



Açıklanamayan infertilitede IUI ilk basamak tedavisi olmalı mıdır ?

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Anabilim Dalı

Açıklanamayan İnfertilite

- Toplumda fertilitenin normal dağılımının azalmış uç grubunu oluştururlar (Subfertilite)
 - Spontan fekundite % 1.3 - 4.1*
 - Hiçbir tedavi verilmese de 3yıda % 33-60 gebelik
 - Yaş ve evlilik süresi ilerledikçe spontan gebelik şansı düşer**
- İnfertil çiftlerin ~ %15-30'u açıklanamayan infertil olarak tanımlanır

*Guzick DS, Fertil Steril 1998

**Dodson WC, Fertil Steril 1987

*** The ESHRE Capri Workshop

Açıklanamayan İnfertilite

- Fekunditeyi bozan çiftlere ait defekt(ler) rutin infertilite araştırmalarıyla tespit edilememektedir.
- Tanısal testler
 - Ovulasyon
 - Tubal açıklık (HSG)
 - Semen analizi

HEPSİ NORMAL

Açıklanamayan İnfertilite

Açıklanamayan infertilite tedavisindeki uygulamalar;

- Bekleme
- Oral veya enjektabl medikasyonlarla superovulasyon (CC / Gonadotropin)
- İntrauterin inseminasyon
- Superovulasyon+İntrauterin inseminasyon
- IVF

IUI vs IVF

- İnfertil çiftlerin tedavi seçim kriterleri;
 - Basit
 - Etkin
 - Gebeliğe kısa sürede ulaşmalı
 - Ödenebilir olmalı
 - Kişisel maliyet
 - Toplumsal maliyet(Sosyal güvenlik,çoğul gebeliğe bağlı prematürite)

İVF ENDİKASYONLARI

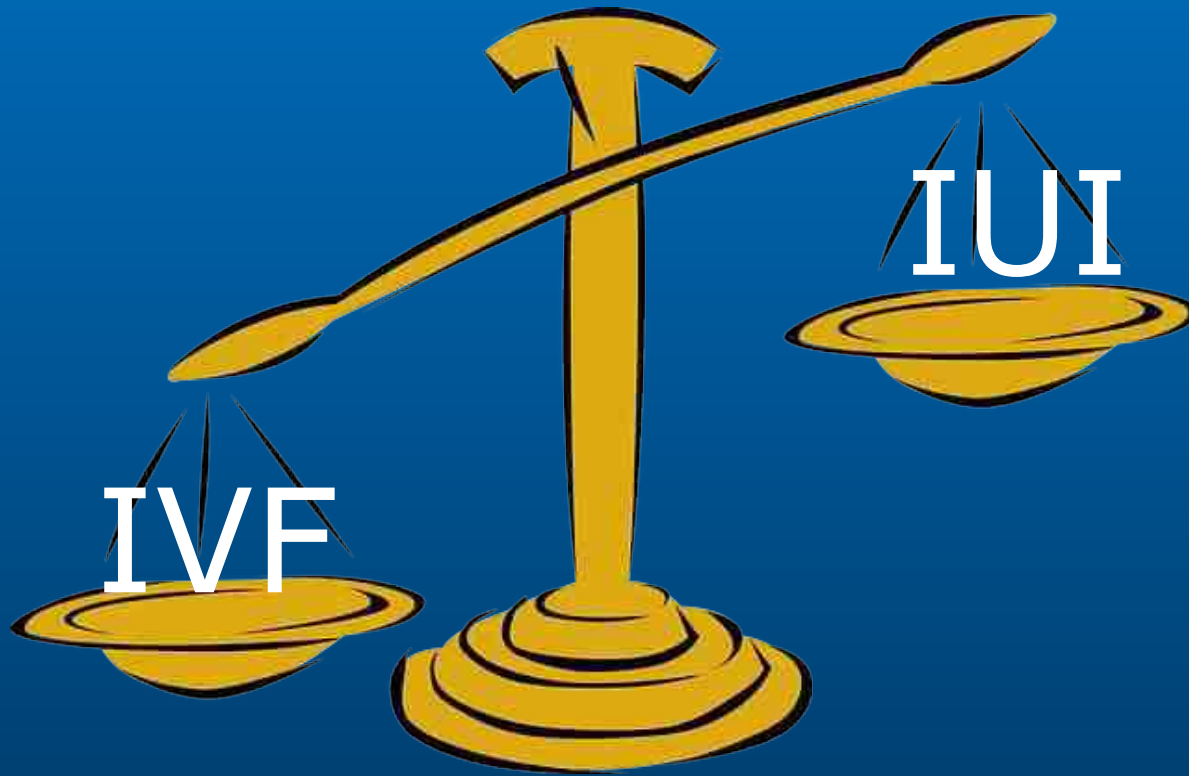
■ Kesin endikasyonlar

- Şiddetli erkek faktörü
- Mekanik/tubal infertilite
- Oosit donasyonu
- PGD

■ İVF'in birinci tedavi seçeneği olmadığı durumlar

- Hipogonadotropik hipogonadizm
- Anovulasyon/PKOS
- Hafif sperm problemleri
- Açıklanamayan infertilite?????

IUI'in geleceği?



« IVF should be offered as first line
therapy to all infertile couples
regardless of the type of infertility»

Gleicher & Karende, 2001

1.8 Unexplained infertility

1.8.1 Ovarian stimulation for unexplained infertility

- 1.8.1.1 Do not offer oral ovarian stimulation agents (such as clomifene citrate, anastrozole or letrozole) to women with unexplained infertility. [new 2013]
- 1.8.1.2 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]
- 1.8.1.3 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]
- 1.8.1.4 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]

- Açıklanamayan infertilitesi olan çiftleri tedavi eden hekimlere öneri:
 - İki yıla kadar bekleme
 - Daha sonra doğrudan IVF tedavisi
 - Halen bu önerinin kanıtı yok

■ NICE kılavuzunu pratikte kullanımı

- İngiliz Fertilite Derneği üyesi 136 hekime online survey
- Sadece % 16'sı IVF'i ilk tedavi önermekte
- Sadece %27'si yeni kılavuza göre uygulamalarını değiştirebileceğini ifade etmekte
- % 30'u uygulamalarını değiştirmeyeceğini, kalanı ise kanıtları beklediğini ifade etmekte

Nandi, Homburg et al Hum Fertility 2014

Intrauterine insemination

The ESHRE Capri Workshop Group¹

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‘Although IUI treatment is cheaper and less demanding on the patient, IVF is the most effective treatment for infertility.

There is a need for management trials to evaluate the order of treatment and overall effectiveness of treatment strategies in more clinical and cost settings.’

Human Reproduction Update, Vol.15, No.3 pp. 265–277, 2009

Açıklanamayan İnfertilite: önce IUI

- IVF tedavisi IUI ile kıyaslandığında
 - Daha invazif
 - Daha komplikatif
 - yüksek çoğul gebelik
 - OHSS
 - OPU komplikasyonları
 - Daha az hasta uyumu
 - Kümülatif drop out oranları daha yüksek
 - Daha maliyetli

Çoğul Gebelik

	IVF	IUI
İKİZ	21	9,5
ÜÇÜZ	0,8	1,0
TOTAL	21,8	10,5

Açıklanamayan İnfertilite: önce IVF

- Tedavi siklusu sayısı az
- Kısa süreli tedavi
- Daha çabuk sonuç
- İleri yaş ve daha çok çocuk isteği
- Daha az psikolojik stress ?
- Risk ?
- Maliyet?

Açıklanamayan İnfertilite: IUI vs IVF

- Terapotik etkinlik
- Maliyet /Cost-effective'lik
- Çoğul gebelik oranları
- Komplikasyonlar
- Drop Out oranları
- Tedavi seçiminde prognostik faktörler

İÜİ:Terapotik Etkinlik

SPERM YIKAMA

- Kötü kalite spermatozoa, lökosit ve hücre artıkları
- Seminal plazma içindeki sitokin, PG, oksijen radikalleri, antijen ve enfeksiyöz maddeler ayrılır
- Kapasitasyon

İÜİ

- Servikal mukusun filtrasyon etkisi önlenir
- Kavite içine daha fazla sayıda motil spermatozoa verilir

Fertilizasyon için ampullada kaliteli spermatozoa sayısı artırılır

SÜPEROVULASYON

İnvivo sperm ile karşılaşan ovum sayısı artar

Homologous Intrauterine Insemination

181

	Vagina	Cervix	Uterus	Tubes
No. of sperm	120-180x10 ⁶	1-3x10 ⁵	1-3x10 ³	1-3x10 ²
day 1				
day 2				
day 3				
day 4				
day 5				

Fig. 2. Passage of spermatozoa through the female genital tract after coitus. Drop in the number of sperm cells between vagina and fallopian tubes. (From Diedrich et al. 1985)

İÜİ:Terapotik Etkinlik

IUI siklus başına gebelik	(%)
- Gonadotropin İÜİ	
Açıklanamayan inf.*	10-20
Açıklanamayan inf. **	20.3

* Hughes EG, Hum Reprod 1997; Guzick DS, Fertil Steril 1998; Guzick DS, NEJM 1999

** Erdem A, RBM Online 2008

Article

Factors affecting live birth rate in intrauterine insemination cycles with recombinant gonadotrophin stimulation

- 278 açıklanamayan infertil/492 siklus
- 75 U rec Gn/prog vag. gel luteal destek
- Siklus başı gebelik % 20,3
- Hasta başı canlı gebelik % 21.1
- Hasta başı canlı gebelik
- Açıklanamayan subfertilite % 25,2
- Erkek faktörü % 15,7
- Spontan gebelik % 6,1
- Hasta başı kümülatif % 30,9
- canlı gebelik (spontan+tedavi)
- Çoğul Gebelik % 11,2

Terapotik etkinlik : IUI vs IVF

Tedavi	Gebelik/ siklus	NNT	Referans
IUI	5	32	Guzick, 1999 Martinez, 1990 Steures, 2007
CC/IUI	7	14	Deaton, 1990
FSH/IUI	12	11	Guzick, 1999
IVF	31	4	Hughes, 2004

The ESHRE Capri Workshop Group, Hum Reprod 2009

ESHRE

Assisted reproductive technology in Europe, 2006: results generated from European registers by ESHRE*.

