Gonadotropinlerle Ovulasyon İndüksiyonu

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ÜYTEM

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Ovulation

Ovulation is the process by which the maternal genetic material can be transferred, by the oocyte, to the next generation.

Health and fertility in WHO group 2 anovulatory Women,
ESHRE Capri Workshop Group
Human Reproduction Update, 2012

Fertility treatments

Regardless of the etiology, infertility treatment has become increasingly"cycle based" whereby ovarian stimulation by oral and/or injectable drugs is combined with a sperm delivery technique, usually IUI, IVF, or ICSI.

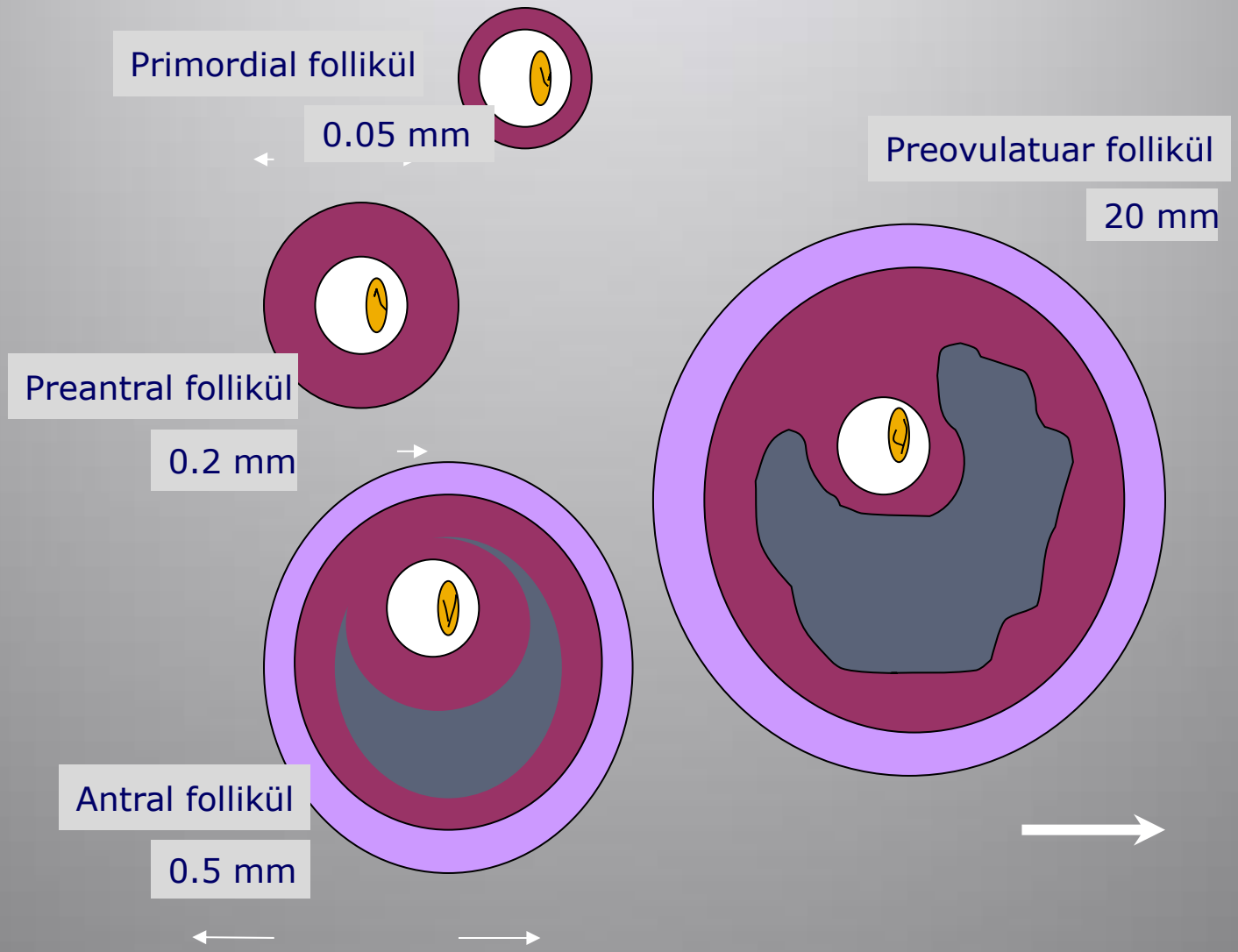
Fertility treatments and outcomes among couples seeking fertility care
J.F. Smith , Fertility and Sterility 2011

Fertility treatments

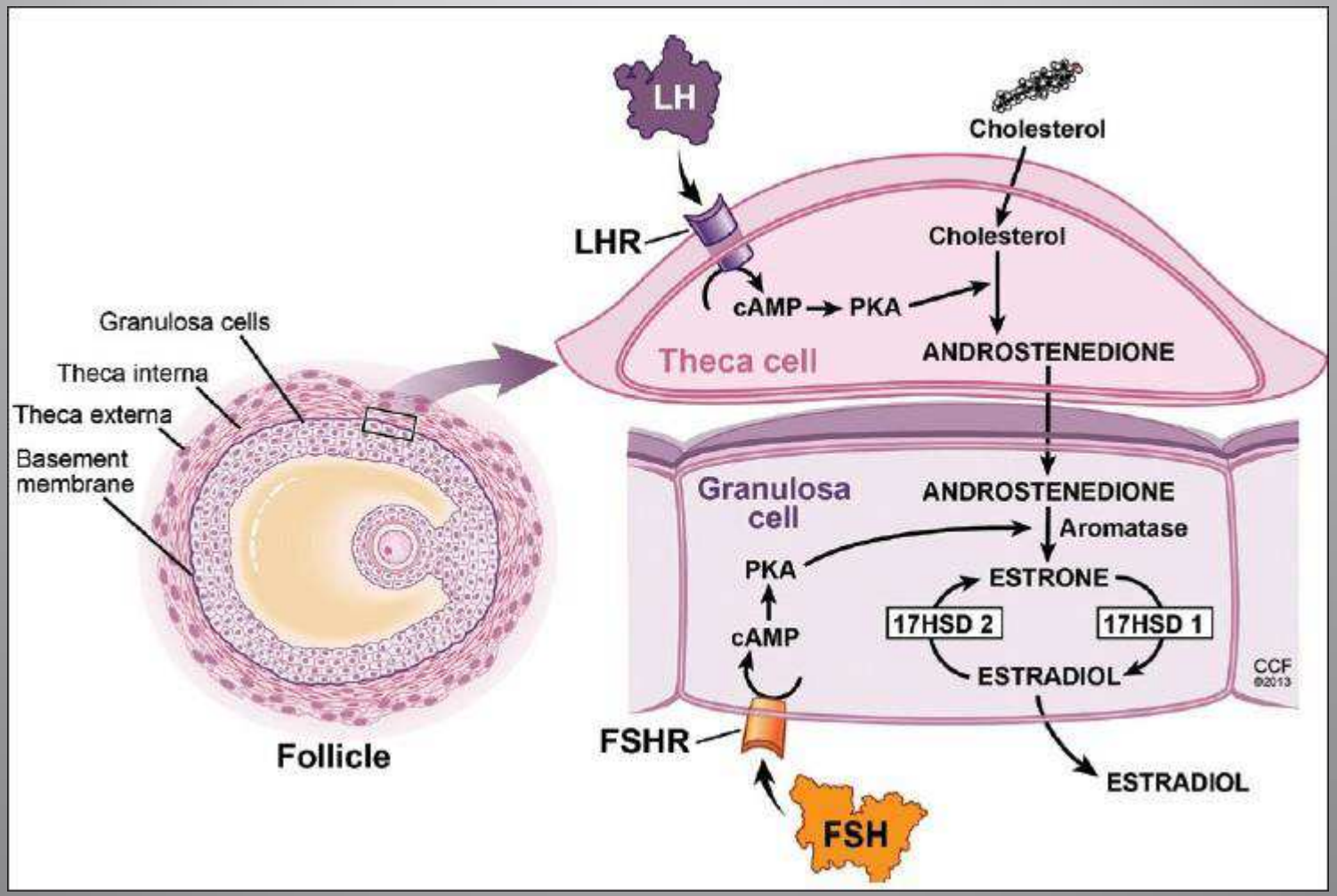
Approximately half of all women who receive fertility care achieve conception leading to a live birth.

Speroff & Fritz, 2005

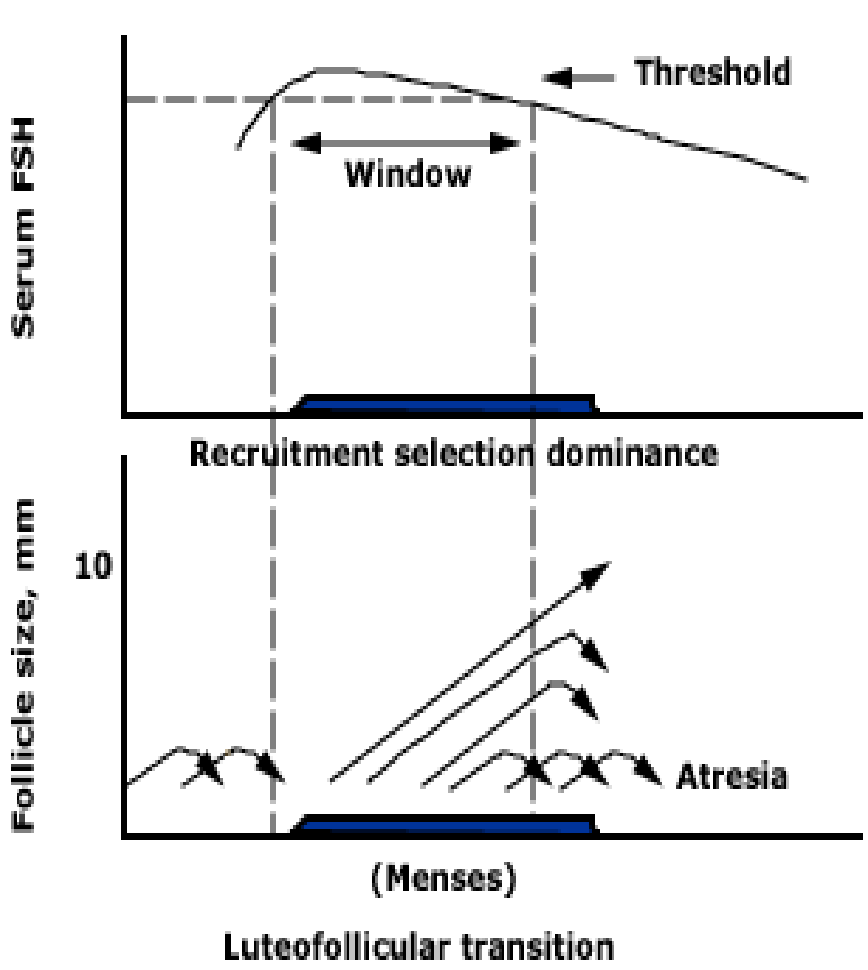
Folliculogenesis

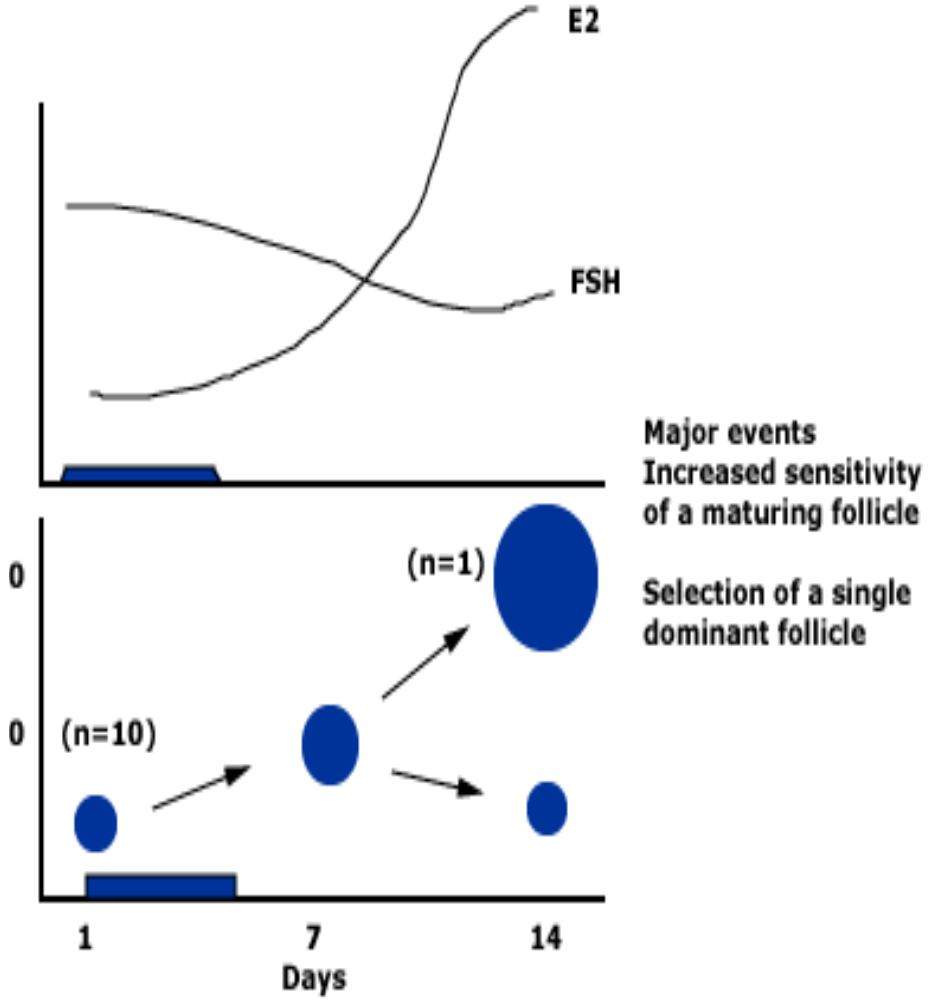


Two cell theory



Follicular development





Infertility treatment

1. Regular, unprotected sexual intercourse
2. CC + IUI
3. Gonadotrophin + IUI
4. IVF

Ovulation induction

- Clomiphene citrate
- Aromatase inhibitor
- Gonadotrophin
- Metformin
- GnRH antagonist
- Pulsatile GnRH
- Dopamine agonist

