



ÜREME TIBBİ ve CERRAHİSİ  
DERNEĞİ

## İnfertilite Tedavisinde Güncel Yaklaşımlar



21 Aralık 2014, Pazar

# ***IUI KİME, NE ZAMAN, KAÇ DEFA ?***

**Prof Dr Bülent Gülekli**

**Dokuz Eylül Üniversitesi**

**Tıp Fakültesi Kadın Hast ve Doğum ABD İZMİR**

# **İnseminasyon - Tarihçe**

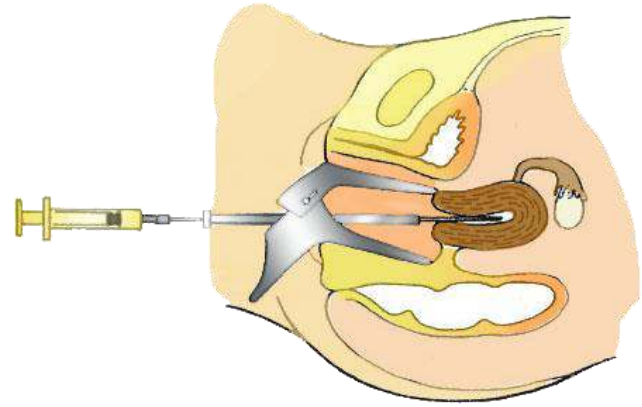
- İlk yayın **1790 John Hunter**
- İlk gebelik **1838 Girault F**
- Donör inseminasyon **1884 Pancost W**
- Yıkanmış sperm **1950 Hanson FM, Rock J**
- Dondurulmuş sperm **1953 Bunge ve Sherman**
- Split ejakulat **1960 Farris E**
- İlk randomize kontrollü çalışma **1984 Kerin JFP**

# **İnseminasyon Tipleri**

- **Intravaginal İnseminasyon** **John Hunter** (1770)
- **İntraservikal inseminasyon**
- **Donor inseminasyon**
- **Intrauterine Insemination**
- **Intrafallopian Insemination**

# Günümüzde IUI

- **Direkt IUI – HAYIR**
  - 1.Kramplar (PG)
  2. Enfeksiyon
- **Split ejakulat – HAYIR**
- **Poliklinik şartlarında**  
Hareketli spermilerin,  
konsantre edildikten  
sonra, steril bir kateter  
yardımıyla serviksin  
geçilerek uterin kaviteye  
verilmesi



# **Assisted reproductive technology in Europe, 2008: results generated from European registers by ESHRE<sup>†</sup>**

**A.P. Ferraretti\*, V. Goossens, J. de Mouzon, S. Bhattacharya, J.A. Castilla, V. Korsak, M. Kupka, K.G. Nygren, A. Nyboe Andersen, The European IVF-monitoring (EIM)<sup>‡</sup>, and Consortium, for the European Society of Human Reproduction and Embryology (ESHRE)**

**Human Reproduction, Vol.27, No.9 pp. 2571–2584, 2012**

➤ **IVF için siklus başına gebelik oranı %28,9**

➤ **IUI için siklus başına gebelik oranı (%12,4)**

➤ **(kliniğimizde 2013 yılı için %14,9)**

# Assisted reproductive technology in Europe, 2010: results generated from European registers by ESHRE<sup>†</sup>

All<sup>a</sup>

176 512

14 750

8.9

**Doğum %**



**KİMLERE  
YAPILMALI?**

# IUI endikasyonları

## ➤ Ejakülatuar yetmezlik

Hypospadius-vaginismus-  
impotans,retrograd ejakülasyon

## ➤ Servikal faktör ???

Mukus uyuşmazlığı, mukus yetersizliği

## ➤ Erkek subfertilitesi

Hafif ve orta derecede erkek  
infertilitesi



# IUI endikasyonları-2

- Açıklanamayan infertilite
- Hafif / orta derecede endometriyozis
- Ovulatuvar nedenlere bağlı infertilite
- HIV (-) kadın ile HIV (+) erkek

IUI, horizontal geçişi önleyebilir.

- Erkekten kanser öyküsü

KT,RT veya orşiektomi öncesi sperm  
kryoprezervasyonu

# Hangi durumlarda önerilmez?

- Bilateral tuba uterinaların blokajı veya hasarı
- Ovaryan yetmezlik
- Ciddi seminal sıvı anormalliği (ciddi oligospermi ..)
- Ciddi endometriyozis
- Servikal atrezi
- Servisit, endometrit

# IUI AVANTAJLARI

- Vajinal asidite ve servikal mukus problemlerini aşar
- Motilite ve kalite açısından göreceli seçilmiş spermin internal tubal açıklığa yaklaşmasını sağlar
- Ovulasyon ve endometriyal kabul için en uygun zaman seçimine olanak tanır
- Ofis şartlarında minimal rahatsızlıkla uygulanma kolaylığı vardır
- Ekonomiktir

# IUI DEZAVANTAJLARI

- Ovaryen Hiperstimulasyon sendromu
- oęul gebelik
- Enfeksiyon



# IUI ÖNCESİ HAZIRLIK

## Sperm Analizi

- Total motil sperm sayısı
- Yıkama sonrası sperm sayısı

## Uterin kavite ve tubaların değerlendirilmesi

- Klasik HSG
- Saline infüzyon sonografi ( SIS)
- Ofis histeroskopi

# IUI ÖNCESİ HAZIRLIK-2

## Ultrasonda minimal değerlendirme

- Her iki over antral follikül sayısının izlenmesi
- Her iki over lateral ve kısmen simetrik yerleşimi
- Uterus morfolojisi
- Endometrium

## Serviks değerlendirilmesi

- Nullipar servikste gerekirse deneme kateterizasyonu
- Serviks aks ve derinliğinin inseminasyon öncesi değerlendirilmesi



**IUI**

**Gebeliğe  
etki eden  
faktörler**

# The Role of Infertility Etiology in Success Rate of Intrauterine Insemination Cycles: An Evaluation of Predictive Factors for Pregnancy Rate

Mahnaz Ashrafi, M.D.<sup>1,2</sup>, Mandana Rashidi, M.D.<sup>1</sup>, Afsaneh Ghasemi, M.D.<sup>1\*</sup>, Arezoo Arabipoor, M.Sc.<sup>2</sup>, Sara Daghighi, B.Sc.<sup>1</sup>, Parisa Pourasghari, M.Sc.<sup>1</sup>, Zahra Zolfaghari, B.Sc.<sup>2</sup>

Int J Fertil Steril. 2013; 7(2): 100-107.