Cyles (IVF+ICSI)	IVF			ICSI		
	Aspirat	Pregn per aspirat (%)	Deliver per aspirat (%)	Aspirat	Pregn per aspirat (%)	Deliver per aspirat (%)
32 852	867	47.9	14.5	31 212	37.3	11.5

* *Hum. Reprod.* (2010)

HFEA

Figure 3: Percentages of couples seeking standard IVF or ICSI treatment, by the reason they sought treatment, 2011

Percentage of cycles started

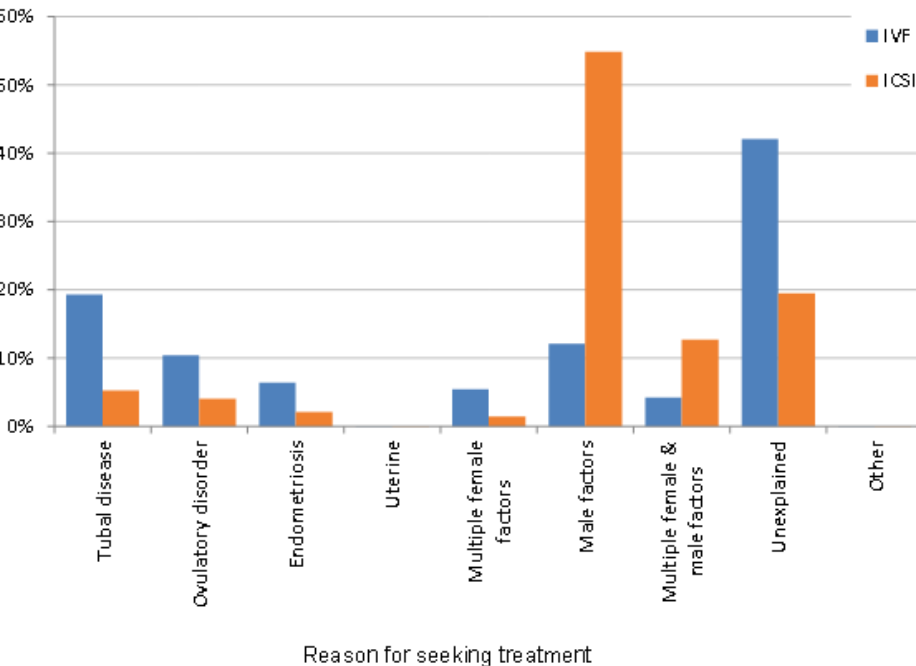
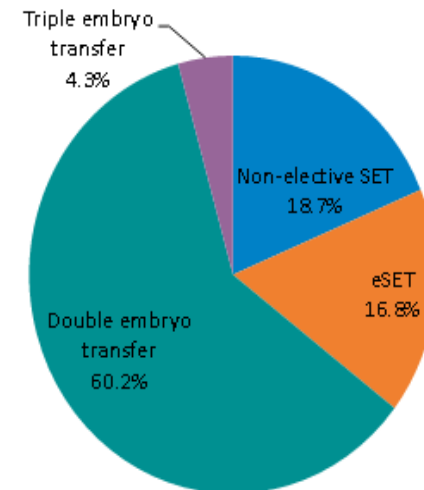


Figure 6: Proportion of all embryo transfers (fresh and frozen), by number of embryos transferred, 2011



Human Fertilisation, Embryology Authority. Latest UK IVF figures - 2009 and 2010. <http://www.hfea.gov.uk/ivffigures-2006.html> (accessed 11 March 2012).

HFEA Database 2011

2011	IVF/ICSI	Live birth rate	IUI	Pregnancy rate
Pregnancies	13,703		572	
Women	48,141	27.2 %		
Cycles	61,726 (\$6K each)	21.1%	4174 (\$1K each)	13.7%
Embryos	89,648	15.3%		

Table 10: Live birth rate, per cycle started, fresh own eggs, 2009 and 2010

Year of treatment:		2009	2010
Age	18 – 34	32.3%	32.2%
	35 – 37	27.2%	27.7%
	38 – 39	19.1%	20.8%
	40 – 42	12.7%	13.6%
	43 – 44	5.1%	5.0%
	45 +	1.5%	1.9%
	All ages	25.2%	25.6%

Açıklanamayan İnfertilite: IUI vs IVF

- IVF vs bekleme
- IVF vs CC
- IVF vs IUI
- IVF vs IUI+superovulation
 - Etkinlik
 - Maliyet (cost-effectivity)

Açıklanamayan İnfertilite: IVF

In vitro fertilisation for unexplained subfertility (Review)

Pandian Z, Gibreel A, Bhattacharya S



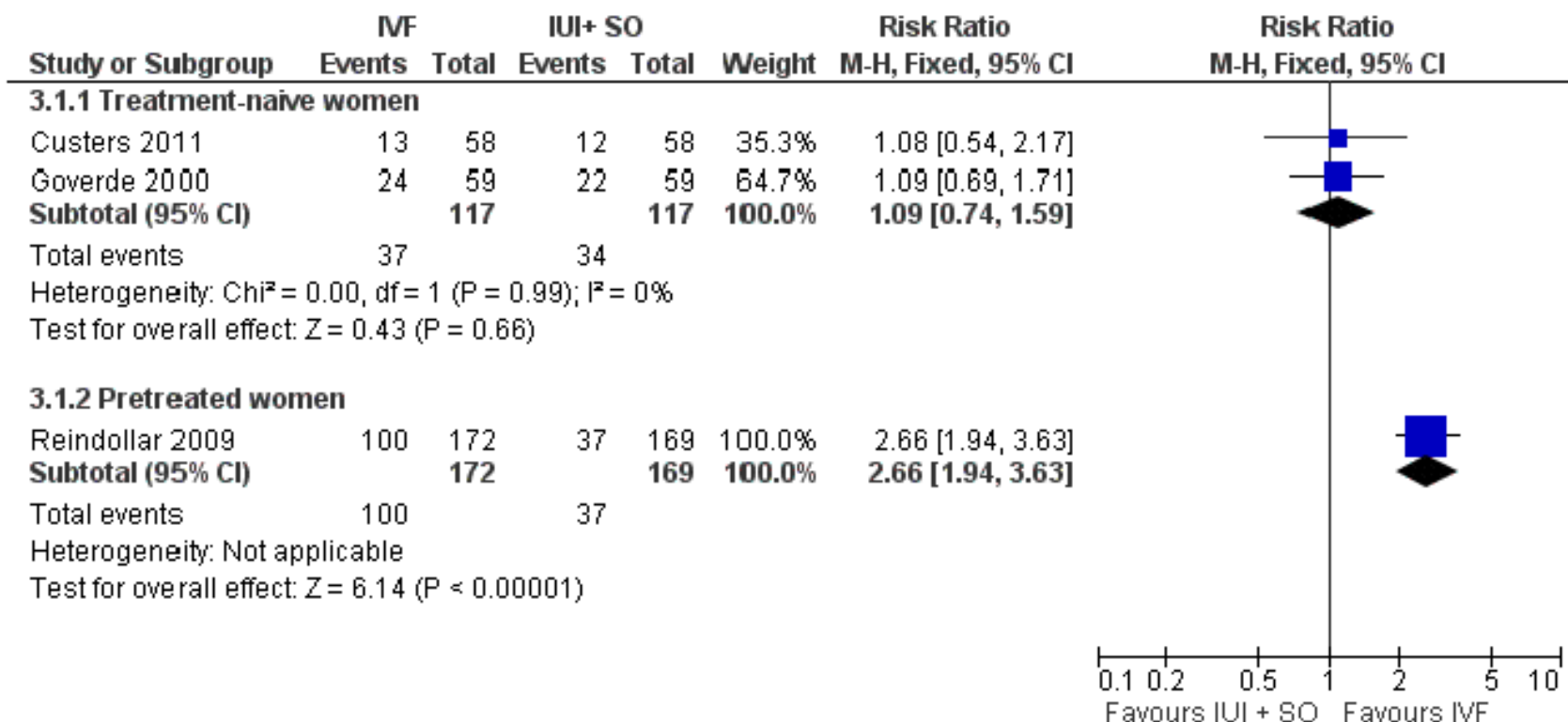
**THE COCHRANE
COLLABORATION®**

Açıklanamayan İnfertilite: IVF

	YAŞ	İNF SÜRE	Hafif erkek faktörü	Intervention
SOLIMAN, 1993	< 40	1 yıl		IVF vs BEKLEME
GOVERDE, 2000	Limit yok	3 yıl	+ Hafif endomet riozis	IVF vs IUI alone IVF vs IUI+SO
HUGHES, 2004	18 - 39	2 yıl		IVF vs BEKLEME
REINDOLLAR 2009	21 - 39	1 yıl	+	IVF vs IUI+SO (her iki grup CC+IUI)
VanRUMSTE, 2011	Limit yok		+	IVF vs IUI+SO
CUSTERS, 2011	< 38	Prog. skor	+	IVF vs IUI+SO

Açıklanamayan Infertilite: IVF vs IUI+SO

Figure 5. Forest plot of comparison: 3 in vitro fertilisation (IVF) versus intrauterine insemination plus ovarian stimulation (IUI+SO), outcome: 3.1 live birth rate per woman.