History of important developments in the production of exogenous gonadotropins

1927	Discovery of gonadotropin in the urine of pregnant women by Aschheim and Zondek
1930	Discovery of gonadotropin in the urine of postmenopausal women by Zondek
1931	Discovery of gonadotropin in the urine of pregnant mares by Cole and Hart
1937	Purified extract of gonadotropin from the urine by Cartland and Nelson
1947	Purified extract from postmenopausal urine (hMG, pergonal) by Piero Donini
1948	Recognition of the placental origin of urinary gonadotropin in pregnant women
1950s	Recognition of the roles of the pituitary and chorionic gonadotropins in ovulation
1959	Clinical use of purified urinary gonadotropins (chorionic and pituitary)
1961	First pregnancy with hMG treatment
1984	Clinical use of GnRH agonists
1985	Clinical use of urinary FSH (purified and highly purified)
1990	Clinical use of recombinant gonadotropins

Gonadotropin induction of ovulation
Saad Amer, *Obstetrics, Gynaecology - Reproductive Medicine, 2007*

Gonadotrophins

- Human menopausal gonadotrophin — Urine — FSH+LH
  - Menogon, Merional, Menopur
- Purified urinary FSH — Urine — FSH
  - Fostimon
- Recombinant FSH — T.CHO — FSH
  - Gonal-F, Puregon, Elonva
- Human Chorionic Gonadotrophin — Urine — hCG
  - Pregnyl, Choragon
- Rec. Human Chorionic Gonadotrophin — T:CHO — hCG
  - Ovitrelle
- Recombinant LH — T.CHO — LH
  - Luveris

Gonadotrophin ovarian induction

- Indications for gonadotropin ovulation induction include hypogonadotrophic hypogonadism and clomiphene-resistant PCOS. The objective of treatment in anovulatory women should be to induce mono-ovulation

- In women with hypogonadotrophic hypogonadism, a small amount of exogenous LH is required for optimal follicular development. A step-up regimen is the usual treatment protocol in this group of women

- Controlled ovarian hyperstimulation in combination with intrauterine insemination is an effective treatment for ovulatory women with unexplained or mild male factor infertility

Gonadotropin induction of ovulation
Saad Amer, *Obstetrics, Gynaecology Reproductive Medicine, 2007*

Women with WHO group II anovulation (mostly PCOS)

- BMI<30
- CC
  - Metformin
- Gonadotrophin
- LOD
- IVF

Assessment and treatment for people with fertility problems
NICE clinical guideline 156, 2013

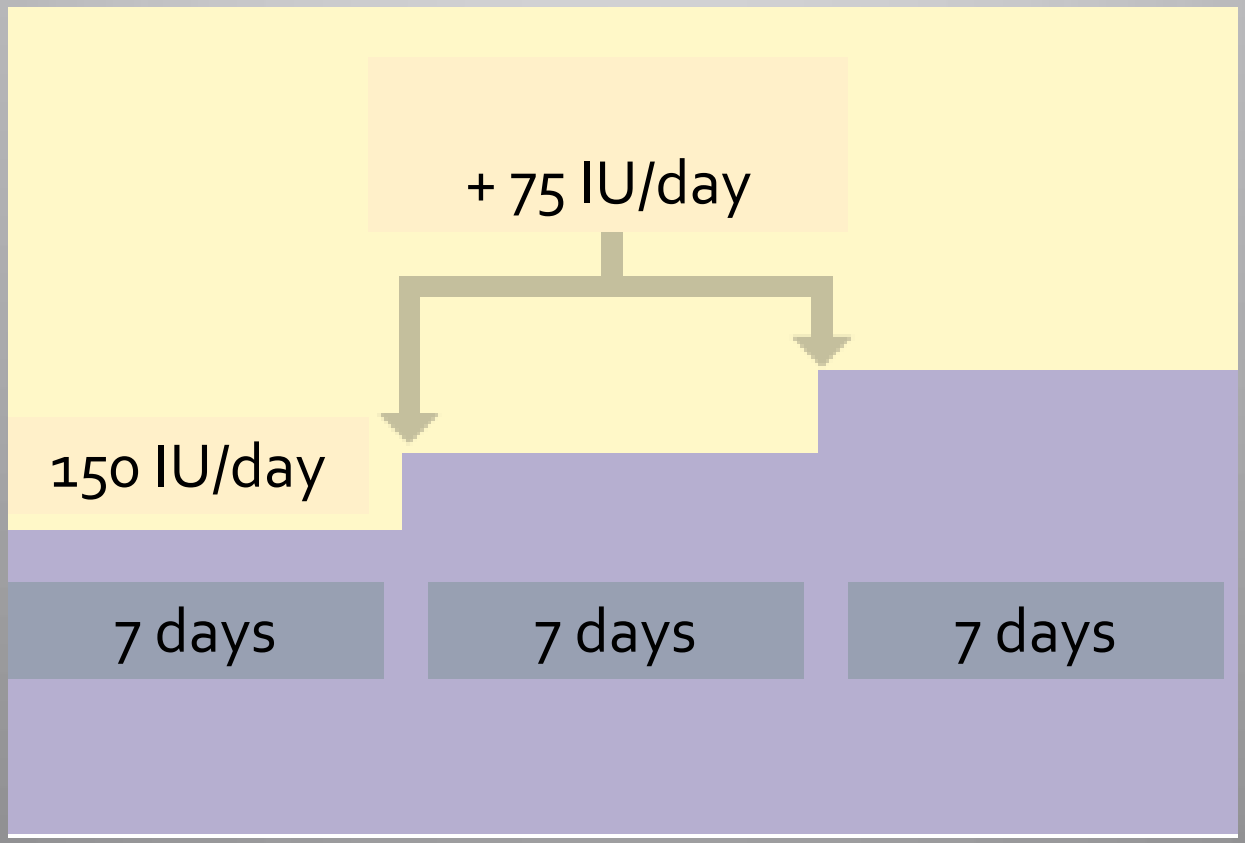
Women with hypogonadotrophic hypogonadism (WHO group I)

- BMI>19
- Moderate exercise

- Pulsatile administration of gonadotrophin-releasing hormone
- Gonadotrophins with LH

Assessment and treatment for people with fertility problems
NICE clinical guideline 156,2013

Conventional protocol



Thompson and Hansen, 1970; Dor et al., 1980; Wang and Gemzell, 1980

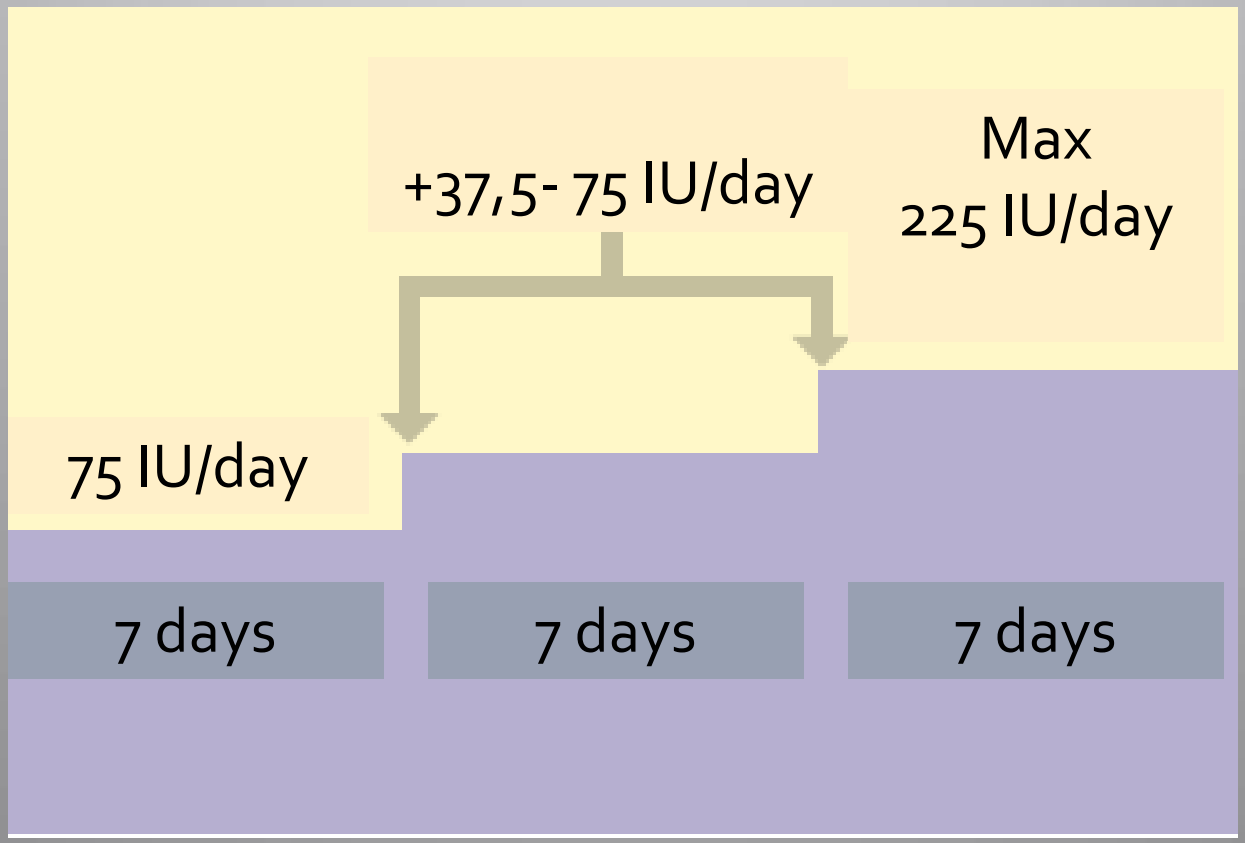
Conventional protocol

- Pregnancy (46%)
- High risk of multiple follicular development,
  - multiple pregnancies (36%),
  - miscarriages (23%)
  - severe OHSS (4.6%)