INTERNATIONAL JOURNAL  
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*Table 3: Logistic regression analysis for predicting the success of intrauterine insemination*

| Variable                                 | OR <sup>a</sup> | CI <sup>b</sup> | P value |
|------------------------------------------|-----------------|-----------------|---------|
| Age (Y) <sup>c</sup>                     |                 |                 |         |
| <40                                      | 2.1             | (1.0-4.5)       | 0.019   |
| Infertility duration (Y) <sup>c</sup>    |                 |                 |         |
| <5                                       | 2.3             | (1.1-4.7)       | 0.015   |
| Infertility etiology <sup>c</sup>        |                 |                 |         |
| Unexplained                              | 1.9             | (0.9-3.5)       | 0.045   |
| Male factor                              | 1.7             | (0.8-3.2)       | 0.05    |
| Number of follicles (>16mm) <sup>c</sup> |                 |                 | 0.02    |
| 2                                        | 3.1             | (1.3-6.4)       |         |
| 3                                        | 3.4             | (1.6-6.9)       |         |
| ≥4                                       | 2.7             | (1.2-5.6)       |         |
| Stimulation regimen <sup>c</sup>         |                 |                 |         |
| CC/ hMG                                  | 2               | (1.03-4.1)      | 0.01    |

<sup>a</sup>; Odds ratio, <sup>b</sup>; Confidence interval and <sup>c</sup>; Odds ratio in contrast to the poorest category.

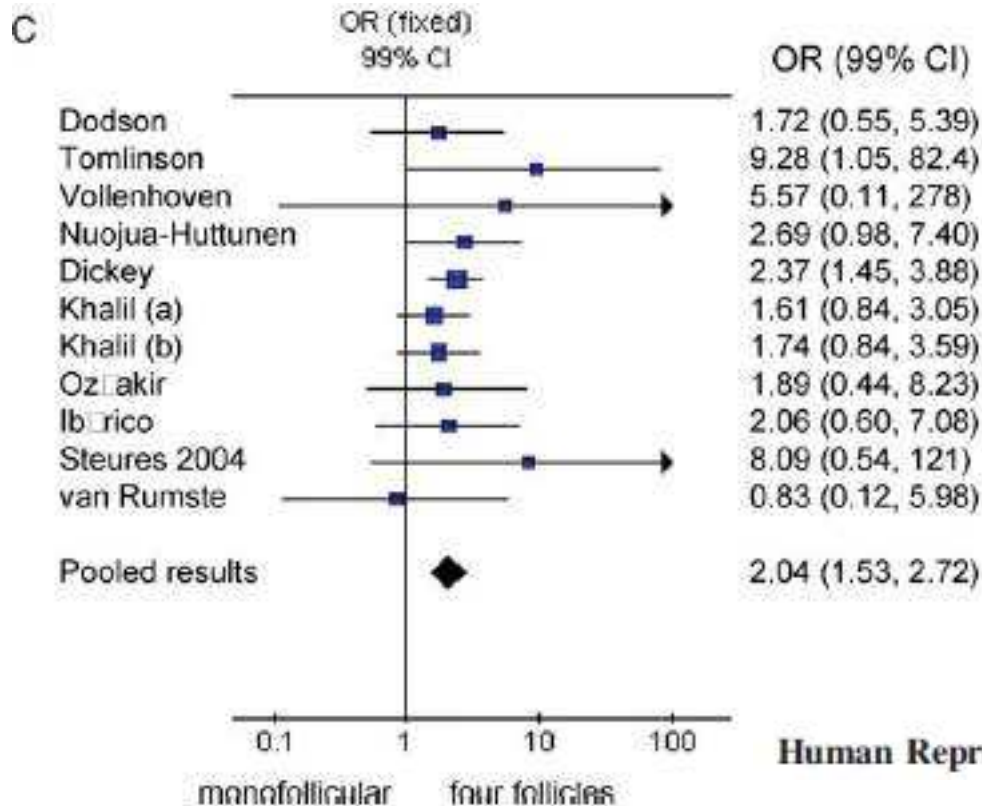


# The influence of the number of follicles on pregnancy rates in intrauterine insemination with ovarian stimulation: a meta-analysis

2 folikül: OR 1.6 (99% CI 1.3–2.0), gebelikte %5 artış

3 folikül: OR 2.0, %8 artış gebelikte

4 folikül: OR 2.0, %8 artış gebelikte



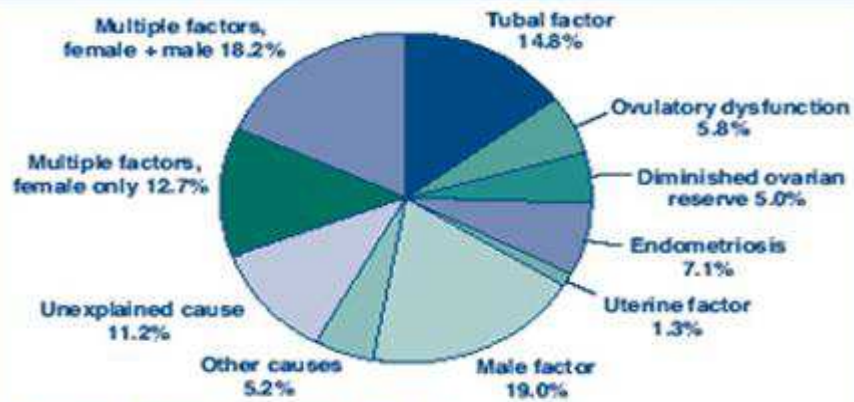
## The effect of ovarian stimulation on the outcome of intrauterine insemination

**Ruth Gomez · Martin Schorsch · Joscha Steetskamp ·  
Thomas Hahn · Kristina Heidner · Rudolf Seufert ·  
Christine E. Skala**

5346 IUI / 2180 hasta

**Table 1** Pregnancy rates after hormonal stimulation/natural cycle before IUI

| Stimulation type | Pregnant (%) | Not pregnant (%) | Total |
|------------------|--------------|------------------|-------|
| Natural cycle    | 49 (11.3)    | 384 (88.7)       | 433   |
| uFSH             | 28 (14.4)    | 166 (85.6)       | 194   |
| rFSH             | 403 (10.0)   | 3,617 (90.0)     | 4,020 |
| Clomiphene       | 44 (7.4)     | 552 (92.6)       | 596   |
| HMG              | 14 (13.6)    | 89 (86.4)        | 103   |



\* Total does not equal 100% due to rounding.

## Minimal-Mild Endometriois-KOH + IUI

**Table 5 Cycle Fecundity Rate and Implantation Rate per Cycle after Intrauterine Insemination in Women with Minimal-Mild Endometriosis and Women with Unexplained Infertility**

| Rate                 | Reference                                  | Minimal-Mild<br>Endometriosis | Unexplained<br>Infertility | P Value |
|----------------------|--------------------------------------------|-------------------------------|----------------------------|---------|
| Cycle fecundity rate | Omland et al, 1998 <sup>53</sup>           | 8/41 (16%)                    | 40/119 (34%)               | < 0.05  |
|                      | Nuojuua-Huttunen et al, 1999 <sup>54</sup> | 9/138 (6%)                    | 63/413 (15%)               | 0.05    |
| Implantation rate    | Omland et al, 1998 <sup>53</sup>           | 9/41 (18%)                    | 52/119 (44%)               | < 0.05  |

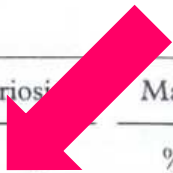
## Success in intrauterine insemination: the role of etiology