Test for subgroup differences: $\text{Chi}^2 = 12.59$, $\text{df} = 1$ ($P = 0.0004$), $I^2 = 92.1\%$

Intrauterine insemination or in-vitro fertilisation in idiopathic subfertility and male subfertility: a randomised trial and cost-effectiveness analysis

Angelique J Goverde, Joseph McDonnell, Jan P W Vermeiden, Roel Schats, Frans F H Rutten, Joop Schoemaker

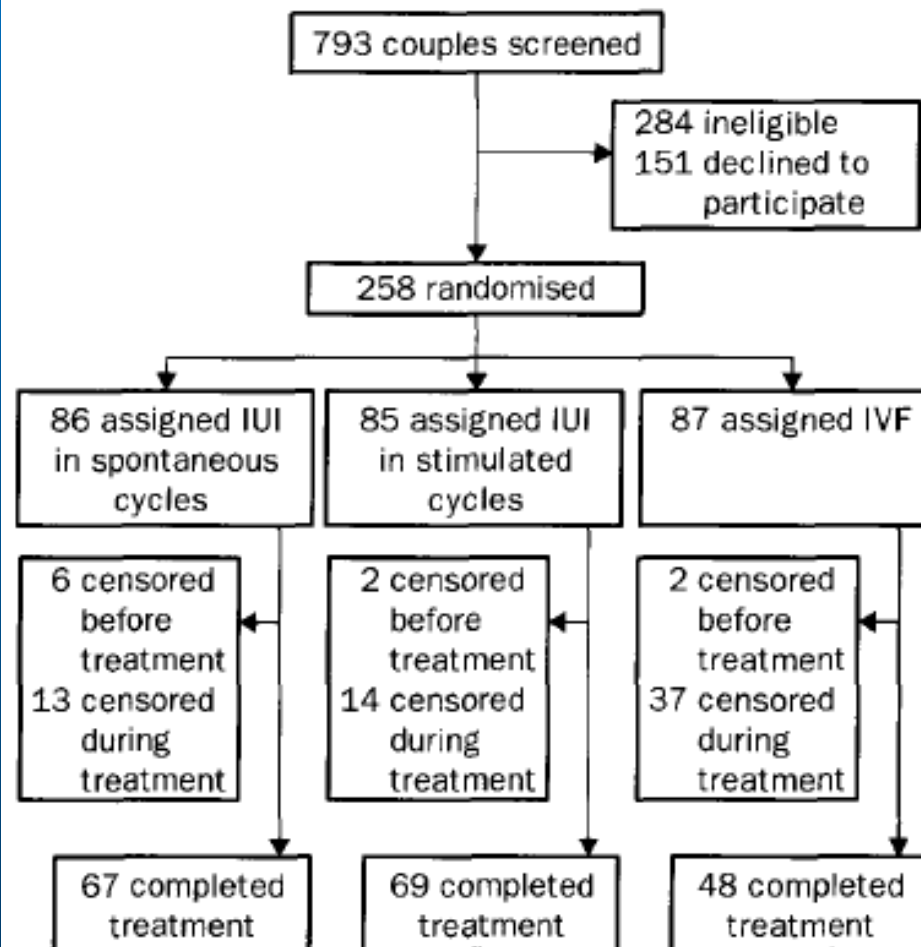


Figure 1: Trial profile

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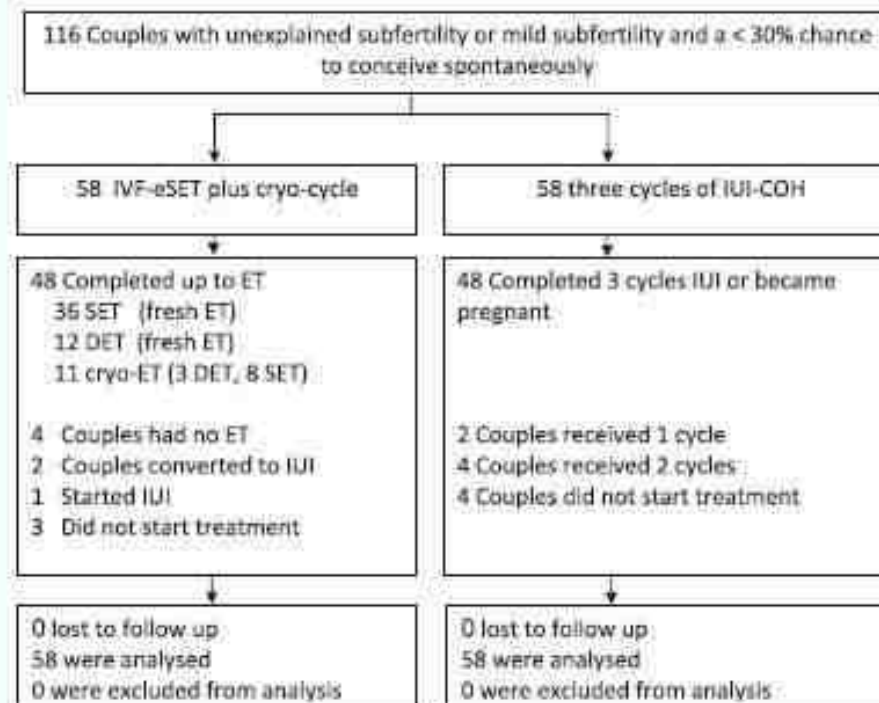
	SİKLUS BAŞI GEBELİK %	KÜMÜLATİF CANLI DOĞUM %	ÇOĞUL GEBELİK %
IUI	7.4	31	4
IUI + SO	8.7	37	29
IVF	12.4*	38	21
	*P=0.09		

Couples with unexplained subfertility and unfavorable prognosis: a randomized pilot trial comparing the effectiveness of in vitro fertilization with elective single embryo transfer versus intrauterine insemination with controlled ovarian stimulation

Inge M. Custers, M.D.,^a Tamar E. König, M.D.,^b Frank J. Broekmans, M.D., Ph.D.,^c Peter G. A. Hompes, Prof.,^b Eugénie Kattijk, M.D., Ph.D.,^d Jur Oosterhuis, M.D., Ph.D.,^e Monique H. Mochtar, M.D.,^a Sjoerd Repping, Prof.,^a Madelon van Wely, Ph.D.,^a Pieter Nel Steures, M.D., Ph.D.,^a Fulco van der Veen, Prof.,^a and Ben W. J. Mol, Prof.^{a,f}

FIGURE 1

Flow chart.



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TABLE 2

Pregnancy outcomes at 4 months from randomization.

Outcome measure	IVF-eSET (n = 58)	IUI-COH (n = 58)	RR (95% CI)
Clinical pregnancies	15	14	1.07 (0.57–2.01)
Ongoing pregnancies	14 (24) ^a	12 (21) ^b	1.17 (0.60–2.30)
Multiple pregnancies	2 (14)	3 (25)	
Twin	2	2	
Triplet	0	1	
Live births	13 ^c (22)	12 (21)	1.08 (0.55–2.16)
Miscarriage	1 (2)	2 (3)	
Ectopic pregnancy	0	1 (2)	

Note: Values are number (percentage).

^a One spontaneous pregnancy (IVF-eSET).

^b Two spontaneous pregnancies (IUI-COH).

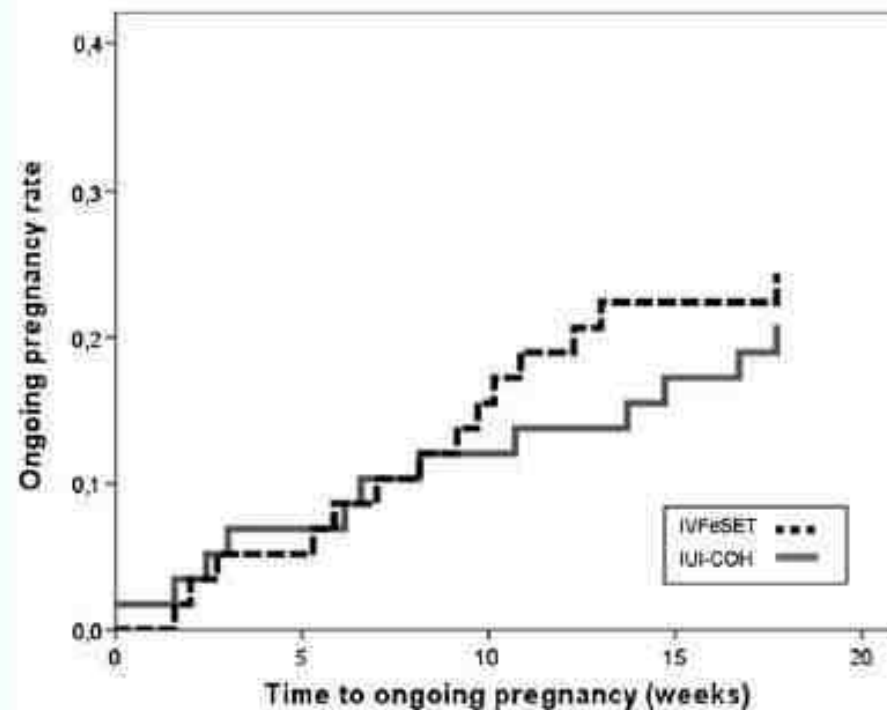
^c One couple was lost to follow-up.

Custers. IVF-eSET or IUI-COS in unexplained subfertility. *Fertil Steril* 2011.

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Cumulative ongoing pregnancy rate over time from one cycle of IVF-eSET or three cycles of IUI-COH.



Custers. IVF-eSET or IUI-COS in unexplained subfertility. *Fertil Steril* 2011.

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, M.D.,^c Kim L. Thornton, M.D.,^d Michael M. Alper, M.D.,^d and Marlene B. Goldman, Sc.D.,^e

- Konvansiyonel tedavi (n:247)
 - 3 siklus CC+IUI
 - 3 siklus rec Gn+IUI
 - 6 siklus IVF (2 siklus thaw)
- Hızlandırılmış tedavi (n:256)
 - 3 siklus CC+IUI
 - 6 siklus IVF (2 siklus thaw)

*Reindollar RH: Fertil Steril 2010; 94(3): 888-99

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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	4	2	6	6	15	18	33	35 ^c	28 ^c
(≥ 20 wks)									
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)

Note: CC = clomiphene citrate; IUI = intrauterine insemination; FSH = gonadotropin.

^a For IVF, 32 of the conventional and nine of the fast track cycles used cryopreserved embryos that had been collected in an earlier IVF cycle and frozen for later use. These cycles, called thaw cycles, are included in the calculation of the pregnancy rates per initiated cycle.