  reported for conventional dose protocols

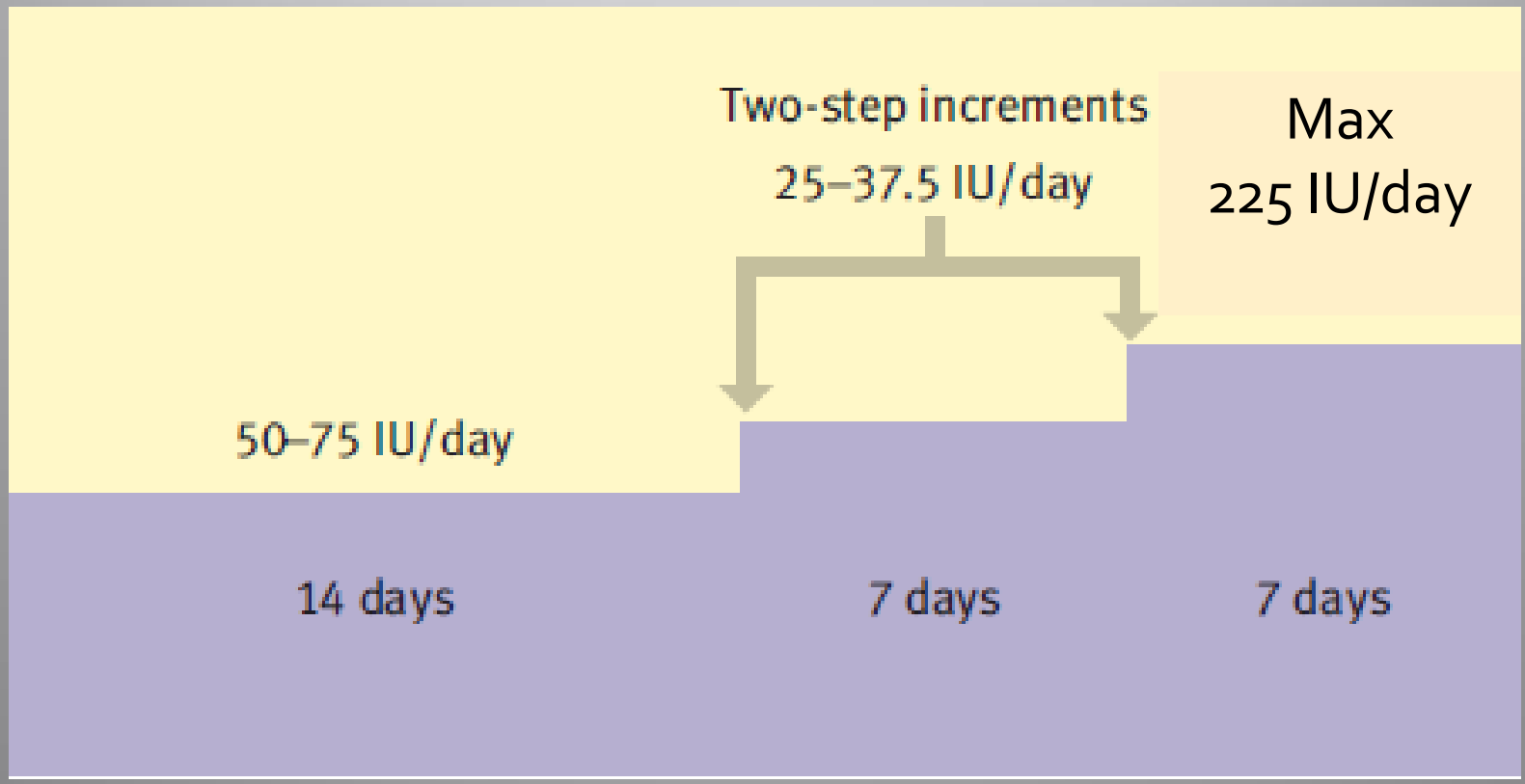
Common problems in induction of ovulation
Baillieres Clin Obstet Gynaecol
Hamilton-Fairley and Franks, 1990

Low dose step-up protocol



White et al., 1996; Hayden et al., 1999; Balasch et al., 2000; Calaf et al., 2003b

Chronic low dose step-up protocol



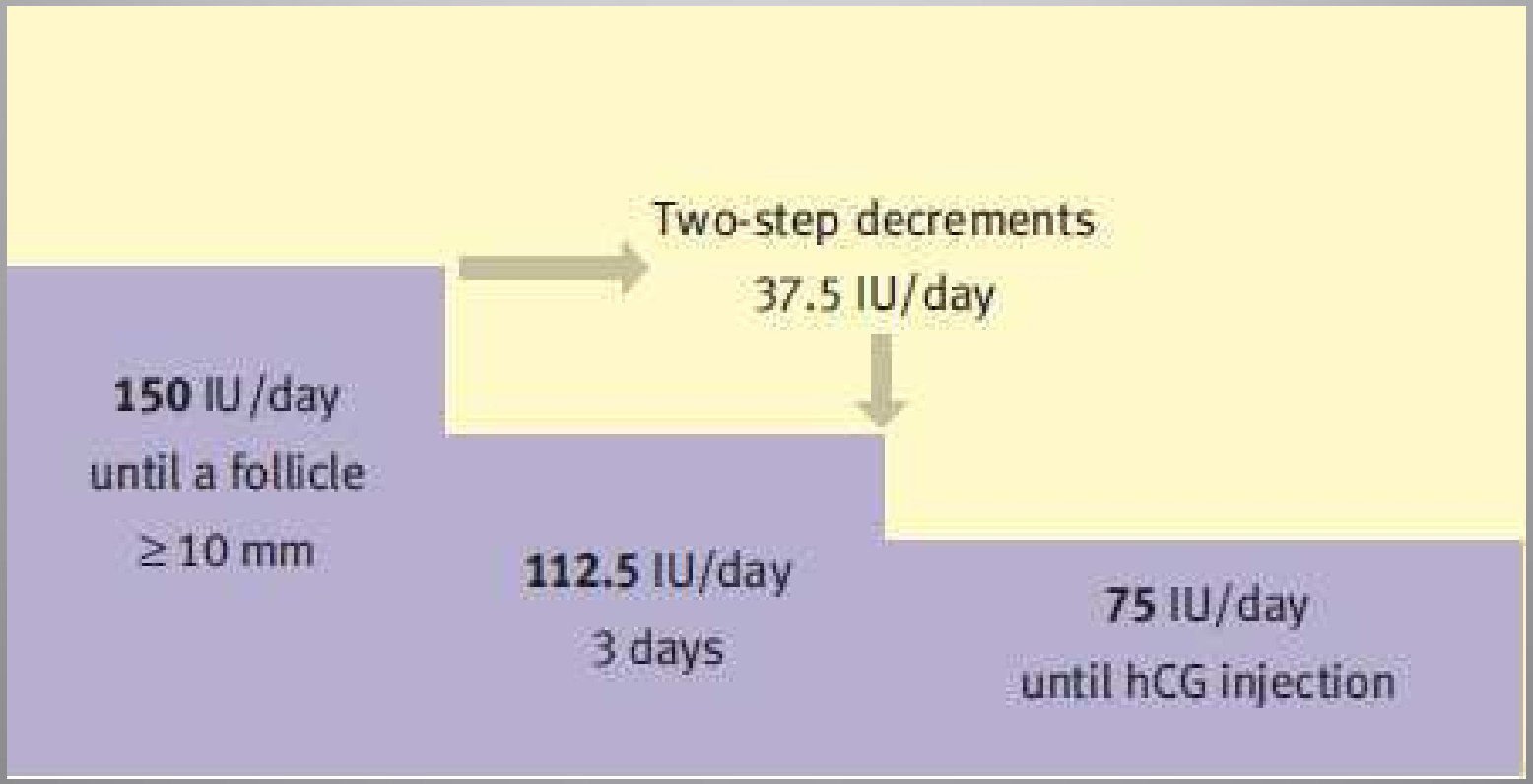
Seibel et al., 1984; Polson et al., 1987; Sagle et al., 1991; Dale et al., 1993

Step-up protocol

- Monofollicular ovulation (~70%)
- Low rates of multiple pregnancies (~5%) and OHSS (<1%),
- Good pregnancy rates (20% per cycle and 40% per patient)

Low-dose FSH therapy for anovulatory infertility associated with polycystic ovary syndrome
Homburg R. Hum Reprod Update 1999

Step-down protocol



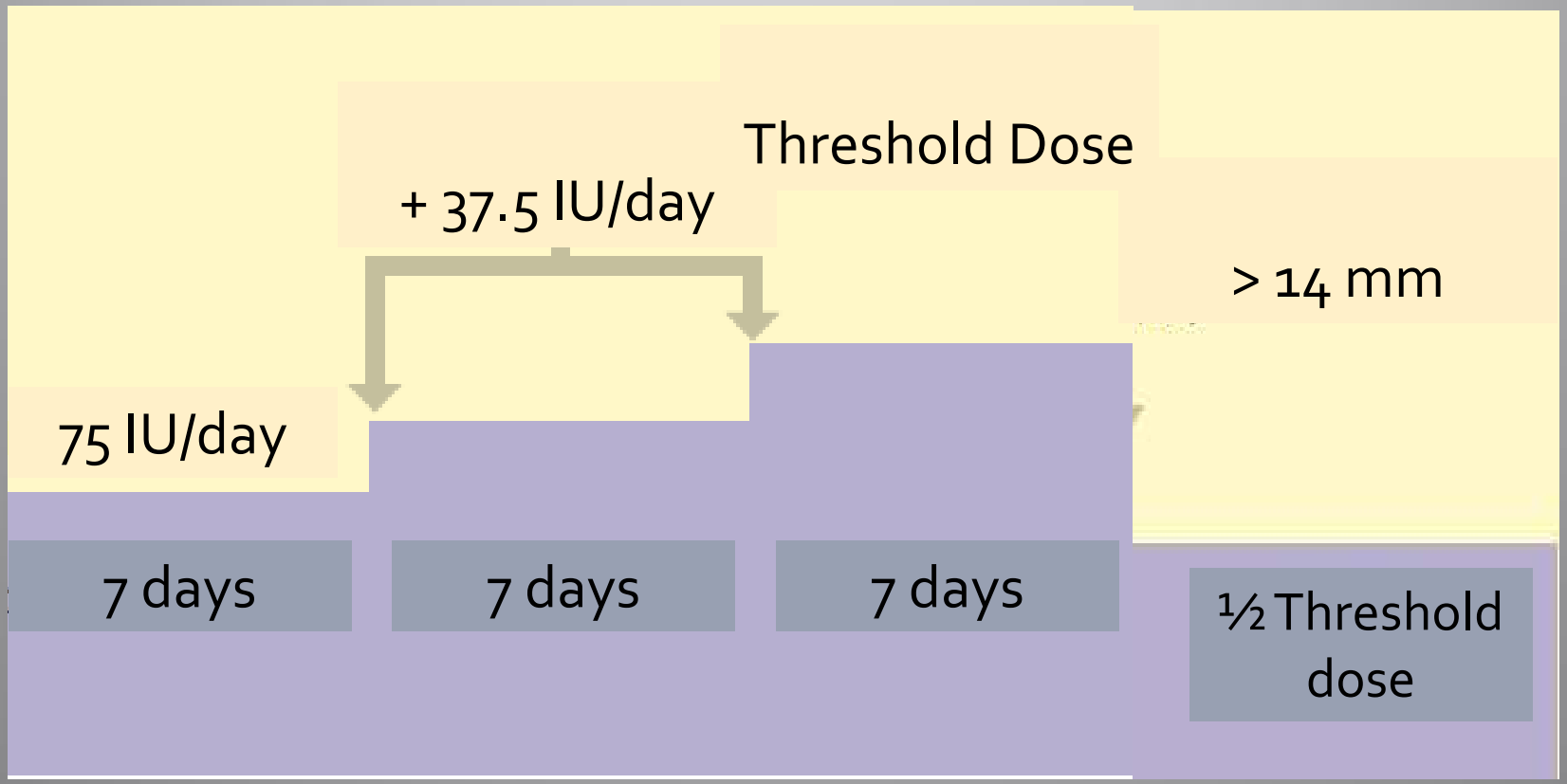
Schoot et al., 1992; van Dessel et al., 1996; Fauser and Van Heusden, 1997

Step-up vs Step-down protokol

	Step-up protocol (n = 85 cycles)	Step-down protocol (n = 72 cycles)	P
Duration of treatment (days)	15.2 ± 7	9.7 ± 3.1	< 0.001
Total amount of rFSH (IU)	951 ± 586	967 ± 458	NS
Rate of monofollicular development (%)	68.2	32	< 0.0001
Rate of bifollicular development (%)	15.3	23.6	NS
Rate of multifollicular (>3) development (%)	4.7	36	< 0.0001
Estradiol plasma value at hCG (pg/ml)	454 ± 465	849 ± 1115	< 0.05
hCG administration (%)	84.6	61.8	0.001
Rate of hyperstimulation (%)	2.25	11	0.001
No response (%)	11.8	8.33	NS
Progesterone > 8ng/ml (%) in luteal phase	70.3	61.7	0.02
Pregnancy/cycle (%)	18.7	15.8	NS

A comparative randomized multicentric study comparing the step-up versus step-down protocol in polycystic ovary syndrome
S.Christin-Maitre. Hum Reprod 2003

Sequential step-up step-down protocol



Hugues et al., 1996, 2006

Sequential step-up step-down protocol

- Reduce the risk of over-response ?