KATJA AHINKO-HAKAMAA<sup>1</sup>, HEINI HUHTALA<sup>2,3</sup> & HELENA TINKANEN<sup>1</sup><sup>1</sup>Department of Obstetrics and Gynaecology, Tampere University Hospital, <sup>2</sup>School of Public Health, University of Tampere, and <sup>3</sup>Research Unit, Tampere University Hospital, Tampere, Finland**Abstract**

**Background.** We aimed to identify the prognostic factors for the highest pregnancy rate and lowest multiple pregnancy rate in different infertility etiology groups among women undergoing insemination treatment. **Methods.** A total of 1,171 cycles among 532 infertile couples were retrospectively studied and the impact of different prognostic factors on pregnancy rate in five different etiology subgroups was analyzed. **Results.** The pregnancy rate/cycle was highest (19.2%) among women with anovulatory infertility and lowest (11.9%) in endometriosis based infertility. Multiple pregnancy rate varied between 3.6% (male infertility) and 13.2% (anovulatory infertility). In unexplained infertility ovarian stimulation resulting in three follicles (pregnancy rate 24.2%) and inseminated motile sperm count  $> 30 \times 10^6$  (pregnancy rate 19.8%) were significant prognostic factors. In anovulatory infertility stimulation with sequential clomiphene citrate and human menopausal gonadotrophin was a positive predictive factor, with a pregnancy rate of 36%. In male infertility stimulation with sequential clomiphene citrate/human menopausal gonadotrophin resulted in the best pregnancy rate (25.0%). In endometriosis-based infertility the pregnancy rate was best with clomiphene citrate stimulation (21.1%) and inseminated motile sperm count  $> 30 \times 10^6$  (24.3%). In combined infertility the highest pregnancy rate was with sequential clomiphene citrate/human menopausal gonadotrophin stimulation and with three follicles (30%), and even 18.2% with inseminated motile sperm count  $< 5.0 \times 10^6$ . **Conclusions.** The etiology of the infertility is important when optimal insemination treatment is planned. The impact of the woman's age, sperm count, stimulation protocol, and the follicle number on the pregnancy rate and multiple pregnancy rate is associated with the etiology of the infertility.

Table I. Pregnancy rates (%) per cycle (n) according to etiology.

|            | Unexplained |     | Male |     | Anovulatory |     | Endometriosis |     | Many reasons |    |
|------------|-------------|-----|------|-----|-------------|-----|---------------|-----|--------------|----|
|            | %           | n   | %    | n   | %           | n   | %             | n   | %            | n  |
| Overall PR | 14.1        | 637 | 18.2 | 154 | 19.2        | 198 | 11.9          | 126 | 17.9         | 56 |



# Endometriosis and infertility: a committee opinion

The Practice Committee of the American Society for Reproductive Medicine  
American Society for Reproductive Medicine, Birmingham, Alabama

## TABLE 1

Cycle fecundity in women with stage I or II endometriosis, according to treatment (reported as percentage).

| Treatment                                  | Group                   |                    |                                      |                    |                     |
|--------------------------------------------|-------------------------|--------------------|--------------------------------------|--------------------|---------------------|
|                                            | Unexplained infertility |                    | Endometriosis-associated infertility |                    |                     |
| Reference                                  | Guzick et al. (55)      | Deaton et al. (41) | Chaffkin et al. (57)                 | Fedele et al. (42) | Kemmann et al. (43) |
| No treatment or intracervical insemination | 2                       | 3.3                | —                                    | 4.5                | 2.8                 |
| IUI                                        | 5 <sup>a</sup>          | —                  | —                                    | —                  | —                   |
| Clomiphene                                 | —                       | —                  | —                                    | —                  | 6.6                 |
| Clomiphene/IUI                             | —                       | 9.5 <sup>a</sup>   | —                                    | —                  | —                   |
| Gonadotropins                              | 4 <sup>a</sup>          | —                  | 6.6                                  | —                  | 7.3 <sup>a</sup>    |
| Gonadotropins/IUI                          | 9 <sup>a</sup>          | —                  | 12.9 <sup>a</sup>                    | 15 <sup>a</sup>    | —                   |
| IVF                                        | —                       | —                  | —                                    | —                  | 22.2 <sup>a</sup>   |

Note: Data presented as percent.

<sup>a</sup>  $P < .05$  for treatment vs. no treatment.

Practice Committee. Endometriosis and infertility. *Fertil Steril* 2012.

# EVRE 1-2 Endometriozis+ IUI

| TEDAVİ               | GEBELİK ORANI |
|----------------------|---------------|
| EXPECTANT MANAGEMENT | %2.8          |
| TIMED INTERCOURSE    | %3.3          |
| GONADOTROPİN         | %7.3          |
| CC+IUI               | %9.5          |
| GONADOTROPİN +IUI    | %15           |

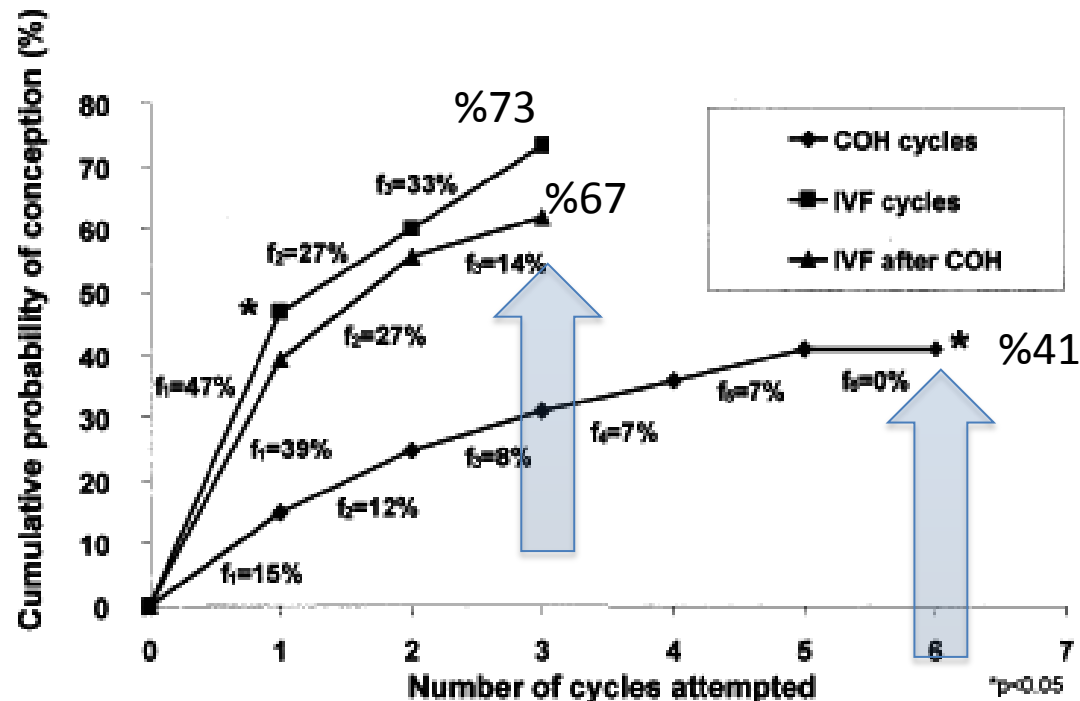
OH+IUI EVRE 1-2 ENDOMETRİOZİSTE UYGULANABİLİR.