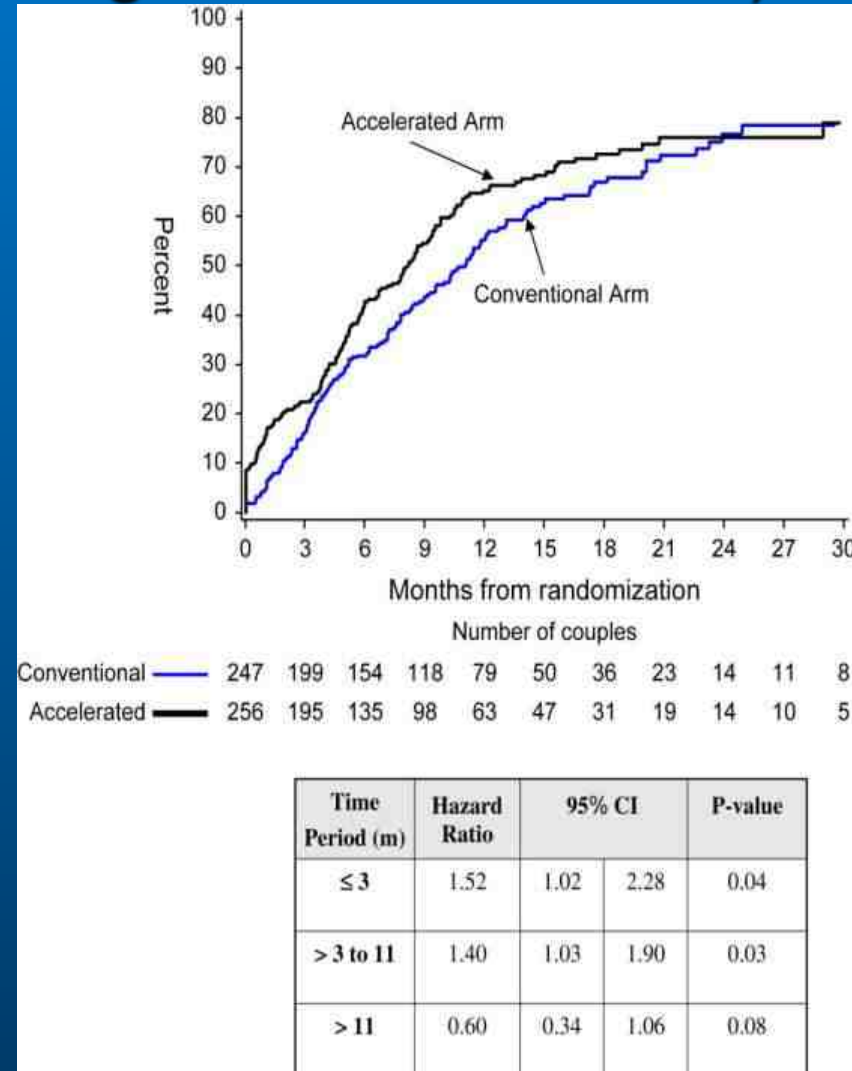
^b Total pregnancies include all ultrasound confirmed pregnancies, including spontaneous abortions.

^c Of these, there were 18 ongoing pregnancies (10 in conventional and 8 in fast track) and 34 live births (14 in conventional and 20 in fast track) that occurred outside of treatment cycles.

FASTT trial

Hasta başı gebelik hızı (canlı doğum + devam eden)

	Gebelik hızı (per couple)	Doğum başı maliyet
CC+IUI	20.6	
FSH+IUI	25.4	
IVF	67.5	
Konvansiyonel	74.9	\$71,399*
Fast track	77.7	\$61,553*
* -9,846 (95% CI, -25,099-3,869)		



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

Marlene B. Goldman, Sc.D.,^{a,b} Kim L. Thornton, M.D.,^c David Ryley, M.D.,^c Michael M. Alper, M.D.,^c June L. Fung, Ph.D.,^a Mark D. Hornstein, M.D.,^d and Richard H. Reindollar, M.D.^{a,e}

- 154 çift (38-42 yaş)
- İlk iki tedavi siklusları randomize
 - CC/IUI
 - FSH/IUI
 - Hemen IVF
- Tüm hastalar ilk iki siklusta gebe kalmaz ise sonraki tedavi IVF ile devam

Goldman MB et al Fertil Steril 2014

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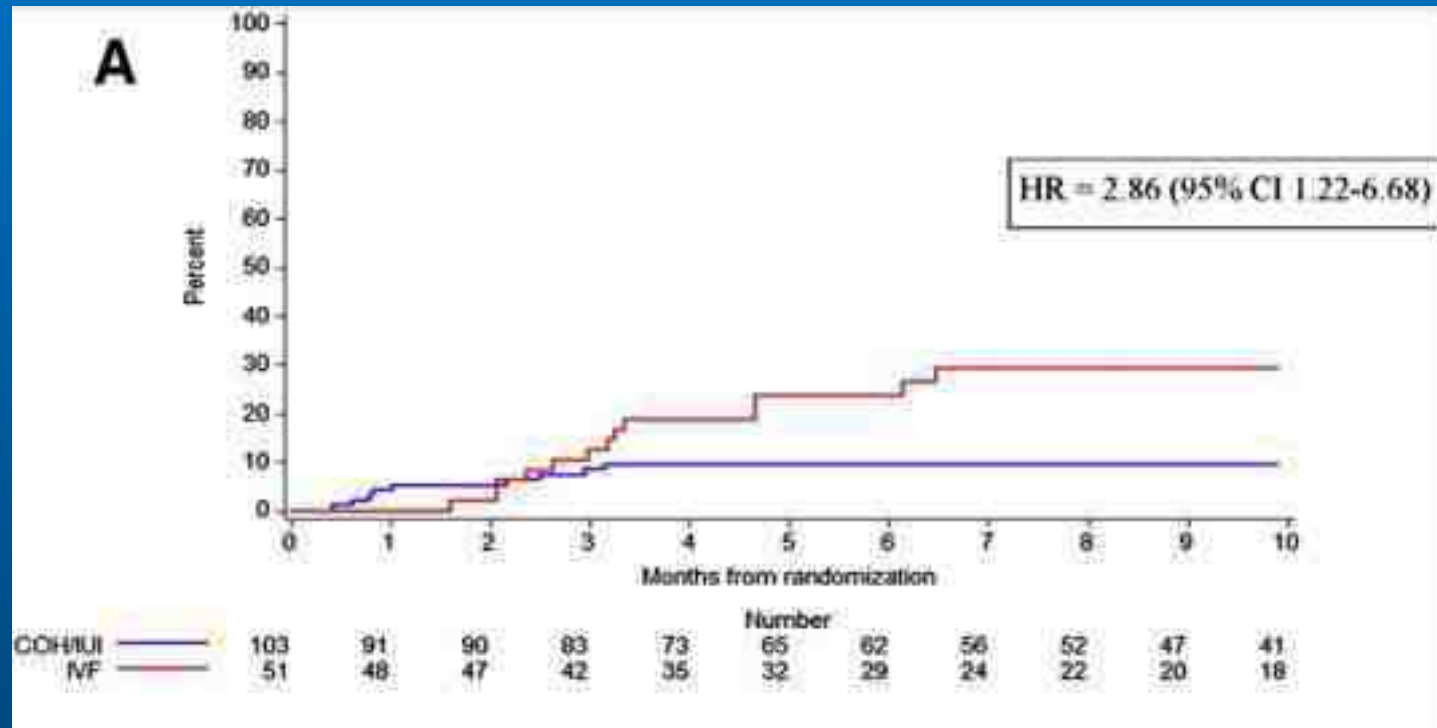
İlk iki siklуста
kümülatif gebelik
oranları

- CC/IUI: % 21,6
- FSH/IUI: % 17,3
- IVF: % 49

- Canlı doğumların % 84,2 si IVF siklusu
- Hemen IVF kolunda tedavi siklusu sayısı %36 daha az
- Hemen IVF kolunda ortalama gebelik elde etme süresi diğerlerine 3,5 ay daha kısa

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

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(A) Kaplan-Meier estimates of cumulative incidence of pregnancy leading to delivery of a live born for the controlled ovarian hyperstimulation arms combined versus the immediate IVF group. Analysis used a Cox proportional hazards model, $P=0.02$.

Maliyet: IUI vs IVF

45 çalışmanın retrospektif analizi

	GEBELİK/SİKLUS %	DOĞUM BAŞI TAHMİNİ MALİYET (\$)
BEKLEME	1.3-4.1	
IUI	3.8	
CC-IUI	8.3	10.000
hMG-IUI	17.1	17.000
IVF-ET	20.7	50.000

Guzick DS, Fertil Steril 1998

Maliyet: IUI vs IVF

	SİKLUS BAŞI MALİYET (NLG)	CANLI DOĞUM BAŞINA MALİYET (NLG)
IUI	623	8423
IUI + SO	931	10661
IVF	3350	27 409

Goverde AJ, Lancet 2000



Maliyet: IUI vs IVF

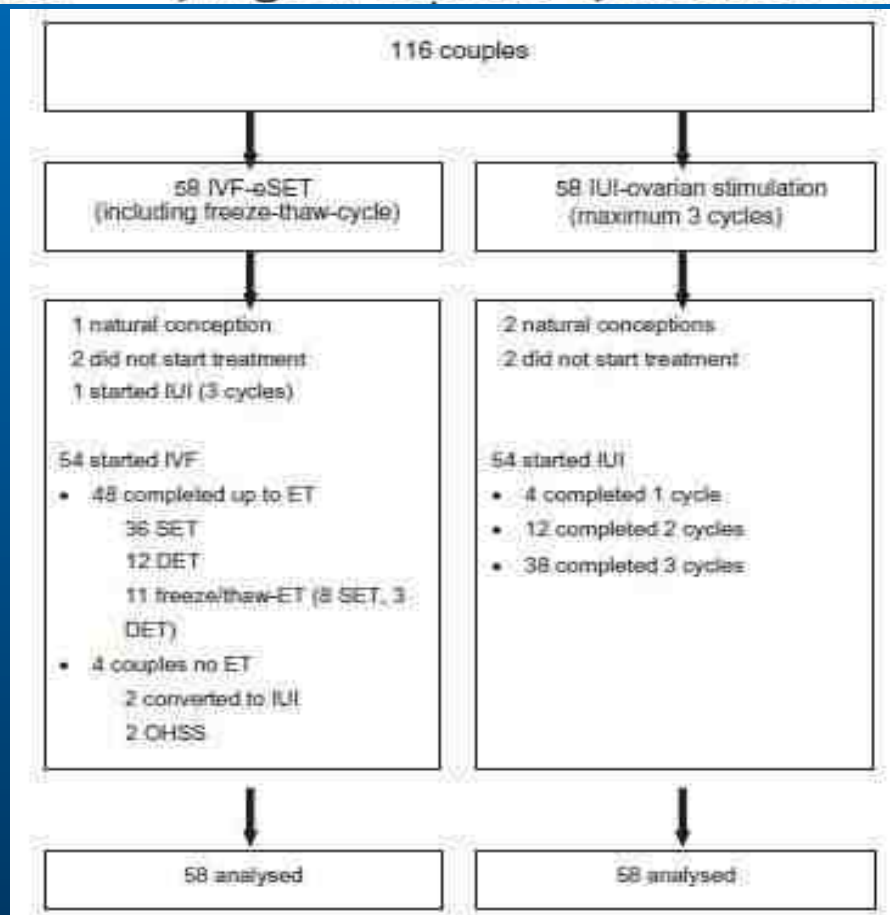


ARTICLE

IVF with planned single-embryo transfer versus IUI with ovarian stimulation in couples with unexplained subfertility: an economic analysis



Minouche ME van Rumste ^{a,b,*}, Inge M Custers ^b, Madelon van Wely ^b,



Maliyet: IUI vs IVF

Table 1 Specified costs per treatment of IVF or IUI—ovarian stimulation.