Sequential step-up and step-down dose regimen: an alternative method for ovulation induction with FSH in PCOS. Hugues JN. Hum Reprod 1996

Complications

- Multiple pregnancy
  - E2 > 1000-1500 pg/ml
  - >3 follicles (16-17)
  - > 10-14 mm follicles
- OHSS
  - E2 > 2500 pg/ml
  - > 10-14 mm follicles
  - hCG
- Cancer
  - Ovarian : not supported
  - Breast : not supported

Arch Gynecol Obstet (2012) 286:1055–1059

Comparison of different starting gonadotropin doses (50, 75 and 100 IU daily) for ovulation induction combined with intrauterine insemination

Robert Streda · Tonko Mardesic · Vladimir Sobotka ·

Table 4 Outcome of the treatment

	50 IU ($n = 31$)	75 IU ($n = 42$)	100 IU ($n = 14$)	p value
Clinical pregnancy rate n (%)[a]	7 (22)	4 (10)	4 (28)	ns
Abortions n (%)[a]	1 (3)	0	0	ns
Ongoing pregnancy rate n (%)[a]	6 (19)	4 (10)	4 (28)	ns
Twins n (%)[a]	0	1 (25)	1 (25)	ns

Human Reproduction Vol.23, No.6 pp. 1424–1430, 2008
doi:10.1093/humrep/den089
Advance Access publication on March 26, 2008

Predicting the FSH threshold dose in women with WHO Group II anovulatory infertility failing to ovulate or conceive on clomiphene citrate

Anders Nyboe Andersen[1,5], Adam Balen[2], Peter Platteau[3], Paul Devro ,

Table II. Statistically significant predictors of FSH threshold dose (univariate and multivariate analysis).

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P*-value[a]	OR (95% CI)	*P*-value[a]
Age (years)	0.91 (0.83–1.00)	0.040	—	—
BMI (kg/m²)	1.10 (1.02–1.19)	0.010	1.17 (1.07–1.29)	<0.001
Failure to ovulate on clomiphene citrate: yes versus no	2.27 (1.14–4.52)	0.020	—	—
Menstrual cycle history		<0.001		<0.001
Amenorrhea versus cycle length 21–35 days	8.33 (2.81–24.7)		11.88 (3.35–42.1)	
Oligomenorrhea versus cycle length 21–35 days	3.48 (1.51–8.03)		2.57 (0.97–6.79)	
Mean ovarian volume (cm^3)	1.18 (1.06–1.31)	0.002	1.22 (1.08–1.37)	<0.001
Free androgen index (nmol/l)	1.25 (1.13–1.38)	<0.001	—	—
Total testosterone (nmol/l)	2.14 (1.14–4.03)	0.018	—	—
LH/FSH ratio (IU/l)	1.59 (1.03–2.45)	0.038	—	—

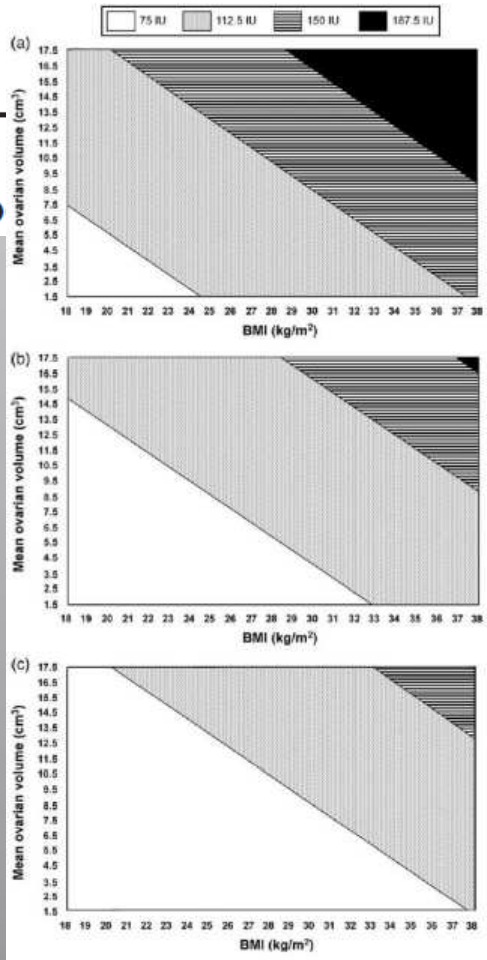


Figure 2: Nomograms for prediction of individual FSH threshold dose in anovulatory patients undergoing ovulation induction with FSH preparations, according to menstrual cycle history, BMI and mean ovarian volume. (a) Amenorrhea, (b) oligomenorrhea and (c) anovulatory cycles with cycle length 21–35 days.

The influence of body weight on response to ovulation induction with gonadotrophins in 335 women with World Health Organization group II anovulatory infertility

RCOG 2006 BJOG An International Journal of Obstetrics and Gynaecology

AH Balen,[a] P Platteau,[b] AN Andersen,[c] P Devroey,[b] P Sørensen,[d] L Helmgaard,[d] J-C Arce[d]

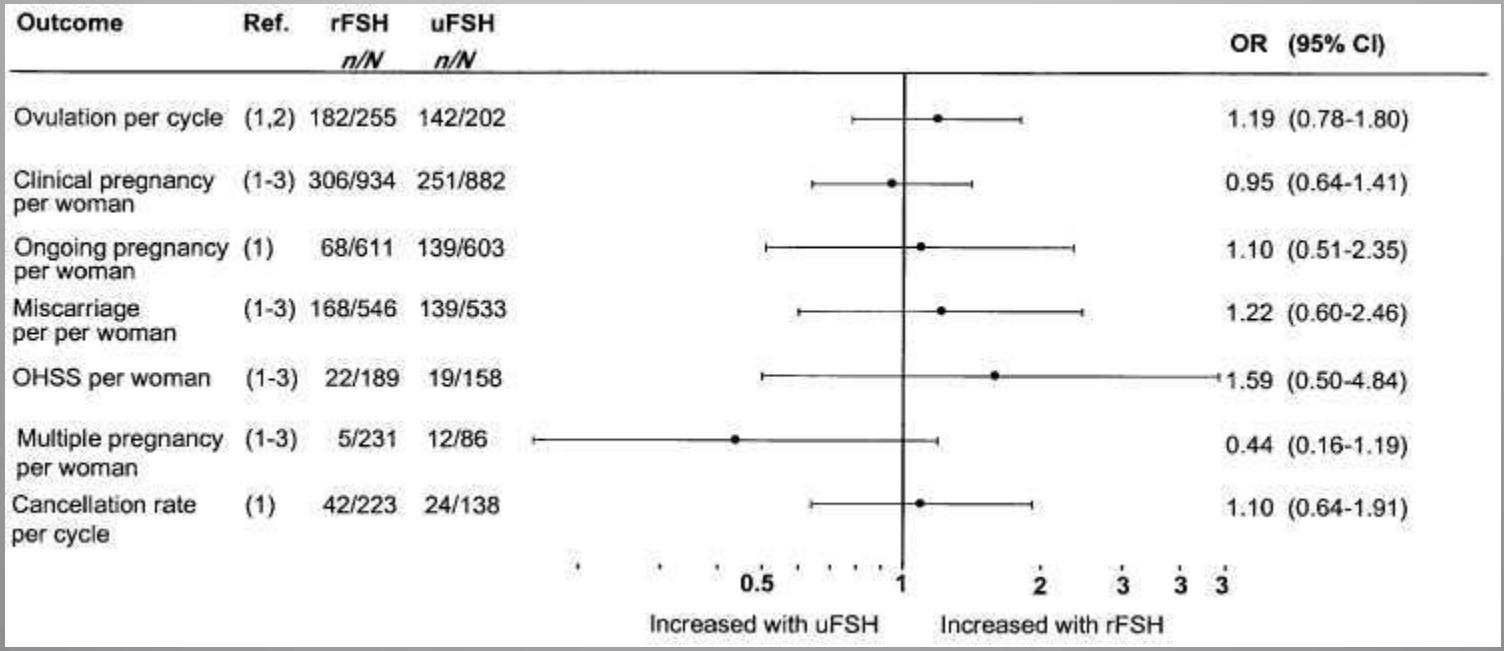
	BMI (kg/m²)			All
	<25	25.1–30	>30.1	
Days of stimulation	12.0 ± 4.4	13.9 ± 6.8	15.9 ± 8.1	13.3 ± 6.2
Total dose of gonadotrophin (iu)	1025 ± 512	1302 ± 899	1633 ± 1279	1220 ± 854
Threshold dose (iu)				
75	64%	56%	45%	58%
112.5	30%	27%	36%	31%
150	5%	14%	10%	8%
187.5	1%	4%	9%	3%
Follicles of size (mm)				
<12	12.8 ± 13.1	12.5 ± 12.2	18.8 ± 15.5	13.9 ± 13.5
12–16	1.6 ± 2.9	1.2 ± 2.4	0.6 ± 1.4	1.3 ± 2.6
17	1.3 ± 0.9	1.0 ± 0.6	1.1 ± 0.6	1.2 ± 0.8
Total follicles	15.7 ± 13.5	14.8 ± 12.3	21.0 ± 15.5	16.5 ± 13.7
Follicular development (%)				
Inadequate	4	9	8	6
Monofollicular	54	54	68	56
Bifollicular/multifollicular	42	38	25	38
Endometrial thickness	8.7 ± 2.1	9.4 ± 2.4	10.0 ± 2.0	9.1 ± 2.2
Ovulation rate (%)	87	83	80	84
Positive hCG (%)	20	24	26	22
Clinical pregnancy rate (%)	17	20	18	18
Continuing pregnancy rate (%)	16	19	17	17

This study confirms the effect of increasing body weight on ovarian response to gonadotrophin stimulation but also indicates that carefully conducted ovulation induction therapy can achieve satisfactory rates of ovulation and pregnancy in women with a BMI up to 35 kg/m^2.

Recombinant FSH in alternative doses or versus urinary gonadotrophins for ovulation induction in subfertility associated with polycystic ovary syndrome: a systematic review based on a Cochrane review

Human Reproduction Vol.18, No.6 pp. 1143–1149, 2003

M.van Wely[1], N.Bayram and F.van der Veen



human reproduction ORIGINAL ARTICLE *Infertility* Vol.27, No.2 pp. 468–473, 2012

Clomifene citrate or low-dose FSH for the first-line treatment of infertile women with anovulation associated with polycystic ovary syndrome: a prospective randomized multinational study

R. Homburg[1,*], M.L. Hendriks[1], T.E. König[1], R.A. Anderson[2],

Table II Results (per-protocol) comparing treatment with clomifene and low-dose FSH.

	CC	FSH	*P*-value
Number of patients randomized	143	159	
Number of patients per protocol	123	132	
Cycles	310	288	
Clinical pregnancies (per patient)	54 (44%)	76 (58%)	0.03
Ongoing pregnancies (per patient)	48 (39%)	68 (52%)	0.04
Clinical pregnancies (per cycle)	54 (17.4%)	76 (26.4%)	0.008
Ectopic pregnancies	1	1	
Miscarriage rate per pregnancy[a]	5 (9.2%)	7 (9.2%)	
Multiple pregnancies (twins only)	0	2 (3.4%)	
Cumulative pregnancy rate			
Cycle 1	12.9%	25.6%	
Cycle 2	29.3%	44.8%	
Cycle 3	41.2%	52.1%	0.02

Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility (Review)

Cantineau AEP, Cohlen BJ

THE COCHRANE COLLABORATION®

Analysis 1.1. Comparison 1 anti-estrogens versus gonadotrophins, Outcome 1 live birth rate per couple.

Review: Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility

Comparison: 1 anti-estrogens versus gonadotrophins

Outcome: 1 live birth rate per couple

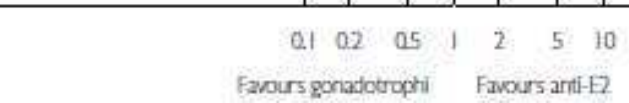
Study or subgroup	anti-estrogens n/N	gonadotrophins n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Dankert 2006	20/71	18/67		100.0 %	1.07 [0.51, 2.26]
Total (95% CI)	**71**	**67**		**100.0 %**	**1.07 [0.51, 2.26]**

Total events: 20 (anti-estrogens), 18 (gonadotrophins)

Heterogeneity: not applicable

Test for overall effect: Z = 0.17 (P = 0.86)

Test for subgroup differences: Not applicable



Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility (Review)

Cantineau AEP, Cohlen BJ

THE COCHRANE COLLABORATION®

Analysis 1.2. Comparison 1 anti-estrogens versus gonadotrophins, Outcome 2 pregnancy rate per couple.