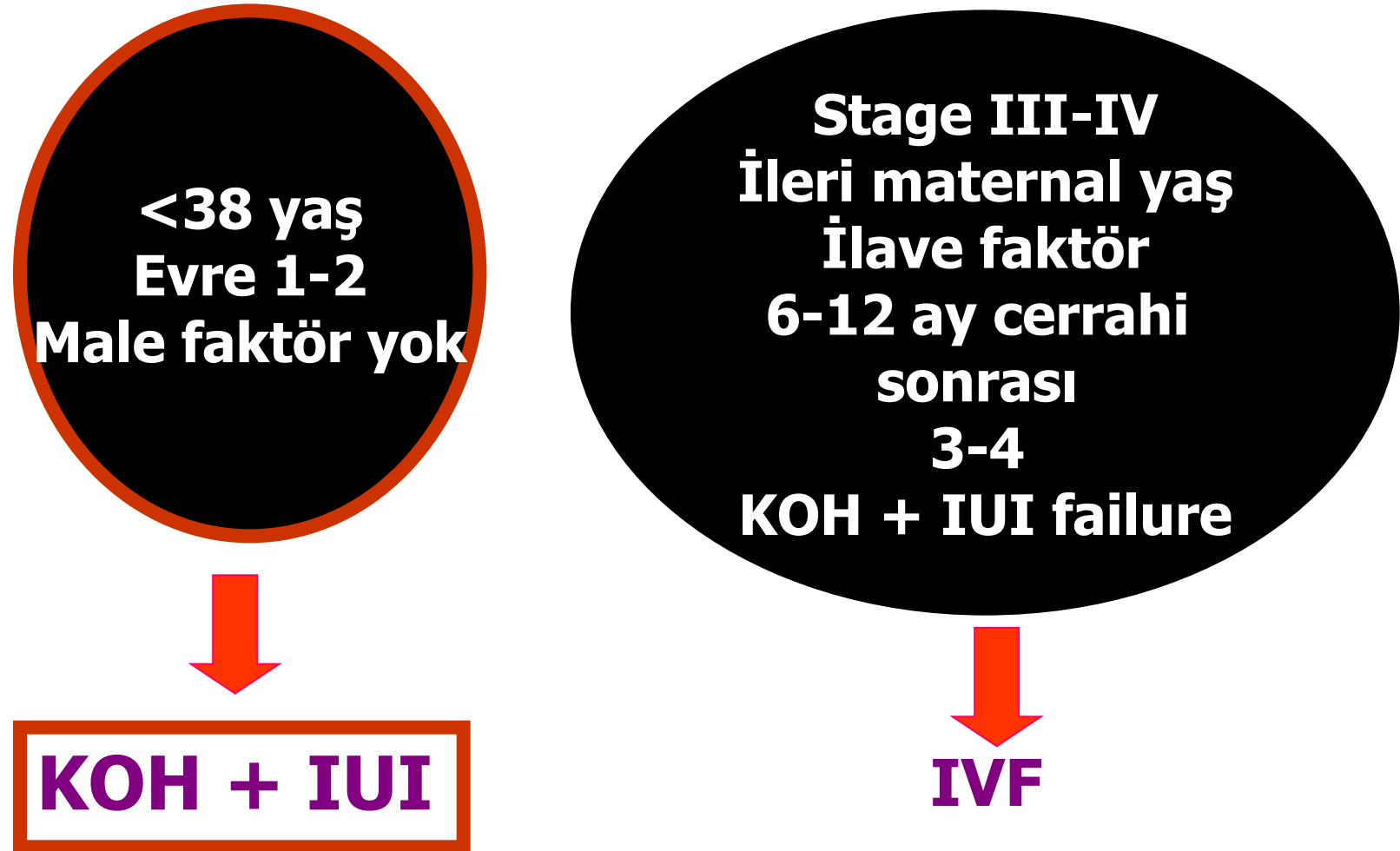
# Cycle-specific and cumulative fecundity in patients with endometriosis who are undergoing controlled ovarian hyperstimulation–intrauterine insemination or in vitro fertilization–embryo transfer

W. Paul Dmowski, M.D., Ph.D., Michelle Pry, M.S.N., Jianchi Ding, Ph.D., and Nasir Rana, M.D., M.P.H.

Cycle and cumulative fecundity in women with endometriosis undergoing COH-IUI, IVF-ET, or IVF-ET after failed COH-IUI.



# Ne zaman KOH + IUI







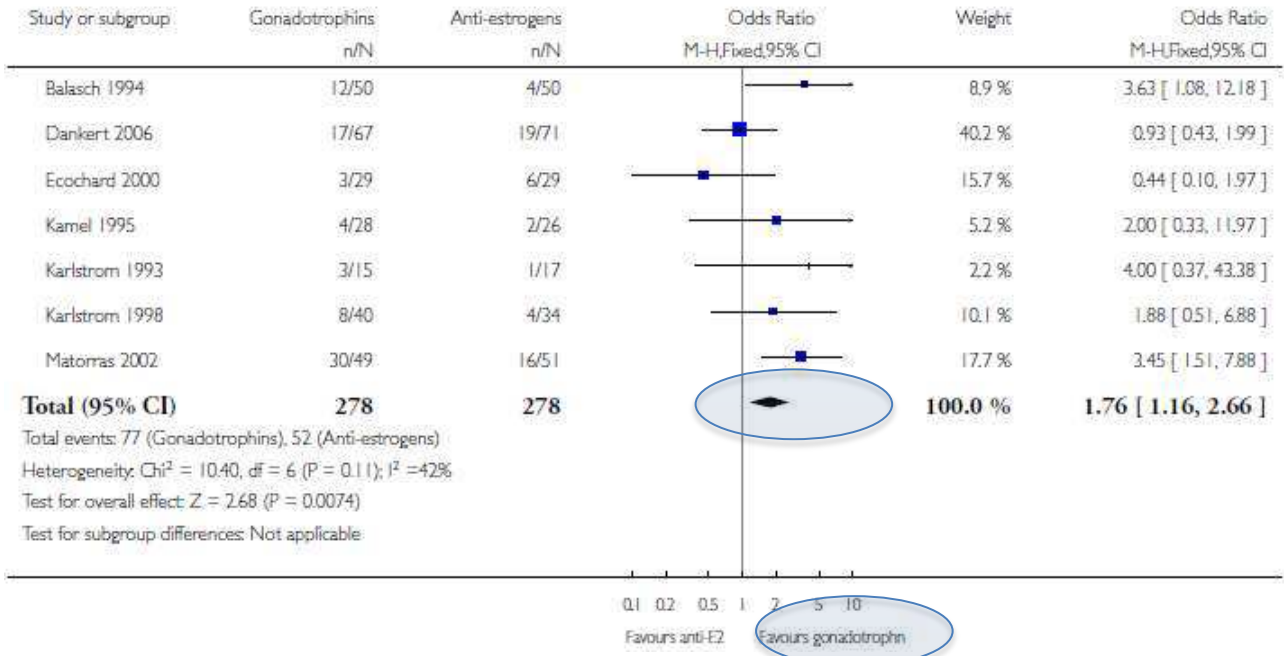
# IUI-Hangi OS?