	IVF—eSET (€)	IUI (€)
Hospital component	1852.20	436.69
Costs without follicle aspiration and ET	1131.37	—
Specialist fee	332.60	66.58
Medication		
50 mg clomiphene citrate	—	0.454
1 IU FSH	0.409	0.409
10,000 IU HCG	8.68	8.68
14 days of progesterone	14	—

eSET = elective single-embryo transfer; ET = embryo transfer; HCG = human chorionic gonadotrophin; IUI = intrauterine insemination.

Maliyet: IUI vs IVF

Table 2 Outcomes per randomized group.

	IVF-eSET (n = 58)					IUI-ovarian stimulation (n = 58)					Difference
	Natural conception	IUI	IVF	Cryo-ET	Total	Natural conception	IUI 1	IUI 2	IUI 3	Total	
Clinical outcomes											
Ongoing pregnancy	1	0	11	2	14 (24)	2	1	5	4	12 (21)	+2
Multiple	0	0	2	0	2 (14)	0	0	2	1	3 (25)	-1
Live birth	1	0	11	1	13 (22)	2	1	5	2	10 (17)	+3
Singleton	1	0	10	1	12 (92)	2	1	3	1	7 (70)	+5
Twin	0	0	1	0	1 (8)	0	0	2	1	3 (30)	-2
Unknown	0	0	1	0	1 (7)	0	0	0	2	2 (17)	
Medication											
Cycles using rFSH	—	3	54	—	54	—	49	45	34	128	—
Total rFSH (IU)	—	1165	98,072	—	99,237	—	30,666	34,103	23,991	88,760	—
Mean rFSH (IU)	—	388	1816	—	1837	—	626	758	706	963	—
Cycles using CC	—	—	—	—	—	—	5	5	5	15	—
Total CC (mg)	—	—	—	—	—	—	2250	2500	2500	7250	—
Mean CC (mg)	—	—	—	—	—	—	450	500	500	483	—
Costs (€)											
Total costs	—	—	—	—	161,327	—	—	—	—	108,808	52,519
Mean costs per couple	—	—	—	—	2781	—	—	—	—	1876	915 ^c
Mean costs per cycle	—	—	—	—	2933	—	—	—	—	761	2172
Mean costs per ongoing pregnancy	—	—	—	—	11,523	—	—	—	—	9067	2456

Values are n or n (%) unless otherwise stated.

CC = clomiphene citrate; eSET = elective single-embryo transfer; ET = embryo transfer; IUI = intrauterine insemination IUI 1, IUI 2, IUI 3 = first, second or third IUI cycle; rFSH = recombinant FSH.

^cBootstrapped mean difference.

Maliyet: IUI vs IVF

Table 3 Scenario analysis for ongoing pregnancy.

IVF- eSET (%)	IUI—ovarian stimulation (%)	Relative risk	Cost- effectiveness	Dominant treatment
24	21	1.17	0.79	IUI
31	21	1.5	1	Neither
38	21	1.83	1.24	IVF

eSET = elective single-embryo transfer; IUI = intrauterine insemination.

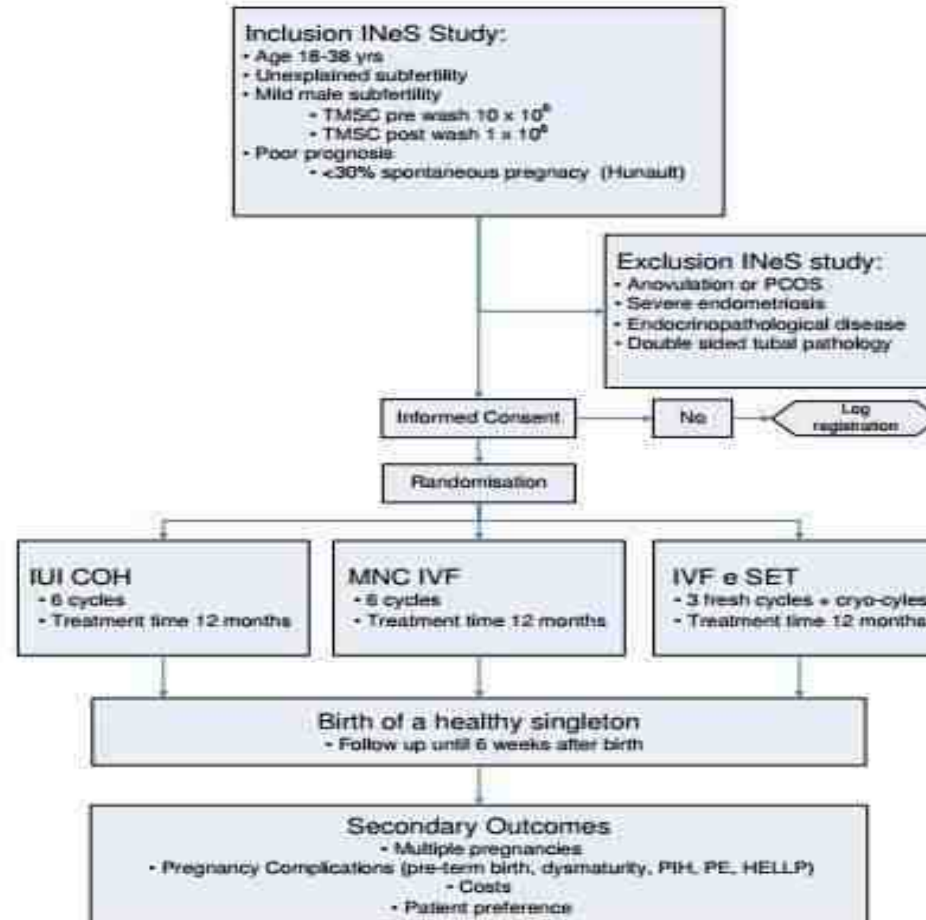
Van Rumste MME, Reprod Biomed Online, 2014

Study protocol

Open Access

The INeS study: prevention of multiple pregnancies: a randomised controlled trial comparing IUI COH versus IVF e SET versus MNC IVF in couples with unexplained or mild male subfertility

Alexandra J Bendsorp*, Els Slappendel, Carolien Koks, Jur Oosterhuis, Annemieke F Jan Peter de I, Nicole Becke Madelon van



PCOS polycystic ovarian syndrome
IUI COH intra uterine insemination + controlled ovarian hyperstimulation
MNC IVF Modified natural cycle IVF
IVF e SET elective single embryo IVF
PIH pregnancy induced hypertension

Is IVF—served two different ways—more cost-effective than IUI with controlled ovarian hyperstimulation?

R.I. Tjon-Kon-Fat¹, A.J. Bendsdorp¹, P.M.M. Bossuyt², C. Koks³, G.J.E. Oosterhuis⁴, A. Hoek⁵, P. Hompes⁶, F.J. Broekmans⁷, H.R. Verhoeve⁸, J.P. de Bruin⁹, R. van Golde¹⁰, S. Repping¹, B.J. Cohlen¹¹, M.D.A. Lambers¹², P.F. van Bommel¹³, E. Slappendel¹⁴, D. Perquin¹⁵, J. Smeenk¹⁶, M.J. Pelinck¹⁷, J. Gianotten¹⁸, D.A. Hoozemans¹⁹, J.W.M. Maas³, H. Groen⁵, M.J.C. Eijkemans²⁰, F. van der Veen¹, B.W.J. Mol²¹, and M. van Wely^{1,*}

Table I Baseline characteristics of the couples.

	IVF-SET (N = 201)	IVF-MNC (N = 194)	IUI-COH (N = 207)
Female age, years, mean (SD)	33 (3.39)	33 (3.50)	34 (3.67)
Primary subfertility, N (%)	160 (80)	141 (73)	157 (76)
Duration of subfertility, mean (SD), years	2.13 (1.73–3.01)	2.14 (1.77–2.81)	2.30 (1.82–3.13)
Total motile sperm count ($\times 10^6$), median (IQR)	51 (25–100)	53 (25–126)	59 (30–124)
Diagnosis subfertility, N (%)			
Unexplained	183 (91)	173 (89)	189 (91)
Male factor	18 (9)	21 (11)	18 (9)

Table II Pregnancy outcomes.

	IVF-SET (N = 201)	IVF-MNC (N = 194)	IUI-COH (N = 207)	IVF-SET versus IUI-COH RR (95% CI)	IVF-MNC versus IUI-COH RR (95% CI)
Pregnancy outcomes					
Healthy child	104 (52)	83 (43)	97 (47)	1.10 (0.91–1.34)	0.91 (0.73–1.14)
Live birth	118 (59)	99 (51)	116 (56)	1.05 (0.89–1.24)	0.91 (0.76–1.09)
Ongoing pregnancy	121 (60)	102 (53)	119 (57)	1.05 (0.89–1.23)	0.91 (0.77–1.09)
Multiple gestation*	7 (6)	5 (5)	8 (7)	1.05 (0.91–1.21)	0.93 (0.80–1.09)

Data are presented as no. (%).