Review: Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility

Comparison: 1 anti-estrogens versus gonadotrophins

Outcome: 2 pregnancy rate per couple

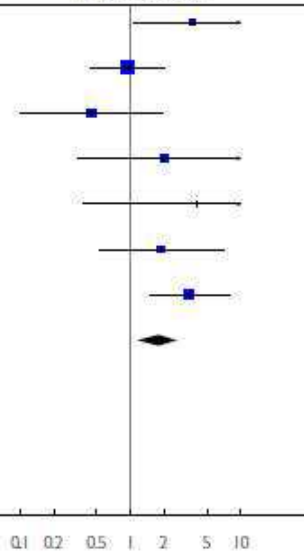
Study or subgroup	Gonadotrophins n/N	Anti-estrogens n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Balasch 1994	12/50	4/50		8.9 %	3.63 [1.08, 12.18]
Dankert 2006	17/67	19/71		40.2 %	0.93 [0.43, 1.99]
Ecochard 2000	3/29	6/29		15.7 %	0.44 [0.10, 1.97]
Kamel 1995	4/28	2/26		5.2 %	2.00 [0.33, 11.97]
Karlstrom 1993	3/15	1/17		2.2 %	4.00 [0.37, 43.38]
Karlstrom 1998	8/40	4/34		10.1 %	1.88 [0.51, 6.88]
Matorras 2002	30/49	16/51		17.7 %	3.45 [1.51, 7.88]
Total (95% CI)	**278**	**278**		**100.0 %**	**1.76 [1.16, 2.66]**

Total events: 77 (Gonadotrophins), 52 (Anti-estrogens)

Heterogeneity: $Chi^2 = 10.40$, $df = 6$ ($P = 0.11$); $I^2 = 42\%$

Test for overall effect: $Z = 2.68$ ($P = 0.0074$)

Test for subgroup differences: Not applicable



Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility (Review)

Cantineau AEP, Cohlen BJ

THE COCHRANE COLLABORATION®

Analysis 1.4. Comparison 1 anti-estrogens versus gonadotrophins, Outcome 4 multiple pregnancy rate per pregnancy.

Review: Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility

Comparison: 1 anti-estrogens versus gonadotrophins

Outcome: 4 multiple pregnancy rate per pregnancy

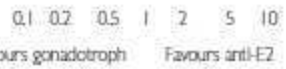
Study or subgroup	gonadotrophins n/N	Anti-estrogens n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
Balasch 1994	0/12	0/4		0.0 [0.0, 0.0]
Dankert 2006	1/23	2/27		0.57 [0.05, 6.70]
Matorras 2002	6/30	2/16		1.75 [0.31, 9.88]
Nakajima 1999	0/4	1/4		0.26 [0.01, 8.52]
Total (95% CI)	**69**	**51**		**0.96 [0.28, 3.28]**

Total events: 7 (gonadotrophins), 5 (Anti-estrogens)

Heterogeneity: $Chi^2 = 1.18$, $df = 2$ ($P = 0.56$); $I^2 = 0.0\%$

Test for overall effect: $Z = 0.06$ ($P = 0.95$)

Test for subgroup differences: Not applicable



Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility (Review)

Cantineau AEP, Cohlen BJ

THE COCHRANE COLLABORATION®

Analysis 1.6. Comparison 1 anti-estrogens versus gonadotrophins, Outcome 6 miscarriage rate per pregnancy.

Review: Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility

Comparison: 1 anti-estrogens versus gonadotrophins

Outcome: 6 miscarriage rate per pregnancy

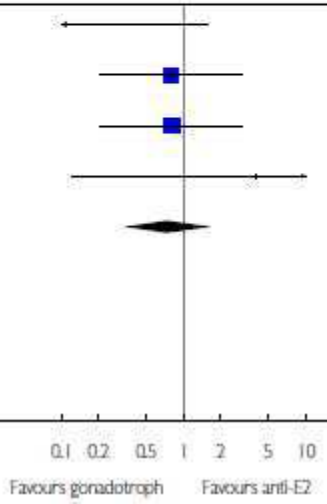
Study or subgroup	gonadotrophins n/N	anti-estrogens n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Balasch 1994	1/12	2/4		21.3 %	0.09 [0.01, 1.55]
Dankert 2006	5/23	7/27		39.0 %	0.79 [0.21, 2.95]
Matorras 2002	8/30	5/16		37.0 %	0.80 [0.21, 3.03]
Nakajima 1999	1/4	0/4		2.7 %	3.86 [0.12, 126.73]
Total (95% CI)	**69**	**51**		**100.0 %**	**0.73 [0.32, 1.67]**

Total events: 15 (gonadotrophins), 14 (anti-estrogens)

Heterogeneity: $Chi^2 = 2.98$, $df = 3$ ($P = 0.39$); $I^2 = 0.0\%$

Test for overall effect: $Z = 0.74$ ($P = 0.46$)

Test for subgroup differences: Not applicable



Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility (Review)

Cantineau AEP, Cohlen BJ

THE COCHRANE COLLABORATION®

Analysis 1.7. Comparison 1 anti-estrogens versus gonadotrophins, Outcome 7 OHSS rate per couple.

Review: Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility

Comparison: 1 anti-estrogens versus gonadotrophins

Outcome: 7 OHSS rate per couple

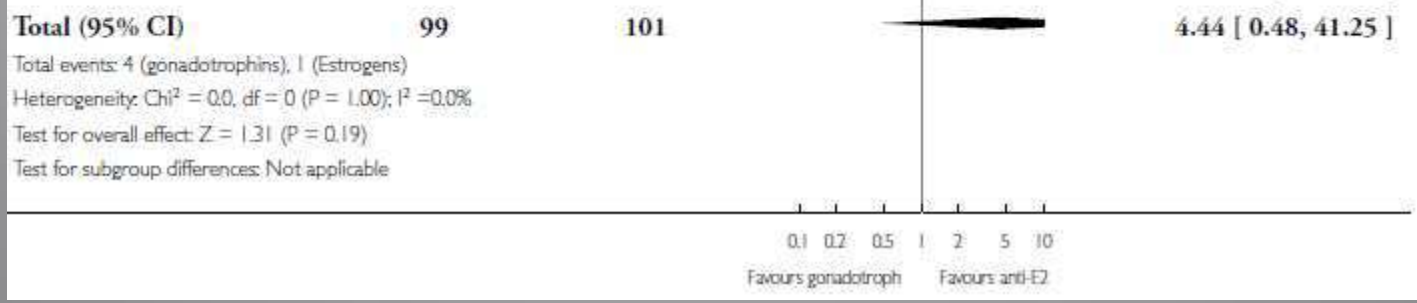
Study or subgroup	gonadotrophins n/N	Estrogens n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
Balasch 1994	0/50	0/50		0.0 [0.0, 0.0]
Matorras 2002	4/49	1/51		4.44 [0.48, 41.25]
Total (95% CI)	**99**	**101**		**4.44 [0.48, 41.25]**

Total events: 4 (gonadotrophins), 1 (Estrogens)

Heterogeneity: $Chi^2 = 0.0$, $df = 0$ ($P = 1.00$); $I^2 = 0.0\%$

Test for overall effect: $Z = 1.31$ ($P = 0.19$)

Test for subgroup differences: Not applicable



Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility (Review)

Cantineau AEP, Cohlen BJ

THE COCHRANE COLLABORATION®

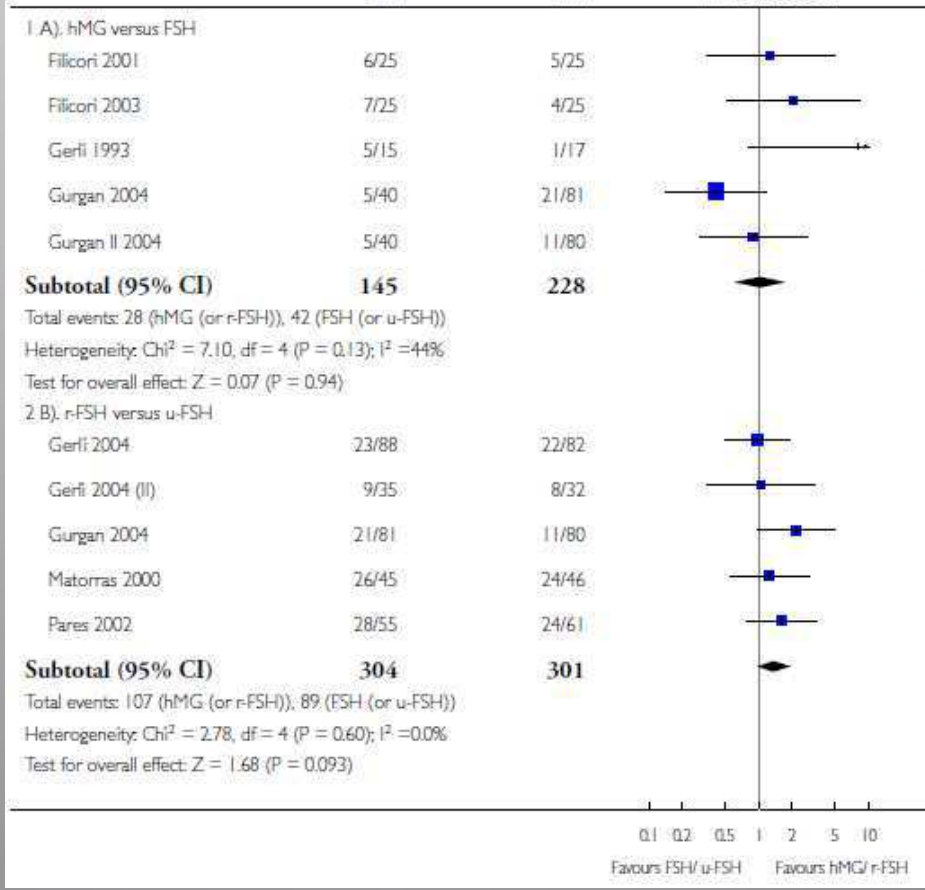
Analysis 5.2. Comparison 5 different types of gonadotrophins, Outcome 2 pregnancy rate per couple.

Review: Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility

Comparison: 5 different types of gonadotrophins

Outcome: 2 pregnancy rate per couple

Study or subgroup	hMG (or r-FSH) n/N	FSH (or u-FSH) n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 A). hMG versus FSH					
Filicori 2001	6/25	5/25		14.7 %	1.26 [0.33, 4.84]
Filicori 2003	7/25	4/25		11.1 %	2.04 [0.51, 8.12]
Gerli 1993	5/15	1/17		2.4 %	8.00 [0.81, 78.83]
Gurgan 2004	5/40	21/81		47.0 %	0.41 [0.14, 1.18]
Gurgan II 2004	5/40	11/80		24.8 %	0.90 [0.29, 2.78]
Subtotal (95% CI)	**145**	**228**		**100.0 %**	**1.02 [0.59, 1.75]**
Total events: 28 (hMG (or r-FSH)), 42 (FSH (or u-FSH))					
Heterogeneity: $Chi^2 = 7.10$, df = 4 (P = 0.13); $I^2 = 44\%$					
Test for overall effect: Z = 0.07 (P = 0.94)					
2 B). r-FSH versus u-FSH					
Gerli 2004	23/88	22/82		32.1 %	0.97 [0.49, 1.91]
Gerli 2004 (II)	9/35	8/32		11.8 %	1.04 [0.34, 3.13]
Gurgan 2004	21/81	11/80		15.6 %	2.20 [0.98, 4.92]
Matorras 2000	26/45	24/46		19.1 %	1.25 [0.55, 2.87]
Pares 2002	28/55	24/61		21.3 %	1.60 [0.76, 3.34]
Subtotal (95% CI)	**304**	**301**		**100.0 %**	**1.36 [0.95, 1.94]**
Total events: 107 (hMG (or r-FSH)), 89 (FSH (or u-FSH))					
Heterogeneity: $Chi^2 = 2.78$, df = 4 (P = 0.60); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.68 (P = 0.093)					



Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility (Review)

Cantineau AEP, Cohlen BJ

THE COCHRANE COLLABORATION®

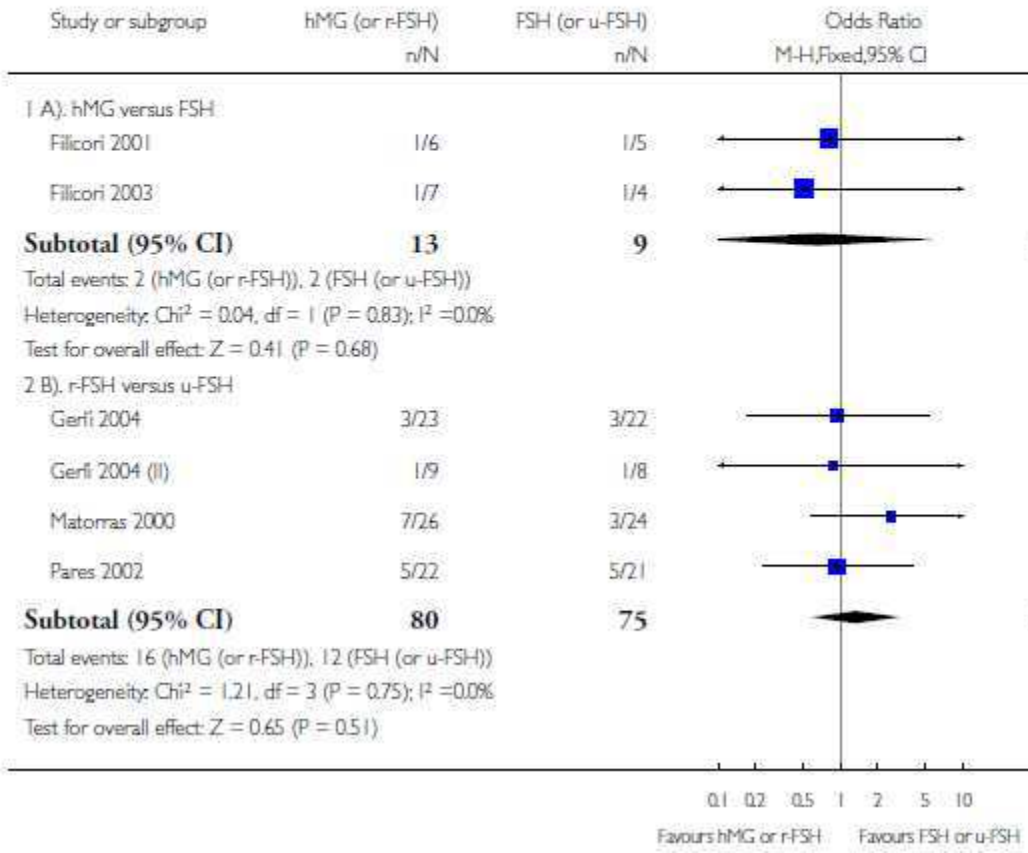
Analysis 5.6. Comparison 5 different types of gonadotrophins, Outcome 6 miscarriage rate per pregnancy.