## 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





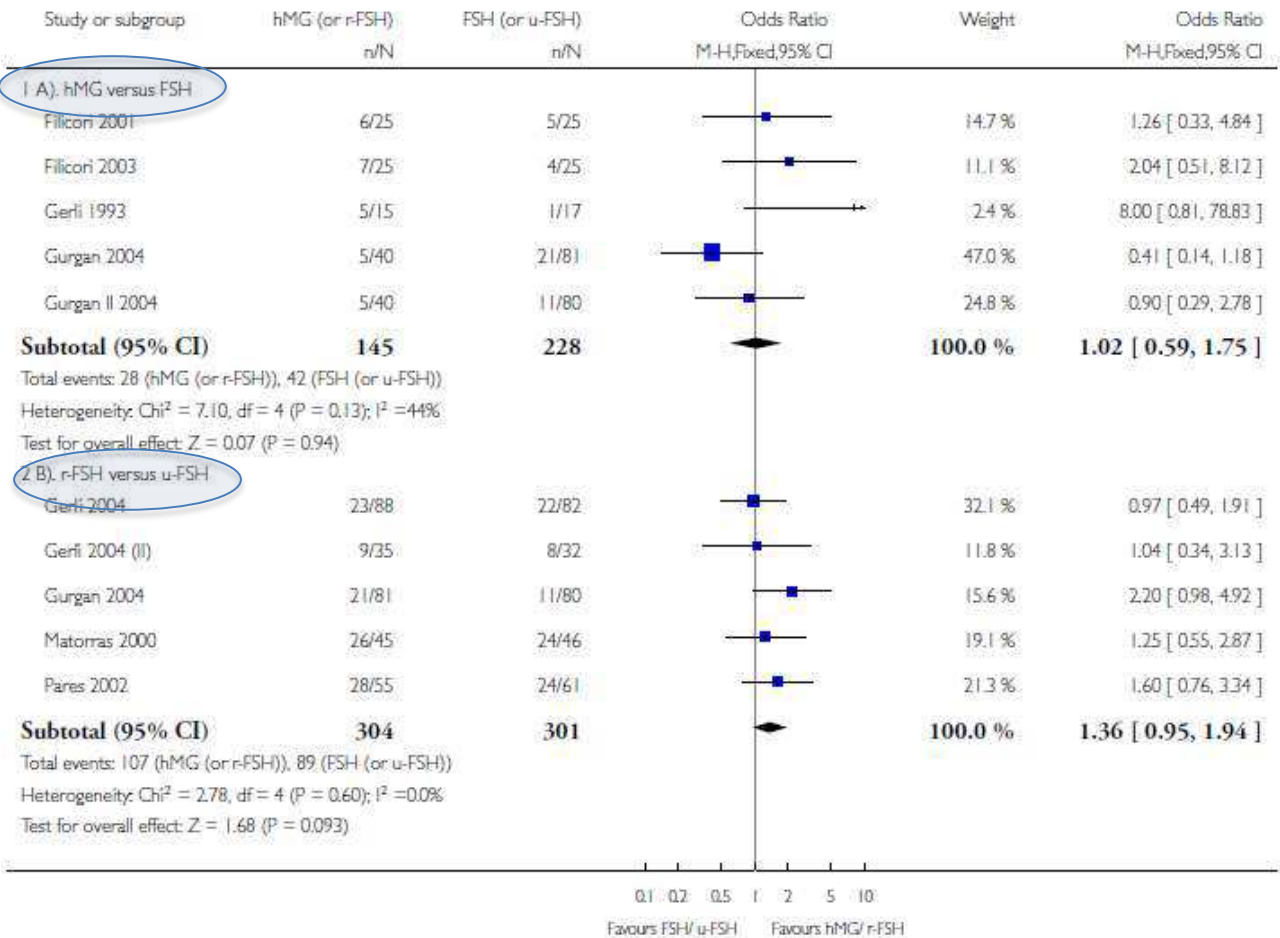
IUI-  
Hangi  
OS?

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



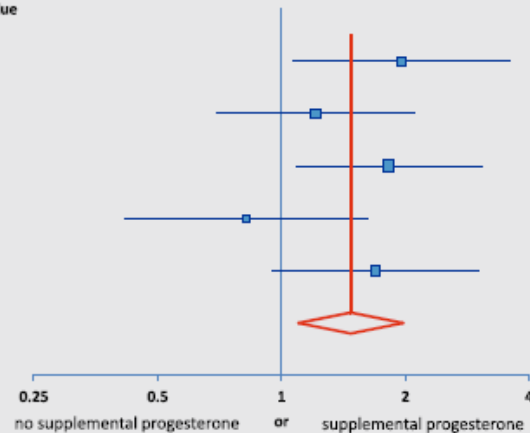
# Progesterone luteal support after ovulation induction and intrauterine insemination: a systematic review and meta-analysis