*Percentage is a ratio of total ongoing pregnancies.

Is IVF—served two different ways—more cost-effective than IUI with controlled ovarian hyperstimulation?

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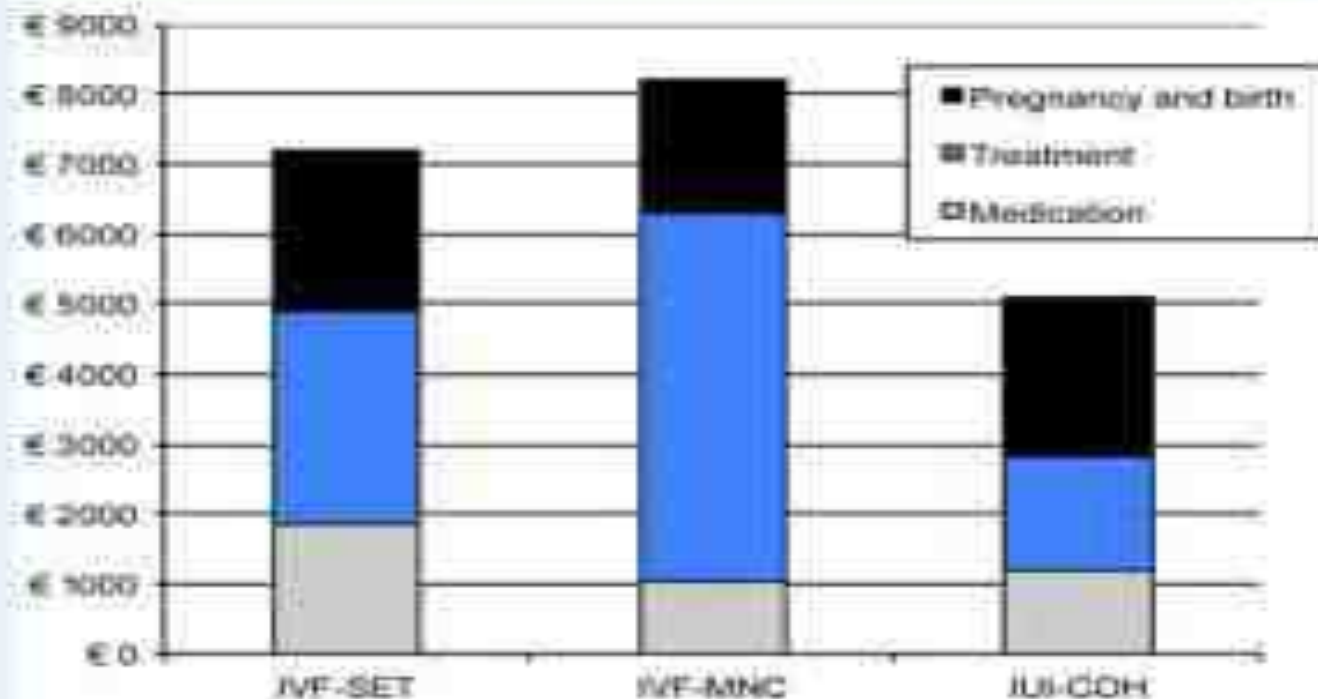


Figure 1 Mean costs per couple.

Cumulative pregnancy probabilities among couples with subfertility: effects of varying treatments

Joseph B. Stanford, M.D.,^a Rafael T. Mikolajczyk, M.D.,^{b,c} Courtney D. Lynch, Ph.D.,^{b,d} and Sara E. Simonsen, M.S.P.H.^a

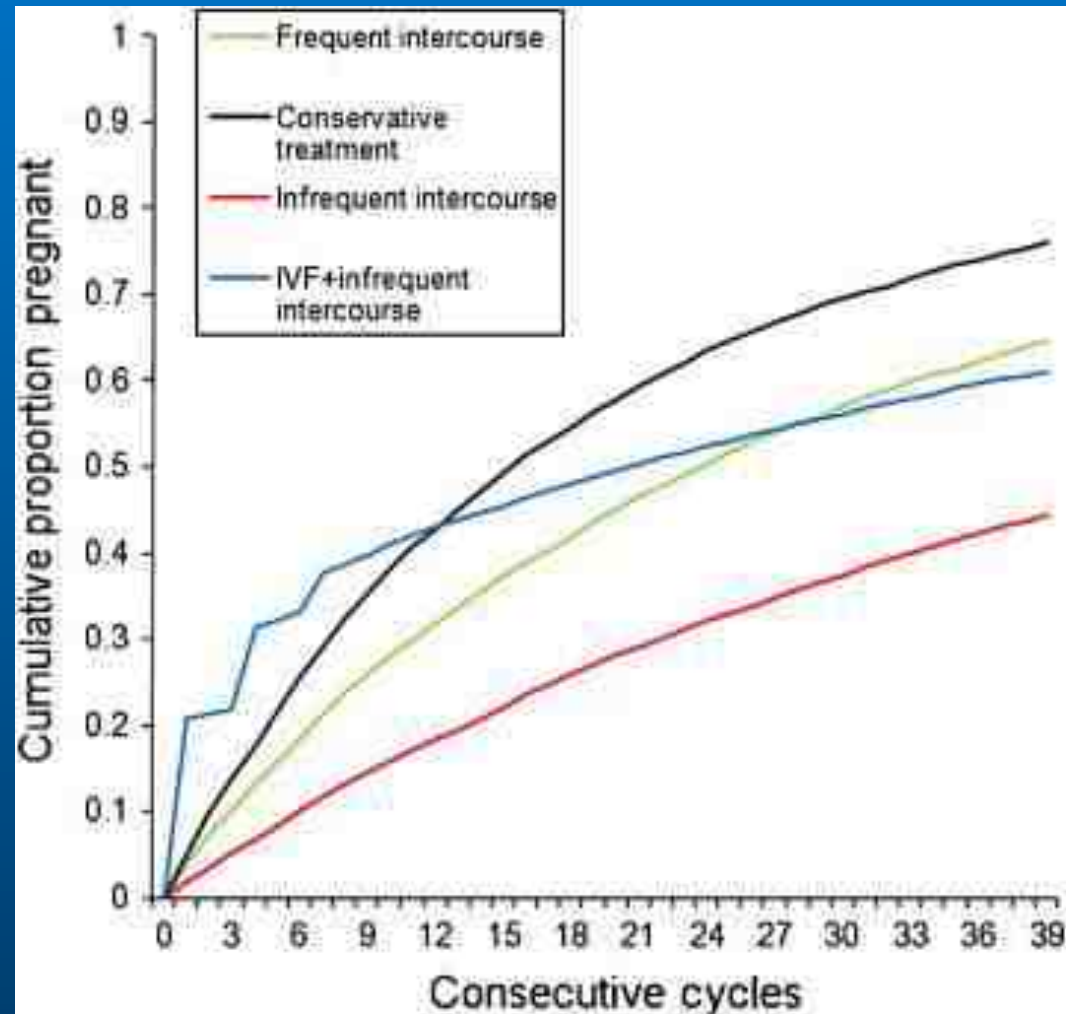
- Baseline fekundite % 25-30
- 12 aylık kumulatif fekundite % 85-95
- Fekundite zamanla azalıyor
- İlk 2 yıl tedavi verilmiyor
- Sonraki üç yıl tedavi

Stanford JB,2010 Fertil Steril

IVF: Etkinlik

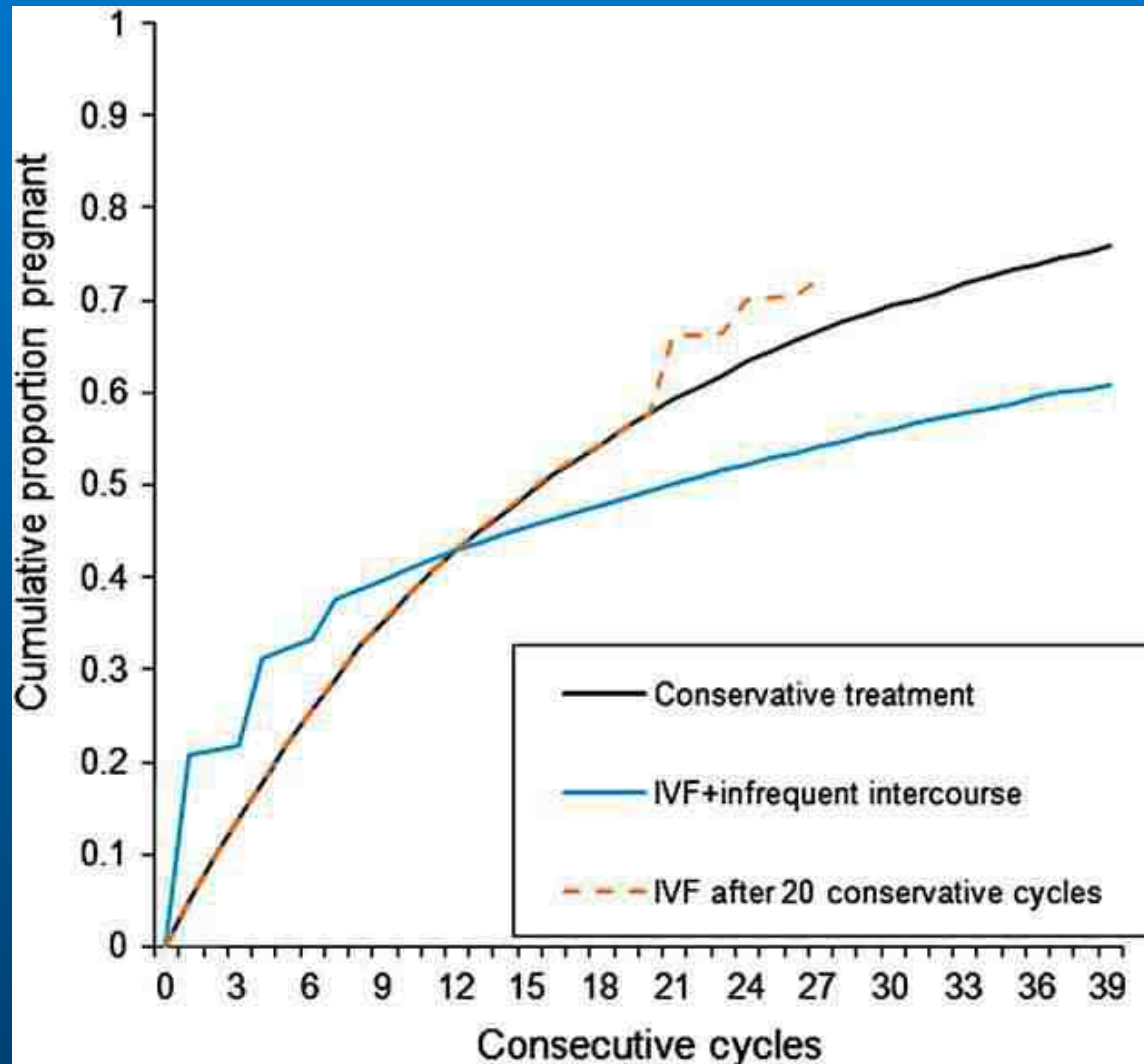
Cumulative pregnancy probabilities among couples with subfertility: effects of varying treatments