Review: Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women wit subfertility

Comparison: 5 different types of gonadotrophins

Outcome: 6 miscarriage rate per pregnancy

Study or subgroup	hMG (or r-FSH) n/N	FSH (or u-FSH) n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 A). hMG versus FSH					
Filicori 2001	1/6	1/5		45.5 %	0.80 [0.04, 17.20]
Filicori 2003	1/7	1/4		54.5 %	0.50 [0.02, 11.09]
Subtotal (95% CI)	**13**	**9**		**100.0 %**	**0.64 [0.07, 5.62]**
Total events: 2 (hMG (or r-FSH)), 2 (FSH (or u-FSH))					
Heterogeneity: Chi^2 = 0.04, df = 1 (P = 0.83); I^2 =0.0%					
Test for overall effect: Z = 0.41 (P = 0.68)					
2 B). r-FSH versus u-FSH					
Gerli 2004	3/23	3/22		27.1 %	0.95 [0.17, 5.30]
Gerli 2004 (II)	1/9	1/8		9.6 %	0.88 [0.05, 16.74]
Matorras 2000	7/26	3/24		23.2 %	2.58 [0.58, 11.42]
Pares 2002	5/22	5/21		40.2 %	0.94 [0.23, 3.87]
Subtotal (95% CI)	**80**	**75**		**100.0 %**	**1.32 [0.58, 3.01]**
Total events: 16 (hMG (or r-FSH)), 12 (FSH (or u-FSH))					
Heterogeneity: Chi^2 = 1.21, df = 3 (P = 0.75); I^2 =0.0%					
Test for overall effect: Z = 0.65 (P = 0.51)					



Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility (Review)

Cantineau AEP, Cohlen BJ

THE COCHRANE COLLABORATION®

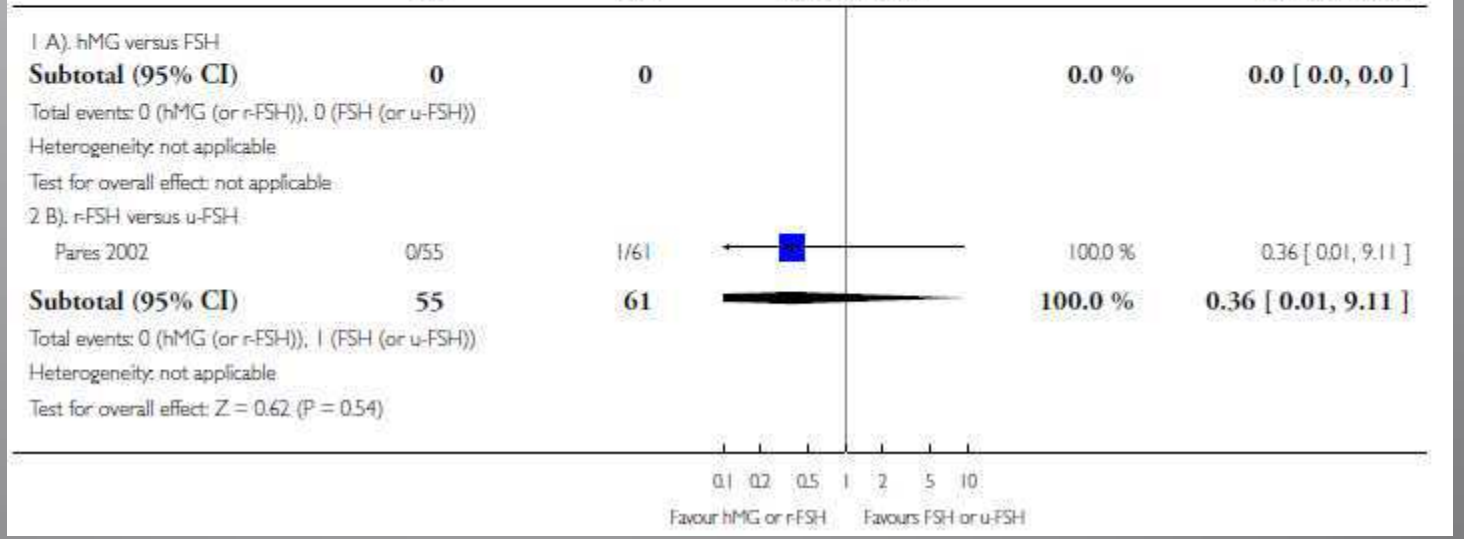
Analysis 5.7. Comparison 5 different types of gonadotrophins, Outcome 7 OHSS rate per couple.

Review: Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility

Comparison: 5 different types of gonadotrophins

Outcome: 7 OHSS rate per couple

Study or subgroup	hMG (or r-FSH) n/N	FSH (or u-FSH) n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 A). hMG versus FSH					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (hMG (or r-FSH)), 0 (FSH (or u-FSH))					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
2 B). r-FSH versus u-FSH					
Pares 2002	0/55	1/61		100.0 %	0.36 [0.01, 9.11]
Subtotal (95% CI)	**55**	**61**		**100.0 %**	**0.36 [0.01, 9.11]**
Total events: 0 (hMG (or r-FSH)), 1 (FSH (or u-FSH))					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.62 (P = 0.54)					



Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility (Review)

Cantineau AEP, Cohlen BJ

THE COCHRANE COLLABORATION®

Analysis 6.2. Comparison 6 gonadotrophins alone versus gonadotrophins with GnRH agonist, Outcome 2 pregnancy rate per couple.

Review: Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility

Comparison: 6 gonadotrophins alone versus gonadotrophins with GnRH agonist

Outcome: 2 pregnancy rate per couple

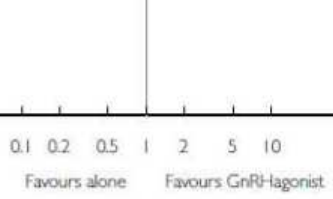
Study or subgroup	Gonadotrophins alone n/N	gonadotrophins+GnRHanta n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Carrera 2002	9/30	5/30		14.9 %	2.14 [0.62, 7.39]
Carrera 2002 (II)	8/30	5/30		15.6 %	1.82 [0.52, 6.38]
Pattuelli 1996	27/104	16/100		51.3 %	1.84 [0.92, 3.68]
Sengoku 1994	7/46	5/45		18.2 %	1.44 [0.42, 4.91]
Total (95% CI)	**210**	**205**		**100.0 %**	**1.81 [1.10, 2.97]**

Total events: 51 (Gonadotrophins alone), 31 (gonadotrophins+GnRHanta)

Heterogeneity: $Chi^2 = 0.21$, $df = 3$ ($P = 0.98$); $I^2 = 0.0\%$

Test for overall effect: $Z = 2.34$ ($P = 0.019$)

Test for subgroup differences: Not applicable



Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility (Review)

Cantineau AEP, Cohlen BJ

THE COCHRANE COLLABORATION®

Analysis 6.4. Comparison 6 gonadotrophins alone versus gonadotrophins with GnRH agonist, Outcome 4 multiple pregnancy rate per pregnancy.

Review: Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility

Comparison: 6 gonadotrophins alone versus gonadotrophins with GnRH agonist

Outcome: 4 multiple pregnancy rate per pregnancy

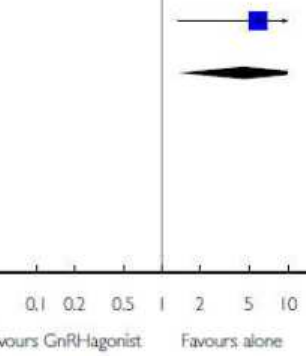
Study or subgroup	Gonadotrophins+GnRHa n/N	gonadotrophins alone n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Carrera 2002	2/9	0/5		17.2 %	3.67 [0.15, 92.65]
Carrera 2002 (II)	3/8	1/5		28.2 %	2.40 [0.18, 32.88]
Pattuelli 1996	8/16	4/27		54.6 %	5.75 [1.36, 24.39]
Total (95% CI)	**33**	**37**		**100.0 %**	**4.45 [1.36, 14.55]**

Total events: 13 (Gonadotrophins+GnRHa), 5 (gonadotrophins alone)

Heterogeneity: $Chi^2 = 0.35$, df = 2 (P = 0.84); $I^2 = 0.0\%$

Test for overall effect: Z = 2.47 (P = 0.014)

Test for subgroup differences: Not applicable



Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility (Review)

Cantineau AEP, Cohlen BJ

THE COCHRANE COLLABORATION®

Analysis 7.1. Comparison 7 gonadotrophins alone versus gonadotrophins with GnRH antagonist, Outcome 1 live birth rate per couple.

Review: Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility

Comparison: 7 gonadotrophins alone versus gonadotrophins with GnRH antagonist

Outcome: 1 live birth rate per couple

Study or subgroup	gonadotrophins+antag n/N	gonadotrophins alone n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Gomez 2005	15/39	7/41		100.0 %	3.04 [1.07, 8.57]
Total (95% CI)	**39**	**41**		**100.0 %**	**3.04 [1.07, 8.57]**

Total events: 15 (gonadotrophins+antag), 7 (gonadotrophins alone)

Heterogeneity: not applicable

Test for overall effect: Z = 2.10 (P = 0.036)

Test for subgroup differences: Not applicable

Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility (Review)

Cantineau AEP, Cohlen BJ

THE COCHRANE COLLABORATION®

Analysis 7.2. Comparison 7 gonadotrophins alone versus gonadotrophins with GnRH antagonist, Outcome 2 pregnancy rate per couple.

Review: Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility

Comparison: 7 gonadotrophins alone versus gonadotrophins with GnRH antagonist

Outcome: 2 pregnancy rate per couple

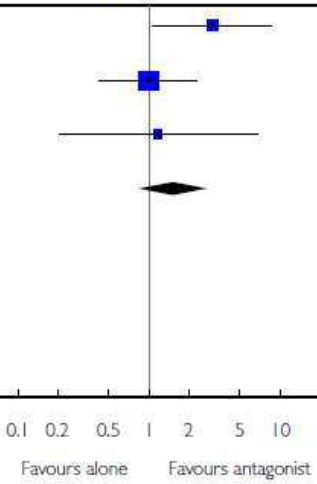
Study or subgroup	gonadotrophins+antag n/N	gonadotrophins alone n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Gomez 2005	15/39	7/41		24.2 %	3.04 [1.07, 8.57]
Lambalk 2006	13/93	12/85		62.2 %	0.99 [0.42, 2.30]
Ragni 2001	3/19	3/22		13.5 %	1.19 [0.21, 6.72]
Total (95% CI)	**151**	**148**		**100.0 %**	**1.51 [0.83, 2.76]**

Total events: 31 (gonadotrophins+antag), 22 (gonadotrophins alone)

Heterogeneity: $Chi^2 = 2.77$, $df = 2$ ($P = 0.25$); $I^2 = 28\%$

Test for overall effect: $Z = 1.34$ ($P = 0.18$)

Test for subgroup differences: Not applicable



European Journal of Obstetrics & Gynecology and Reproductive Biology 166 (2013) 168–172

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European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Effectiveness of GnRH antagonist in intrauterine insemination cycles

Mohan S. Kamath, Ramya R., Priya Bhave, Muthukumar K., Aleyamma T.K., Korula George

Parameters	Antagonist group (%)	Control group (%)	*P* value	OR (95%CI)
Premature LH surge	3/60 (5)	6/58 (10.3)	0.45	2.19 (0.52–9.21)
Premature luteinization	3/60 (5)	8/58 (13.8)	0.31	3.04 (0.76–12.08)
Clinical pregnancy rate[a]	2/71 (2.8)	7/70 (10)	0.12	3.83 (0.76–19.14)