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

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

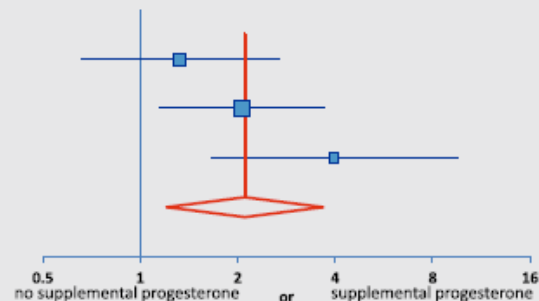
## A Clinical Pregnancy

| 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     |

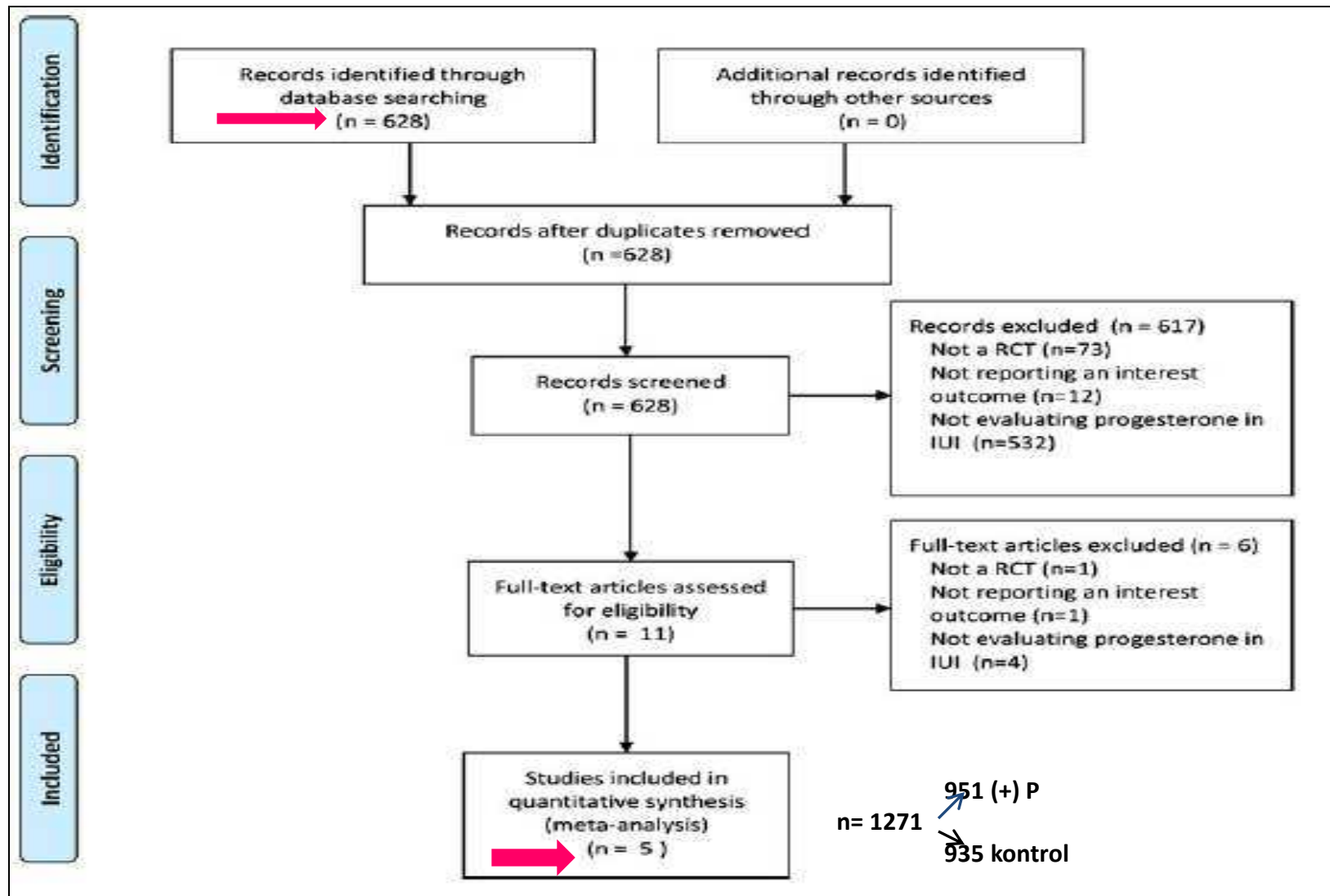


# Efficacy of luteal phase support with vaginal progesterone in intrauterine insemination: a systematic review and meta-analysis

Ester Miralpeix • Mireia González-Comadran •  
Ivan Solà • Dolors Manau • Ramon Carreras •  
Miguel A. Checa

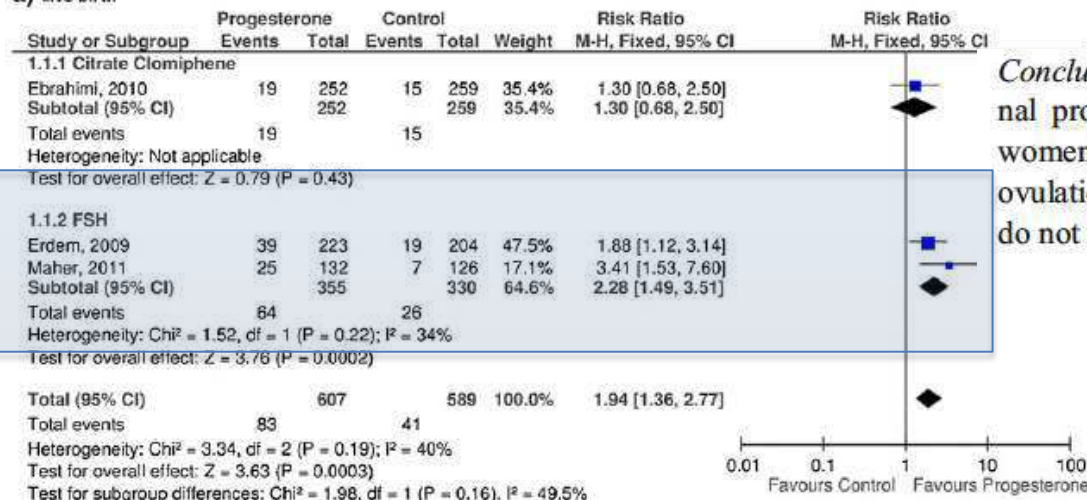
J Assist Reprod Genet (2014) 31:89–100  
DOI 10.1007/s10815-013-0127-6