- Sık İlişki: haftada 2
- Daha az sık ilişki: haftada 1
 - %40 kümülatif gebelik oranı azalır
- Konservatif tedavi: CC
 - kümülatif gebelik oranı 1,5 kat artar
- IVF: ortalama hasta başı 1.8 siklus
 - 1 siklus sonrası %30, 2 siklus sonrası % 43 drop-out



Cumulative pregnancy probabilities among couples with subfertility: effects of varying treatments

- Önce IVF sadece gebelik oluşumunu hızlandırır
- Ek maliyet ve advers etkileri ise dezavantajları



Two new prediction rules for spontaneous pregnancy leading to live birth among subfertile couples, based on the synthesis of three previous models

							Score 3-sample	Score 2-sample
Woman's age (y)	21-25	26-31	32-35	36-37	38-39	40-41		
3-sample model	0	3	7	10	13	15		
2-sample model	0	2	6	9	11	12		
Duration of subfertility (y)	1	2	3-4	5-6	7-8			
3-sample model	0	3	7	12	18			
2-sample model	0	2	5	9	13			
Type of subfertility		Secondary	Primary					
3-sample model		0	8					
2-sample model		0	6					
Motility (%)	≥ 60	40-59	20-39	0-19				
3-sample model	0	2	4	6				
2-sample model	0	2	4	6				
Referral status	Secondary-care couple		Tertiary-care couple					
3-sample model		0	4					
2-sample model		0	4					
Post-Coital-Test		Normal	Abnormal					
2-sample model		0	14					
Prognostic Index Score (Sum)								

Two new prediction rules for spontaneous pregnancy leading to live birth among subfertile couples, based on the synthesis of three previous models

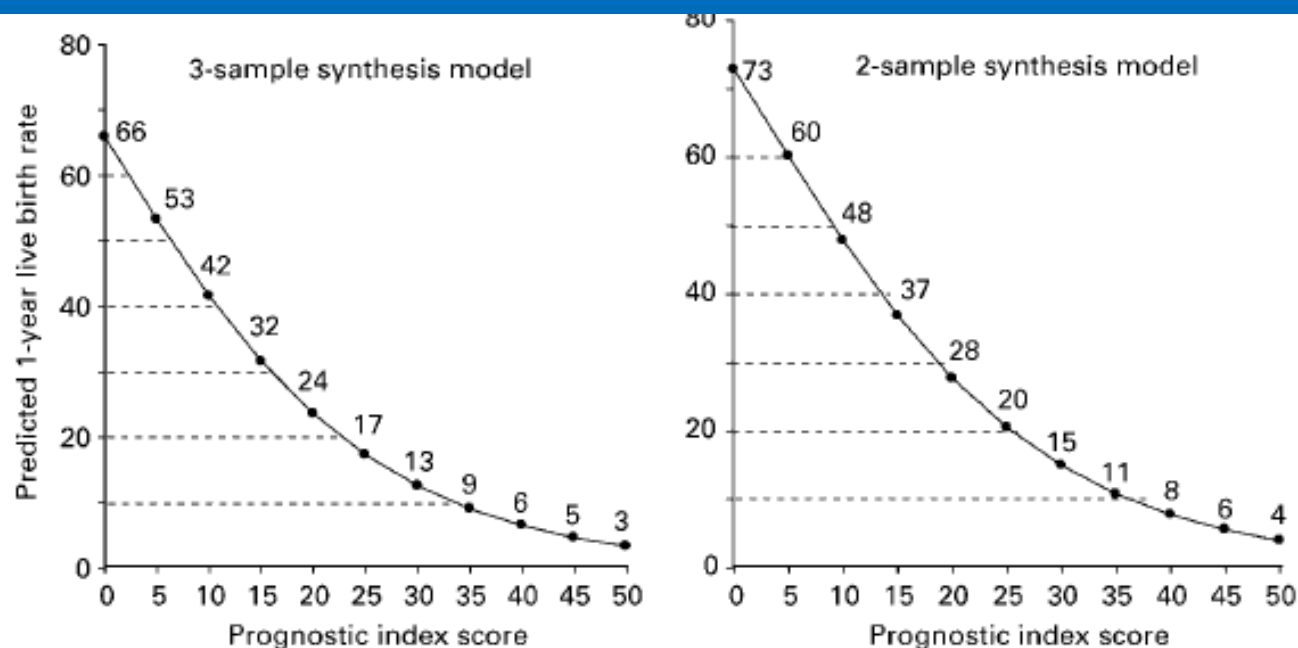


Figure 1. Score chart of the 3-sample and 2-sample synthesis models to estimate the chance of spontaneous pregnancy within 1 year after intake resulting in live birth. Upper part: calculating the score; lower part: predicting 1-year pregnancy rate.

Two new prediction rules for spontaneous pregnancy leading to live birth among subfertile couples, based on the synthesis of three previous models

Table IV. Predicted probabilities and observed proportions of 1 year pregnancy leading to live birth, when applying the synthesis models
(a). Three-sample synthesis model, applied to all three samples ($n = 2455$).

Predicted probability	<i>n</i>	(%)	Observed	95% CI
<20%	991	(40%)	13%	11–16%
20–40%	1256	(51%)	29%	26–31%
>40%	208	(9%)	50%	42–58%
All	2455	(100%)	24%	22–26%

Hunault C et al. Hum. Reprod. 2004;19:2019-2026

İÜİ:Prognostik faktörler

- **İnfertil çiftte ait faktörler**
 - İnfertilite süresi
 - İnfertilite cinsi (primer vs sekonder)
 - **Kadına ait parametreler**
 - Kadın yaşı
 - Over rezervi
 - Tubal faktör
 - Endometriozis
 - **Erkeğe ait parametreler**
 - Semen parametreleri

Article

Factors affecting live birth rate in intrauterine insemination cycles with recombinant gonadotrophin stimulation



Ahmet Erdem MD is associate professor of Obstetrics and Gynecology at the University of Gazi, Turkey. He is a graduate of the University of Hacettepe Medical School in Turkey and completed his residency at University of Gazi School of Medicine Department of Obstetrics and Gynecology in Ankara, Turkey. Since 1998, he is also a clinician and researcher at the Assisted Reproductive Technologies Unit of the University of Gazi Center for Reproductive Health, Infertility and Family Planning. His research activity focuses on clinical IVF, intrauterine insemination and ovarian reserve testing.

Article

Factors affecting live birth rate in intrauterine insemination cycles with recombinant gonadotrophin stimulation

- 278 açıklanamayan infertil/492 siklus
- 75 U rec Gn/prog vag. gel luteal destek
- Siklus başı gebelik % 20,3
- Siklus başı canlı doğum % 11,4
- **Hasta başı canlı gebelik % 25,2**
- Spontan gebelik % 6,1
- **Hasta başı kümülatif % 30,9**
canlı gebelik (spontan+tedavi)
- Çoğul Gebelik % 11,2

Erdem et al RBM Online. 2008;17:199-206

Article

Factors affecting live birth rate in intrauterine insemination cycles with recombinant gonadotrophin stimulation

	Canlı Doğum	Gebe olmayan	P
İnfertilite süresi (yıl)	3.9 ± 2.8	4.8 ± 3.6	0.001
Unexplained	14	86	0.003
Erkek faktörü	7.8	92.2	
hCG öncesi dominant folikül sayısı	2.1 ± 1.3	1.7 ± 1.1	0.01
Swim up öncesi sperm motilite(%)	59.2±16.2	53.8 ± 16.6	0.003

Multivariat Logistik Regresyon Analizi

Unexplained infertil hastalarda (278 hasta)
“canlı doğumu” öngören bağımsız
değişkenler

- **İnfertilite süresi**
(OR = 0.898, 95% CI = 0.820–0.934, $P=0.022$)
- **Tedavi yapılan siklus sayısı**
(bir siklus vs iki, üç, veya >4)
OR = 0.518, 95% CI = 0.392–0.683, $P = 0.0001$)
- **HCG öncesi dominant folikül sayısı**
(bir dominant follicle vs üç veya fazla folikül)
OR = 2.077, 95% CI = 1.138–3.792, $P = 0.017$)

OVULATION INDUCTION

Role of antral follicle count in controlled ovarian hyperstimulation and intrauterine insemination cycles in patients with unexplained subfertility

Mehmet Erdem, M.D., Ahmet Erdem, M.D., Ismail Guler, M.D., and Songul Atmaca, M.D.