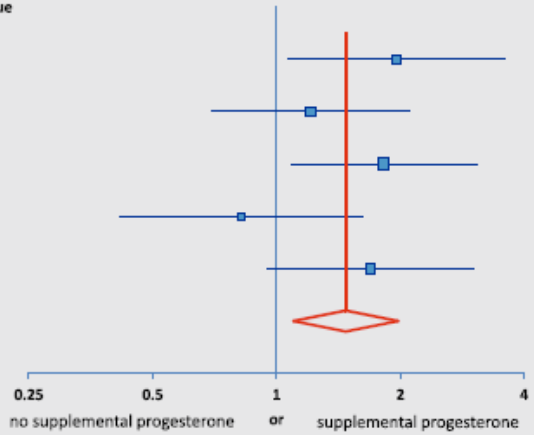
Progesterone luteal support after ovulation induction and intrauterine insemination: a systematic review and meta-analysis

Fertility and Sterility® Vol. 100, No. 5, November 2013

Micah J. Hill, D.O.,[a] Brian W. Whitcomb, Ph.D.,[b] Terrence D. Lewis, M.D.,[c] Mae Wu, D.O.,[c] Nancy Terry,[d] Alan H. DeCherney, M.D.,[a] Eric D. Levens, M.D.,[e] and Anthony M. Propst, M.D.[c]

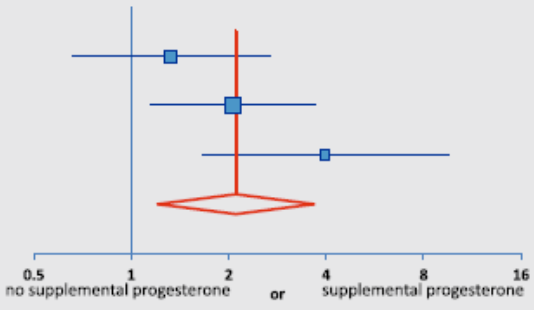
A Clinical Pregnancy

Author	Sample size	Measure (CI)	Weight	*P* value
Agha-Hosseini	290	1.96 (1.07; 3.59)	18.91	.03
Ebrahimi	511	1.21 (0.69; 2.11)	21.52	.5
Erdem	427	1.83 (1.08; 3.08)	23.7	.02
Kyrou	452	0.82 (0.41; 1.62)	15.48	.57
Maher	258	1.69 (0.95; 3.01)	20.4	.07
Synthesis	1938	1.47 (1.1; 1.98)	100	.01



B Live Birth

Author	Sample size	Measure (CI)	Weight	*P* value
Ebrahimi	511	1.33 (0.66; 2.67)	33.79	.43
Erdem	427	2.06 (1.15; 3.7)	40.36	.02
Maher	258	3.97 (1.65; 9.56)	25.85	0
Synthesis	1196	2.11 (1.21; 3.67)	100	.01



Use of exogenous gonadotropins in anovulatory women: a technical bulletin

The Practice Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

This Technical Bulletin reviews the indications for gonadotropin treatment in anovulatory women; outlines the recommended pretreatment evaluation, treatment regimens, and monitoring; describes the alternatives and adjuncts to treatment with gonadotropins; and summarizes the complications of gonadotropin treatment. (Fertil Steril® 2008;90:S7–12. ©2008 by American Society for Reproductive Medicine.)

Gonadotropin Regimens in PCOS

In women with PCOS, only FSH activity is required, because endogenous LH levels are adequate, although added LH does not appear to be harmful (1, 7). There is no significant advantage to using any specific gonadotropin preparation. A meta-analysis concluded that the outcomes of treatment achieved with hMG and with FSH alone were similar (20). Others have observed that treatment with rFSH or urinary FSH yields similar results (21).

The risk of OHSS and multiple pregnancy is greater among women with PCOS than among those with HA, primarily because gonadotropin treatment generally stimulates development of larger follicular cohorts in women with PCOS (22). Consequently, exogenous gonadotropins must be administered judiciously (23–29). The recommended approach in the first dose-finding cycle is to begin with a low dose of gonadotropin, typically 37.5–75 IU/day, increasing after 7 days or more if no follicle >10 mm has yet emerged, in small increments, at intervals, until evidence of progressive follicular development is observed. The maximum required daily dose of FSH/hMG seldom exceeds 225 IU/day (23).

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- Among women not previously treated with exogenous gonadotropins, treatment generally should begin at a relatively low dose (e.g., 37.5–75 IU/day). In subsequent cycles, treatment generally begins at the threshold of response previously determined.
- Ovulation of a mature ovarian follicle may be triggered with either purified (5,000–10,000 IU IM or SC) or recombinant (250 μg SC) hCG. A GnRH agonist (leuprolide 500 μg SC; triptorelin 200 μg SC) also may be used to trigger ovulation, except in women with HA and those who have received GnRH agonist treatment earlier during the course of gonadotropin treatment.
- Luteal support after OI is most clearly indicated and recommended in women with HA and those who receive treatment with a GnRH agonist, because, in these cases, endogenous gonadotropin secretion may be inadequate to support normal luteal function.

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Ovulatory women undergoing IUI Unexplained/mild male factor infertility

- Regular unprotected sexual intercourse for a total of 2 years
- Clomiphene citrate, anastrozole or letrozole(? ? ?)
- Gonadotrophin + IUI (? ? ?)
- IVF

Assessment and treatment for people with fertility problems
NICE clinical guideline 156,2013

Best practices of ASRM and ESHRE
L. Gianaroli Human Reproduction, 2012

RBM online - Vol 9. No 6. 2004 664-672 Reproductive BioMedicine Online; www.rbmonline.com/Article/1560 on web 2 November 2004

Article

Gonadotrophin ovarian stimulation and intrauterine insemination for unexplained infertility

Juan Balasch
Institut Clínic of Gynecology, Obstetrics and Neonatology, Hospital Clínic-Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Faculty of Medicine, University of Barcelona, Barcelona, Spain

Table 5. Aggregate pregnancy rates of 20 randomized controlled trials comparing alternative treatments for unexplained infertility. Figures in parentheses are percentages.

Comparison	*No. (%) of pregnancies per cycle*	*OR (95% CI)*
FSH + IUI versus FSH + TI	170/929 (18) versus 76/711 (11)	1.71 (1.28–2. 28)
FSH + IUI versus IUI	107/478 (22) versus 59/466 (13)	1.77 (1.26–2.49)
FSH + IUI versus FSH + cervical insemination	127/476 (27) versus 74/517 (14)	1.86 (1.36–2.54)

Adapted from Aboulghar *et al.* (2003).

human reproduction update

Vol.15, No.3 pp. 265–277, 2009

Intrauterine insemination

The ESHRE Capri Workshop Group[1]

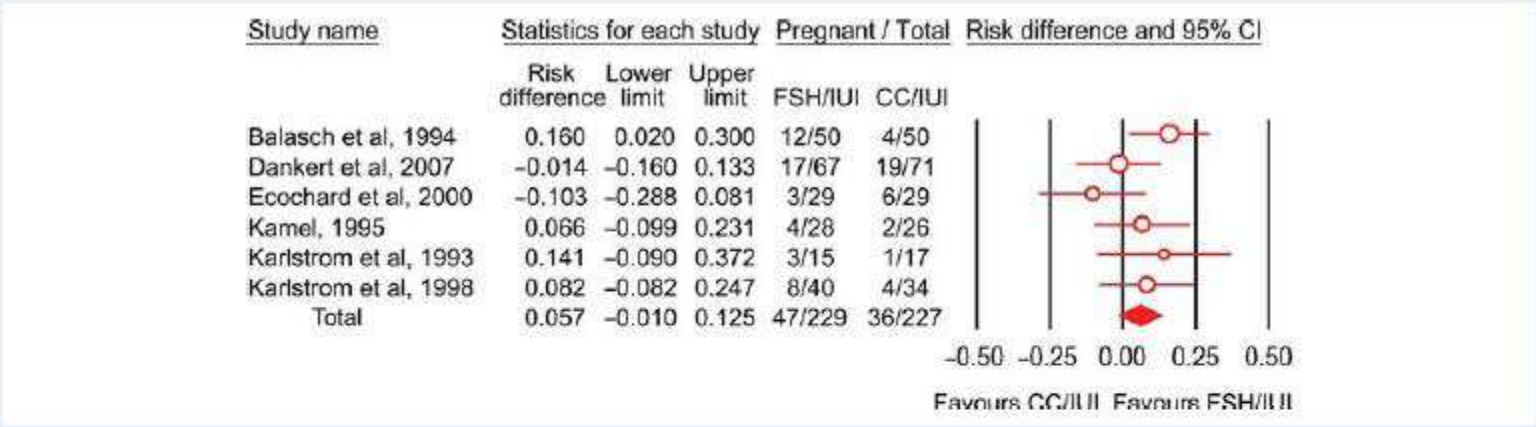


Figure 1 Pregnancy rates following IUI combined with ovarian stimulation using either anti-estrogens or FSH. Live birth rates could not be assessed (Cantineau *et al.*, 2007).

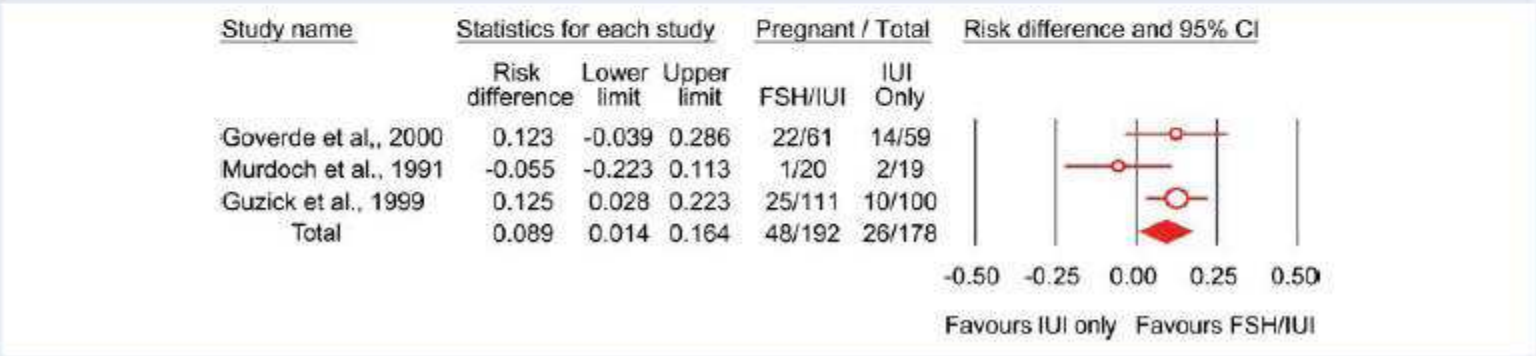


Figure 2 Live birth rate per couple following IUI with or without FSH ovarian stimulation (Verhulst *et al.*, 2006).

Fertility and Sterility® Vol. 94, No. 3, August 2010

A randomized clinical trial to evaluate optimal treatment for unexplained infertility: the fast track and standard treatment (FASTT) trial

Richard H. Reindollar, M.D.,[a] Meredith M. Regan, Sc.D.,[b] Peter J. Neumann, Sc.D.,[c] Bat-Sheva Levine,

TABLE 2

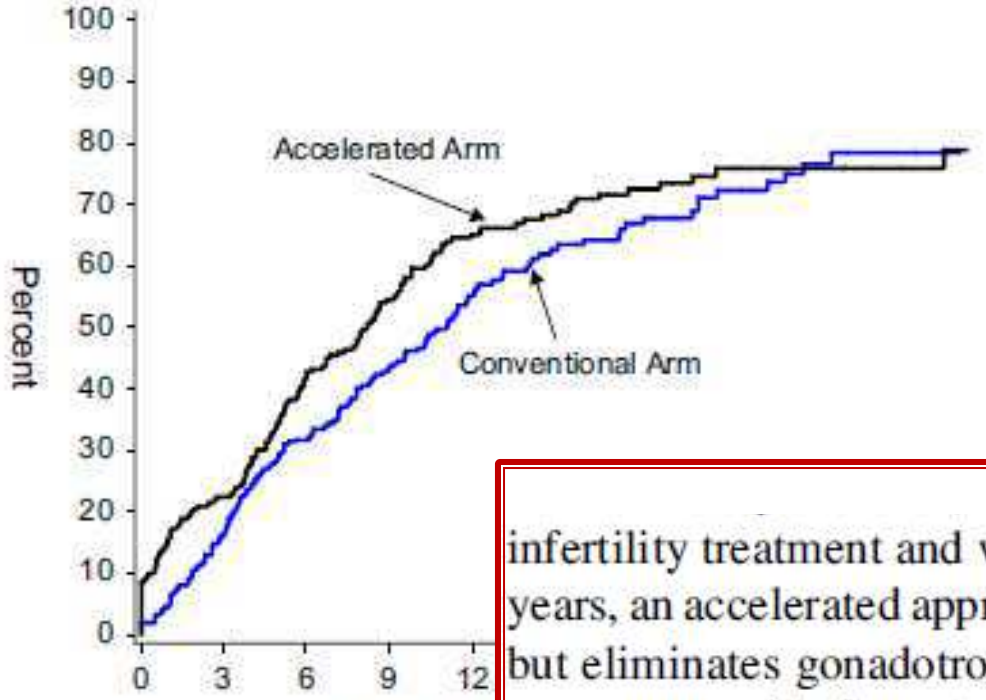
Number of couples initiating treatment cycles, total number of cycles initiated, and pregnancy rates by treatment group as of April 30, 2006.