ASSISTED REPRODUCTION TECHNOLOGIES



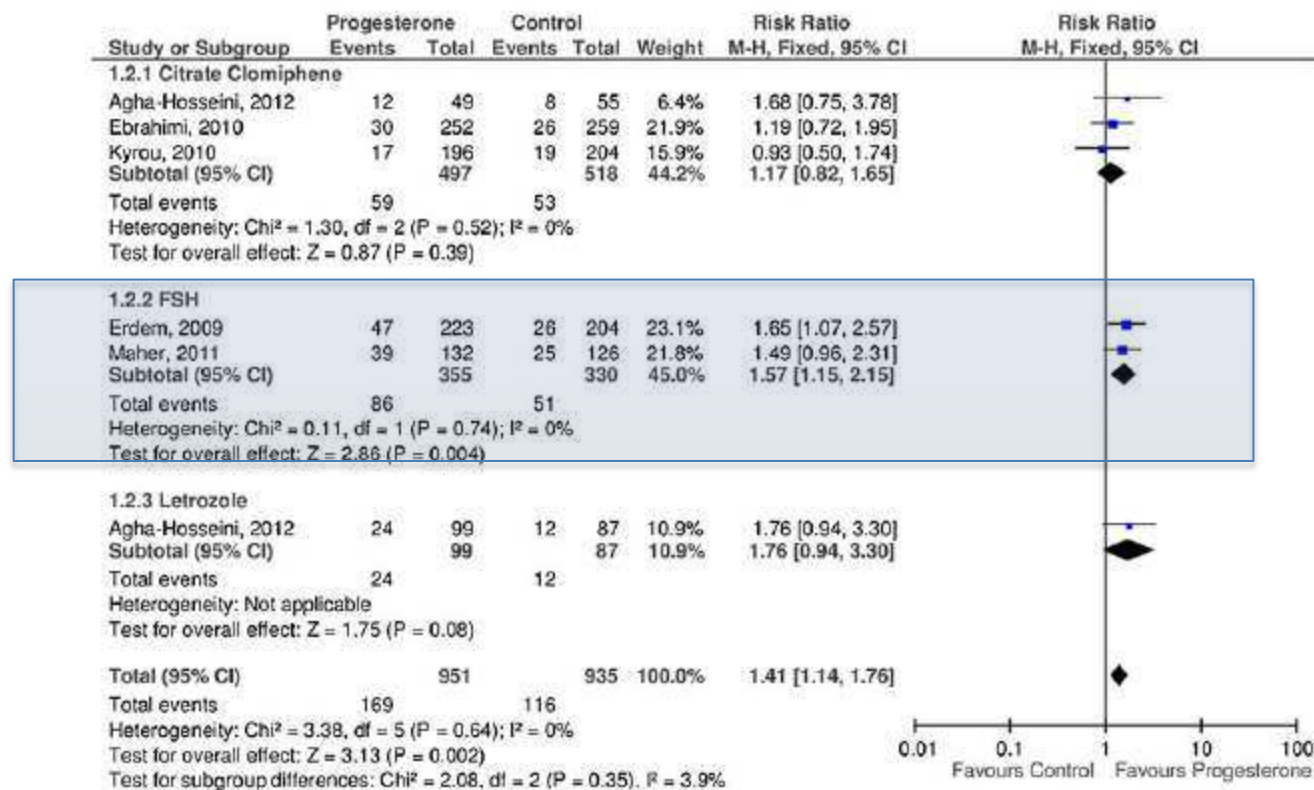


### a) Live birth



**Conclusions** The supplementation of luteal phase with vaginal progesterone significantly increases live birth among women undergoing IUI when receiving gonadotropins for ovulation induction. Women receiving CC to induce ovulation do not seem to benefit from this treatment.

### b) Clinical pregnancy



# Prognosis factors of pregnancy after intrauterine insemination with the husband's sperm: conclusions of an analysis of 2,019 cycles

Laka Dinelli, M.D.,<sup>a</sup> Blandine Courbière, M.D., Ph.D.,<sup>a,b</sup> Vincent Achard, M.D., Ph.D.,<sup>a,c</sup> Elisabeth Jouve, M.Sc.,<sup>d</sup> Carole Deveze, M.D.,<sup>a</sup> Audrey Gnisci, M.D.,<sup>a</sup> Jean-Marie Grillo, M.D., Ph.D.,<sup>a,c</sup> and Odile Paulmver-Lacroix, M.D., Ph.D.,<sup>a,c</sup>

[Fertil Steril® 2014

**Predictive factors of pregnancy according to the results of multivariate analysis.**

| Factor                         | OR    | 95% CI      | P value |
|--------------------------------|-------|-------------|---------|
| Female infertility             | 1.694 | 1.291–2.275 | .001    |
| Woman's age (y)                | 0.933 | 0.901–0.965 | .001    |
| Triggering ovulation           | 1.467 | 1.086–1.96  | .013    |
| Woman's secondary infertility  | 1.455 | 1.080–1.962 | .014    |
| Basal FSH levels $\leq 7$ UI/L | 1.434 | 1.056–1.947 | .021    |

Note:  $P < .05$  was considered statistically significant. CI = confidence interval; OR = odds ratio.

## **Factors influencing the outcome of intrauterine insemination (IUI): Age, clinical variables and significant thresholds**

B. E. Speyer<sup>1</sup>, B. Abramov<sup>2</sup>, W. Saab<sup>2</sup>, A. Doshi<sup>2</sup>, U. Sarna<sup>2</sup>, J. C. Harper<sup>1,2</sup> & P. Serhal<sup>2</sup>

<sup>1</sup>*UCL Centre for PG&D, IFWH, University College London and* <sup>2</sup>*Centre for Reproductive and Genetic Health, London, UK*

To conclude, the most significant factors for predicting live-birth outcome in this group of patients were female age, FSH and AMH. On the male side, the importance of sperm concentration and motility was shown by the highly significant relationship between TMC and live-birth.

# Indications of Intrauterine Insemination for Male and Non–Male Factor Infertility

**Table 2** Predictive factors for pregnancy after intrauterine insemination

|                                                                 | Good                      | Bad                          |
|-----------------------------------------------------------------|---------------------------|------------------------------|
| Cause of infertility <sup>23,28</sup>                           | Anovulatory               | Endometriosis or male factor |
| Age <sup>29–32,37,38</sup>                                      | < 25–35 y old             | > 35–40 y old                |
| <sup>a</sup> Total motile sperm count <sup>23,30,35,37,38</sup> | > 10–30 × 10 <sup>6</sup> | < 1.0–5.0 × 10 <sup>6</sup>  |
| Duration of infertility <sup>28,42–44</sup>                     | < 3–4 y                   |                              |

<sup>a</sup>Controversial.



***SPERM***

# Morfoloji ve IUI

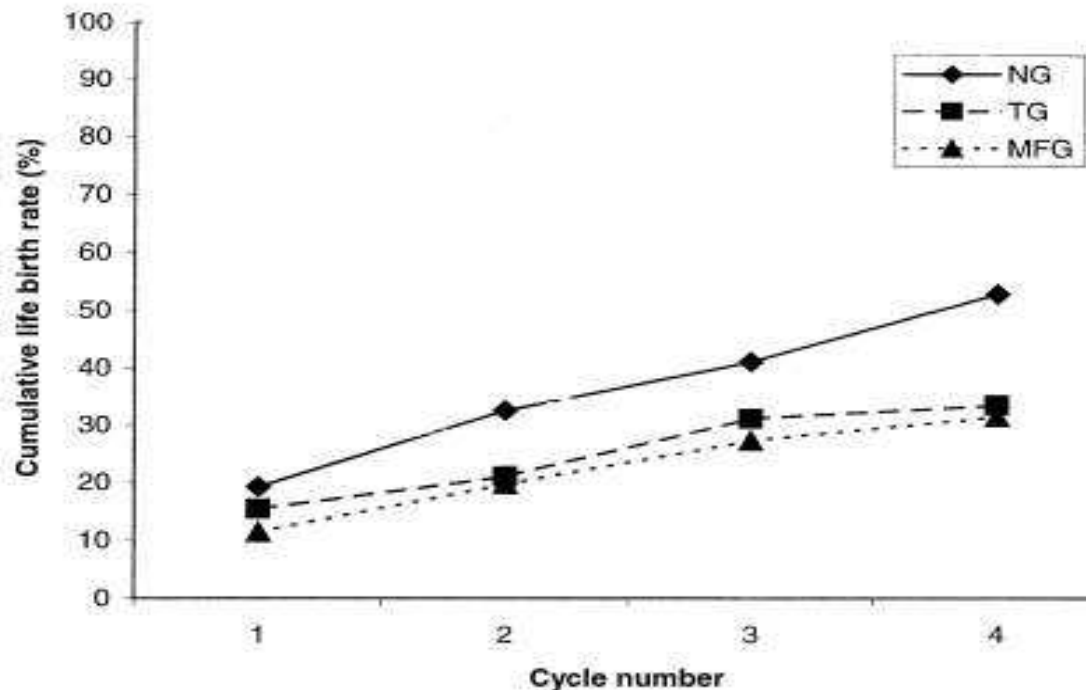
**Table 2.** Pregnancy rate after intrauterine insemination in the three groups

| Normal morphology forms (%)    | Poor<br>( $< 4$ ) | Good<br>(4–14) | Normal<br>( $> 14$ ) |
|--------------------------------|-------------------|----------------|----------------------|
| No. of couples                 | 19                | 83             | 6                    |
| No. of pregnancies             | 2                 | 30             | 3                    |
| Pregnancy rate (per couple, %) | 11.1              | 36.1           | 50.0                 |

$P=0.008$ ;  $\chi^2$  test.

