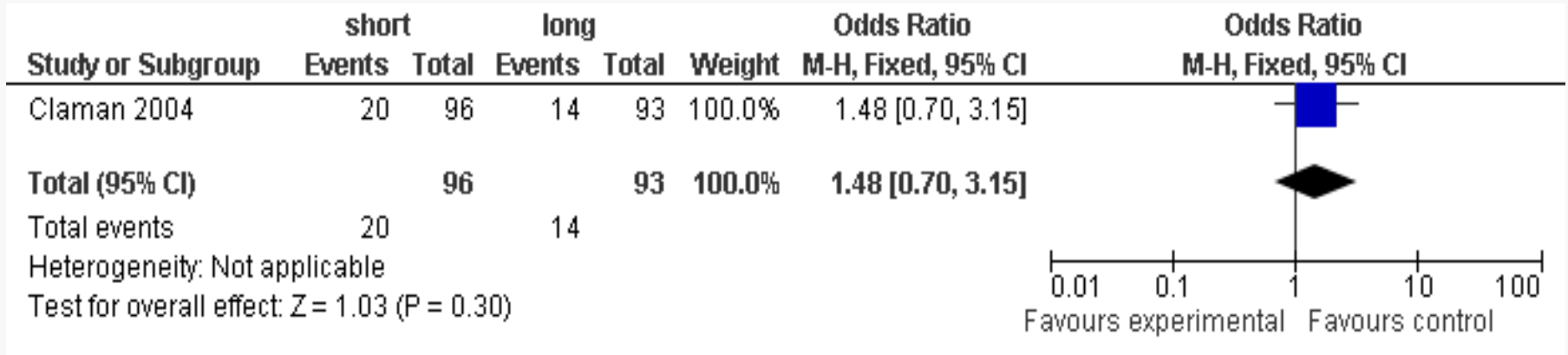Optimal time-interval between hCG and IUI

- 12, 24, 48 hours?

Or…

- double insemination?

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32-34 hours versus 38-40 hours

Study or Subgroup	short Events	short Total	long Events	long Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Claman 2004	20	96	14	93	100.0%	1.48 [0.70, 3.15]
Total (95% CI)		96		93	100.0%	1.48 [0.70, 3.15]
Total events	20		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.03 (P = 0.30)						

Cantineau et al Cochrane database submitted

Single versus double IUI

| | Double IUI | | Single IUI | | | Odds Ratio | Odds Ratio |
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Casadei 2006	9	39	5	43	4.4%	2.28 [0.69, 7.52]	
Liu 2006	124	624	70	633	66.5%	1.99 [1.45, 2.74]	
Ng 2003	11	30	11	30	8.3%	1.00 [0.35, 2.86]	
Ragni 1999a	28	92	6	45	6.7%	2.84 [1.08, 7.48]	
Ragni 1999b	10	91	7	45	10.0%	0.67 [0.24, 1.90]	
Zeyneloglu 2002	4	40	4	42	4.2%	1.06 [0.25, 4.54]	
Total (95% CI)		916		838	100.0%	1.81 [1.39, 2.36]	
Total events	186		103				

Heterogeneity: Chi² = 6.60, df = 5 (P = 0.25); I² = 24%
Test for overall effect: Z = 4.39 (P < 0.0001)

Cantineau et al Single versus double IUI Cochrane database updated

Conclusions

- No difference in pregnancy rates between timing with hCG and LH surge detection

- Significant more pregnancies when GnRH antagonist is added to ovarian stimulation

- Optimal time-interval after hCG is not defined (yet)

- Double insemination for male subfertility seems more effective than single IUI

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Questions?