	Treatment type and randomization strategy								
	CC/IUI			FSH/ IUI	IVF			Total	
	Conventional	Fast track	All	Conventional	Conventional	Fast track	All	Conventional	Fast track
No. couples initiating	233	242	475	169	111	172	283	247	256
No. of cycles initiated	646	648	1294	439	261[a]	361[a]	622	1346	1009
No. of pregnancies									
Total[b]	55	68	123	50	95	145	240	200	213
Losses	10	15	25	7	22	27	49	39	42
Ongoing (≥ 20 wks)	4	2	6	6	15	18	33	35[c]	28[c]
Live birth	41	51	92	37	58	100	158	150[c]	171[c]
Pregnancy rates (live birth + ongoing)									
Per initiated cycle	7.0 (4.8-10.0)	8.2 (5.8-11.4)	7.6 (6.2-9.2)	9.8 (6.8-14.0)	28.0 (21.8-35.2)	32.7 (27.0-38.9)	30.7 (27.1-34.5)		
Per couple	19.3 (14.5-25.0)	21.9 (16.9-27.7)	20.6 (17.1-24.6)	25.4 (19.1-32.7)	65.8 (56.2-74.5)	68.6 (61.1-75.5)	67.5 (61.7-72.9)	74.9 (69.0-80.2)	77.7 (72.1-82.7)

Fertility and Sterility® Vol. 94, No. 3, August 2010

A randomized clinical trial to evaluate optimal treatment for unexplained infertility: the fast track and standard treatment (FASTT) trial

Richard H. Reindollar, M.D.,[a] Meredith M. Regan, Sc.D.,[b] Peter J. Neumann, Sc.D.,[c] Bat-Sheva Levine,



Compared with conventional infertility treatment and when the woman is younger than 40 years, an accelerated approach to IVF that starts with CC/IUI, but eliminates gonadotropin/IUI, results in a shorter time to pregnancy, with fewer treatment cycles, and at a suggested cost savings.

INFERTILITY

Fertility and Sterility® Vol. 94, No. 3, August 2010

A randomized clinical trial to evaluate optimal treatment for unexplained infertility: the fast track and standard treatment (FASTT) trial

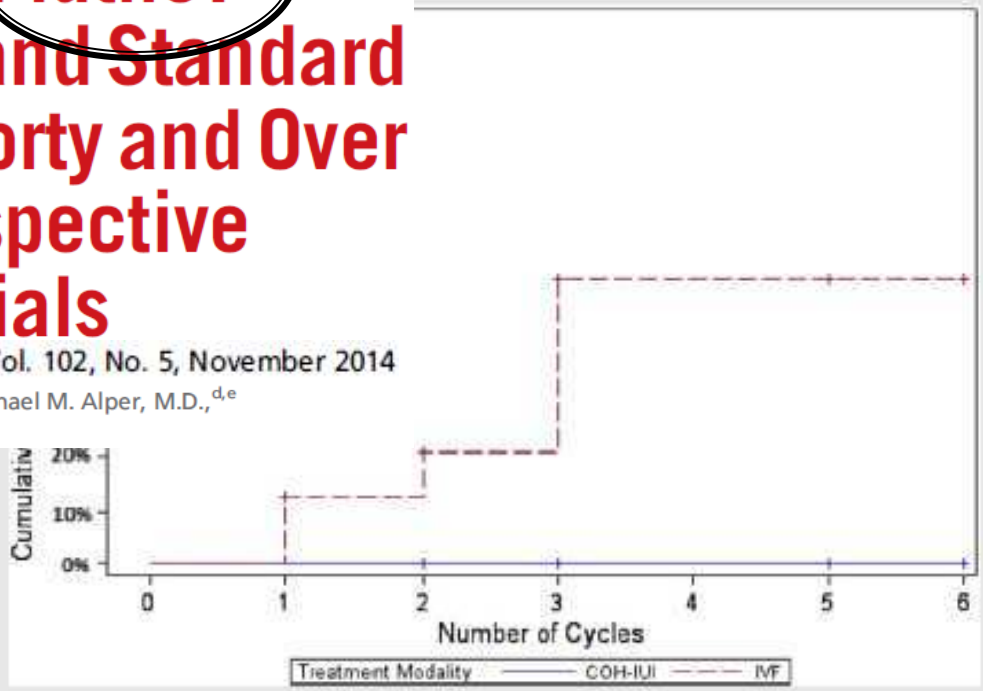
Richard H. Reindollar, M.D.,[a] Meredith M. Regan, Sc.D.,[b] Peter J. Neumann, Sc.D.,[c] Bat-Sheva Levine,

- The accelerated approach to IVF resulted in a shorter time to pregnancy with an equivalent cumulative percentage of pregnancies occurring in less treatment cycles and with cost savings, suggesting that FSH/IUI was of no added value
- Accelerated approach to IVF (that eliminates FSH/IUI, but starts with CC/IUI) represents the best treatment option.

When is clomiphene or gonadotropin intrauterine insemination futile? Results of the Fast Track and Standard Treatment Trial and the Forty and Over Treatment Trial, two prospective randomized controlled trials

Fertility and Sterility® Vol. 102, No. 5, November 2014

Daniel J. Kaser, M.D.,[a] Marlene B. Goldman, Sc.D.,[b,c] June L. Fung, Ph.D.,[b] Michael M. Alper, M.D.,[d,e] and Richard H. Reindollar, M.D.[b]



Kaplan-Meier estimates of the cumulative incidence of live births after COH-IUI vs. IVF for patients in group 2B (FSH, 10–15 mIU/mL; and E_2

(13, 14). The observation that no live births occurred among women with an FSH of 10–15 mIU/mL and $E_2 \geq 40$ pg/mL treated with IUI challenges the current paradigm of stepwise treatment for these patients in mandated states, where several cycles of CC-IUI may still be required by some insurers before the initiation of IVF.

Fertility

NHS National Institute for Health and Clinical Excellence

Issued: February 2013

Assessment and treatment for people with fertility problems

NICE clinical guideline 156

guidance.nice.org.uk/cg156

Do not offer oral ovarian stimulation agents (such as clomifene citrate, anastrozole or letrozole) to women with unexplained infertility. **[new 2013]**

Inform women with unexplained infertility that clomifene citrate as a stand-alone treatment does not increase the chances of a pregnancy or a live birth. **[new 2013]**

Advise women with unexplained infertility who are having regular unprotected sexual intercourse to try to conceive for a total of 2 years (this can include up to 1 year before their fertility investigations) before IVF will be considered. **[new 2013]**

Offer IVF treatment (see recommendations 1.11.1.3–4) to women with unexplained infertility who have not conceived after 2 years (this can include up to 1 year before their fertility investigations) of regular unprotected sexual intercourse. **[new 2013]**

A randomized clinical trial to determine optimal infertility treatment in older couples: the Forty and Over Treatment Trial (FORT-T)

Fertility and Sterility® Vol. 101, No. 6, June 2014

Marlene B. Goldman, Sc.D.,[a,b] Kim L. Thornton, M.D.,[c] David Ryley, M.D.,[c] Michael M. Alper, M.D.,[c]

Clinical pregnancy and live birth rates per couple, by randomization assignment for the first two treatment cycles and at the end of all treatment.

		First two treatment cycles		Duration of study	
Randomized treatment arm	No. of couples (%)	No. of clinical pregnancies[a,b] (%, 97.5% CI)	No. of live births[c] (%, 97.5% CI)	No. of clinical pregnancies[d] (%, 97.5% CI)	No. of live births[d] (%, 97.5% CI)
CC/IUI	51 (33.1)	11 (21.6, 10.2–37.3)	8 (15.7, 6.2–30.5)	38 (74.5, 58.4–86.9)	25 (49.0, 32.9–65.2)
Gonadotropin (FSH)/IUI	52 (33.8)	9 (17.3, 7.3–32.2)	7 (13.5, 4.9–27.6)	34 (65.4, 49.0–79.5)	22 (42.3, 27.1–58.7)
Immediate IVF	51 (33.1)	25 (49.0, 32.9–65.2)	16 (31.4, 17.7–47.9)	38 (74.5, 58.4–86.9)	24 (47.1, 31.2–63.4)
Total[e]	154	45 (29.2, 21.3–38.2)	31 (20.1, 13.4–28.4)	110 (71.4, 62.5–79.3)	71 (46.1, 37.0–55.4)

Note: Includes treatment-independent pregnancies. CC = clomiphene citrate; CI = confidence interval; FSH = follicle-stimulating hormone; IUI = intrauterine insemination; IVF = in vitro fertilization.

[a] Number of clinical pregnancies includes all ultrasound confirmed pregnancies, including pregnancy losses.

[b] For clinical pregnancy rate after first two treatment cycles: $P=.0067$ for comparison between CC/IUI and immediate IVF; $P=.0007$ for comparison between FSH/IUI and immediate IVF.

[c] For live-birth rate after first two treatment cycles: $P=.101$ for comparison between CC/IUI and immediate IVF; $P=.035$ for comparison between FSH/IUI and immediate IVF.

[d] For clinical pregnancy and live-birth rates after all treatment, there are no statistically significant differences, reflecting subsequent IVF treatment in all arms.

[e] Of these, there were 5, 2, and 4 clinical pregnancies and 5, 1, and 3 live births in the CC/IUI, FSH/IUI and immediate IVF arms, respectively, that occurred before treatment was initiated or between treatment cycles one and two. Over the duration of the study there were 11, 3, and 9 clinical pregnancies and 7, 1, and 6 live births in the CC/IUI, FSH/IUI, and immediate IVF arms, respectively, that occurred outside of treatment cycles.

Goldman. Forty and Over Treatment Trial (FORT-T). Fertil Steril 2014.

the data show that for couples who present at the end of their reproductive years and who demonstrate a reasonable chance for continued success, the most successful treatment is immediate IVF. About half will have a live birth (more than 80% of

A randomized clinical trial to determine optimal infertility treatment in older couples: the Forty and Over Treatment Trial (FORT-T)

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Marlene B. Goldman, Sc.D.,[a,b] Kim L. Thornton, M.D.,[c] David Ryley, M.D.,[c] Michael M. Alper, M.D.,[c]

- Immediate treatment with two cycles of IVF for older women (38–42 years) results in significantly higher pregnancy and live birth rates compared with two cycles of either CC/IUI or FSH/IUI

Gonadotropin therapy: a 20th century relic

Richard H. Reindollar, M.D., and Marlene B. Goldman, Sc.D. Fertility and Sterility® Vol. 97, No. 4, April 2012

Superovulation with IUI has become the mainstay of treatment for unexplained and mild male factor infertility. Historically, therapy was initiated with clomiphene and IUI, and when not pregnant, couples moved in a step wise fashion through gonadotropin and IUI treatments to IVF. This progression seemed logical as an initial literature-wide review (primarily observational studies) reported success rates of 1.3% to 4% for no treatment, 8.3% for CC/IUI, 17.1% for hMG/IUI, and 20.7% for IVF (6).

Gonadotropin therapy: a 20th century relic

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comparing the use of CC vs. low dose recombinant FSH in a SO/IUI protocol (9). Live birth rates per couple over a maximum of four treatment cycles for CC/IUI and FSH/IUI were 28% and 27%, respectively, and per cycle were 10% for CC/IUI and 8.7% for FSH/IUI. The Dankert study demonstrated that, for their mild protocol, FSH/IUI was no better than CC/IUI.

Gonadotropin therapy: a 20th century relic

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The FASTT and FORT-T trials have demonstrated that there is really no place for the routine use of gonadotropins in SO/IUI protocols today. Other studies have similarly demonstrated that even when given as mild protocols for SO/IUI, gonadotropin therapy is not helpful; in fact, in such protocols observation performed equally as well. The only current use for gonadotropin therapy before IVF is in anovulatory patients either resistant to clomiphene or for whom clomiphene is not effective (i.e., hypothalamic patients). These patients, especially those with PCOS, have a high risk for multiple births and OHSS. Clearly, new tech-

Gonadotropin therapy: a 20th century relic

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We need to continue to develop infertility treatments that decrease the cost, time involvement, stress, and dangers and do not limit infertility treatment to couples of higher socioeconomic status. In so doing, we believe gonadotropin therapy will be considered a relic of the twentieth century.

Dr. Bora Cengiz