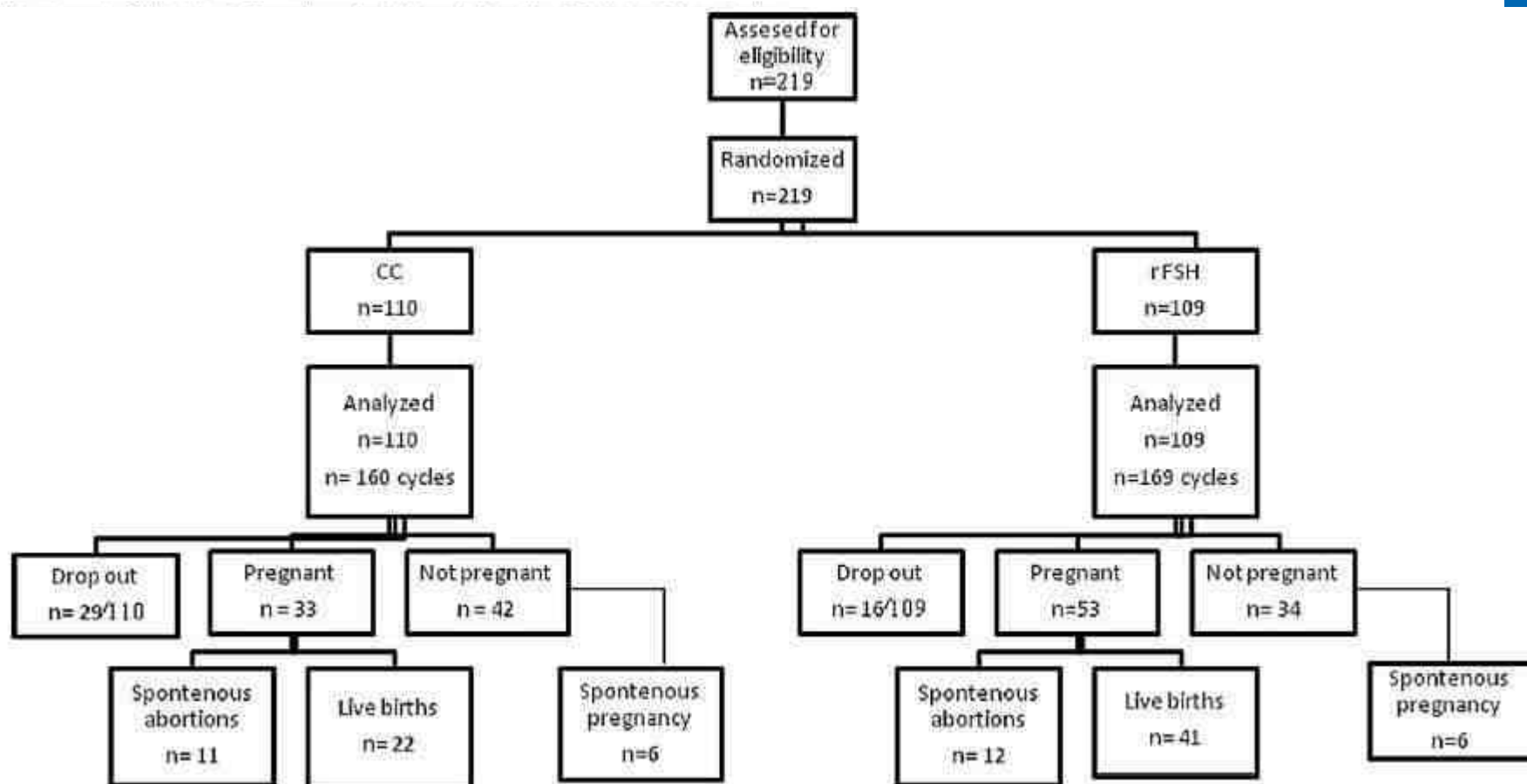
Department of Obstetrics and Gynecology, Gazi University School of Medicine, Ankara, Turkey

	Canlı Doğum	Gebe olmayan	P
Total antral folikül sayısı	9.4 ± 3.5	6.9 ± 2.4	0.0001
Değişken	OR	% 95 CI	P
Bazal AFC	1.33	1.10-1.60	0.003
Bazal FSH	1.23	0.99-1.0	0.057
Yaş	0.95	0.85-1.06	0.95
Total Gn dozu	0.99	0.99-1.0	0.27
hCG günü dominant folikül sayısı	0.72	0.39-1.53	0.47

Recombinant FSH increases live birth rates as compared to clomiphene citrate in intrauterine insemination cycles in couples with subfertility: a prospective randomized study



Mehmet Erdem^a, Seraf Abay^a, Ahmet Erdem^a, Mehmet Firat Mutlu^{b,*}, Esra Nas^a, Ilknur Mutlu^c, Mesut Oktem^a



Recombinant FSH increases live birth rates as compared to clomiphene citrate in intrauterine insemination cycles in couples with subfertility: a prospective randomized study

Table 2

Treatment outcomes of the study groups.

	rFSH protocol <i>n</i> = 109	CC protocol <i>n</i> = 110	<i>p</i> value
E ₂ level on the day of hCG (pg/ml)	742.1 ± 619	667.4 ± 460	NS
Progesterone level on the day of hCG (ng/ml)	1.10 ± 0.66	1.04 ± 0.64	NS
LH level on the day of hCG (IU/ml)	12.8 ± 11.6	12.0 ± 7.1	NS
Endometrial thickness on hCG day (mm)	10.5 ± 2.2	8.1 ± 2.0	<0.001*
Follicle number (≥14 mm) on hCG day	1.8 ± 1.1	1.7 ± 1.0	NS
Clinical pregnancy rate per cycle (%)	48/169 (28.4%)	32/160 (20%)	NS
Live birth rate per cycle (%)	41/169 (24.3%)	22/160 (13.8%)	<0.05*
Clinical pregnancy rate per patient (%)	47/109 (43.1%)	31/110 (28.2%)	<0.05*
Live birth rate per patient (%)	41/109 (37.6%)	22/110 (20%)	<0.01*
Live birth rate per patient ^a (%)	47/109 (43.1%)	28/110 (25.5%)	<0.01*
Live birth rate in 1st cycle (%)	26/106 (24.5%)	18/103 (17.5%)	NS
Spontaneous abortion rate	12/53 (22.6%)	11/33 (33.3%)	NS
Multiple pregnancies	5/48 (10.4%)	4/32 (12.5%)	NS

^a Live births resulting from spontaneous pregnancy are included.

* Shows significant difference.

IUI : Prognostik Faktörler

- İyi prognoz faktörleri
 - Kısa süreli infertilite
 - Gonadotropinlere multifoliküler yanıt
 - İlk tedavi ayı
 - Sekonder infertilite
 - Kadın yaşının genç olması
- Kötü prognoz faktörleri
 - Erkek subfertilitesi
 - Tubal hastalık
 - Endometriozis

Açıklanamayan İnfertilite: IUI

People are having less sex than they were in the 1990s

■ Men ■ Women

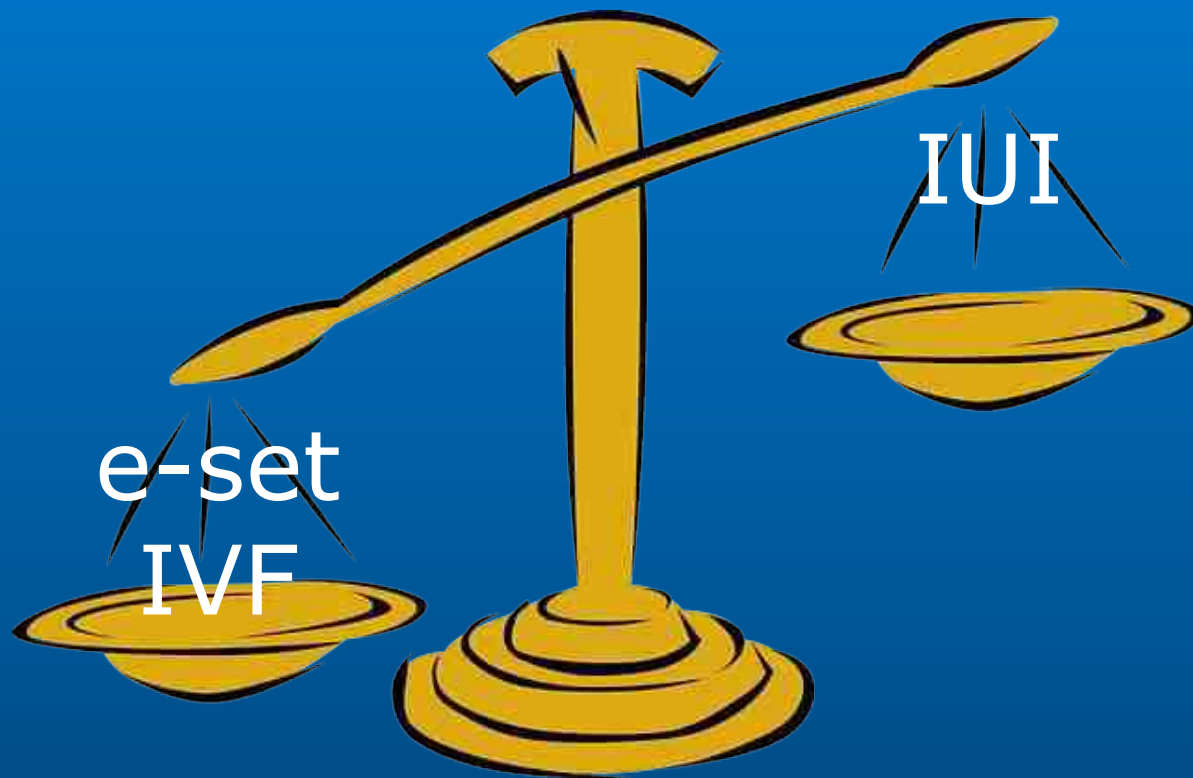
Average number of times per month



Source: National Survey of Sexual Attitudes and Lifestyles

SONUÇLAR

- IVF'in siklus başı tedavi etkinliği diğer yöntemlere göre (IUI) belirgin yüksektir.
- IVF ilk tedavi seçeneği olarak giderek daha çok oranda hekim ve hasta tarafından tercih edilmektedir.
- Ancak eldeki veriler henüz IVF'in açıklanamayan infertil çiftlerin tümünde ilk basamak uygulanmasının etkin ve cost-effectif olacağını desteklememektedir.
- İyi prognozlu hastalarda IUI ilk basamak uygulanabilir
- Kadın yaşı, infertilite süresi ve tipi, AFC, önemli prognostik faktörlerdir.





TEŞEKKÜRLER