# Isolated teratozoospermia and intrauterine insemination

Cumulative live birth rate during four cycles for the normozoospermic group (NG), teratozoospermic group (TG), and male factor infertility group (MFG).

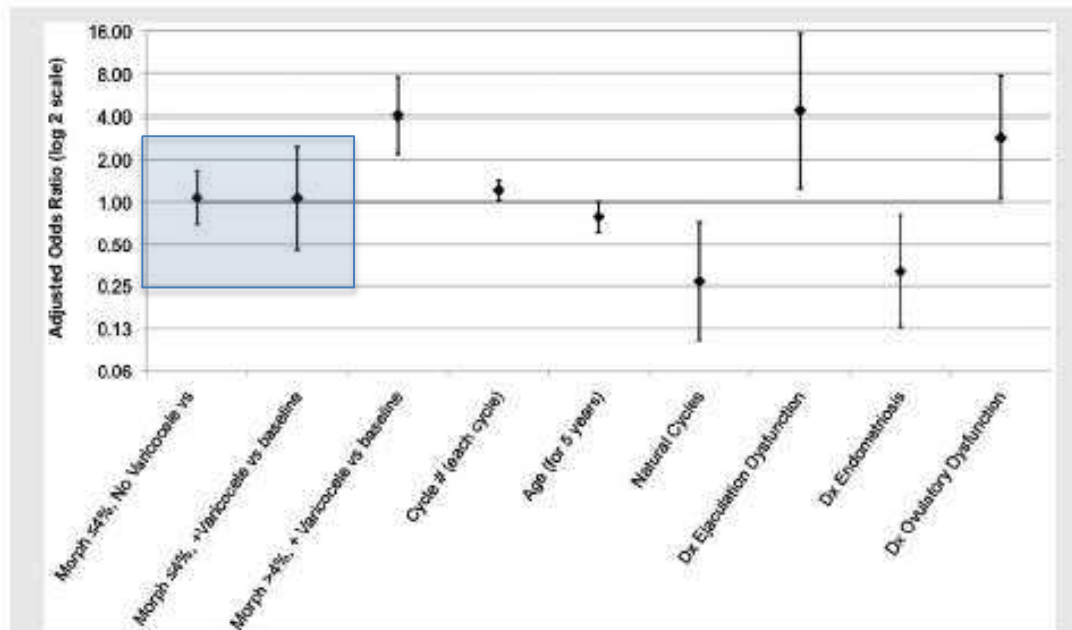


# İZOLE TERATOSPERMİ

- İzole teratospermi astenospermi veya oligospermi gibi ilk IUI siklusu sonucunda düşük başarı ile ortaya çıkmaktadır.
- Bu tip olgularda sınırlı sayıda IUI  $\leq 3$  uygulanmalı ve IVF/ICSI düşünülmelidir.
- Fertility and Sterility Vol. 83, No. 3, March 2005

# Impact of sperm morphology on the likelihood of pregnancy after intrauterine insemination

Nicolette E. Deveneau, M.D.,<sup>a</sup> Omar Sinno, M.D.,<sup>a</sup> Miriam Krause, M.D.,<sup>b</sup> Daniel Eastwood, M.S.,<sup>c</sup> Jay I. Sandlow, M.D.,<sup>d</sup> Paul Robb, M.D.,<sup>a</sup> Amy Granlund, B.A.,<sup>a</sup> and Estil Y. Strawn Jr., M.D.<sup>a</sup>



- Sperm morfoloji <%4 ile IUI gebelikleri arasında belirgin ilişki yok
- Morfoloji <%4 olanlara direkt IVF önermek doğru değil...

Adjusted odds ratios for pregnancy using multivariate logistic regression with generalized estimating equations. Dx = diagnosis.

Deveneau. Impact of sperm morphology on IUI. Fertil Steril 2014.

102 NO. 6 / DECEMBER 2014

# Total motil sperm- gebelik oranları

Clinical pregnancy rates and live birth rates of infertility treatments based on average total motile sperm counts in the ejaculate.

| Treatment                                                  | Average total motile sperm count |               |                 | $\chi^2$ P value |
|------------------------------------------------------------|----------------------------------|---------------|-----------------|------------------|
|                                                            | <10 million                      | 10–30 million | >30 million     |                  |
| No. of patients who got pregnant/total no. of patients (%) |                                  |               |                 |                  |
| 1st cycle of IUI                                           | 1/68 (1.5)                       | 16/152 (10.5) | 98/819 (12.0)   | 0.03             |
| 1st cycle of IVF                                           | 29/71 (40.9)                     | 14/40 (35.0)  | 139/313 (44.4)  | 0.49             |
| All cycles of IUI                                          | 5/214 (2.3)                      | 42/502 (8.4)  | 274/2,763 (9.9) |                  |
| All cycles of IVF                                          | 37/99 (37.4)                     | 18/59 (30.5)  | 167/393 (42.5)  |                  |
| No. of live births/total no. of patients (%)               |                                  |               |                 |                  |
| 1st cycle of IUI                                           | 1/68 (1.5)                       | 13/152 (8.6)  | 62/819 (7.6)    | 0.15             |
| 1st cycle of IVF                                           | 24/71 (33.8)                     | 11/40 (27.5)  | 120/313 (38.3)  | 0.35             |
| All cycles of IUI                                          | 3/214 (1.4)                      | 29/502 (5.8)  | 194/2,763 (7.0) |                  |
| All cycles of IVF                                          | 32/99 (32.3)                     | 15/59 (25.4)  | 147/393 (37.4)  |                  |

Van Voorhis. Motile sperm count and IUI effectiveness. *Fertil Steril* 2001.

TMSS >30 milyon olan grupta, 1. IUI siklusunda gebelikler anlamlı fazla

# The effect of post-wash total progressive motile sperm count and semen volume on pregnancy outcomes in intrauterine insemination cycles: a retrospective study

Elvan Koyun Ok, Ömer Erbil Doğan, Recep Emre Okyay, Bülent Gülekli

Division of Reproductive Medicine, Department of Obstetrics And Gynecology, Dokuz Eylül University Medical Faculty, İzmir, Turkey

**Table 3. Comparison of sperm parameters (post-wash TPMSC and semen volume) between groups**

|                                     | pregnant   | non-pregnant |         |
|-------------------------------------|------------|--------------|---------|
| Post-wash TPMSC (x10 <sup>6</sup> ) | n (%)      | n (%)        | p value |
| <1                                  | 3 (7)      | 8 (7.1)      | 0.08    |
| 1-4.9                               | 10 (23.30) | 41 (36.3)    | 0.00    |
| 5-9.9                               | 9 (20.90)  | 33 (29.2)    | 0.001   |
| 10 and > 10                         | 21 (48.80) | 31 (27.4)    | 0.16    |
| Post-wash semen volume (mL)         | n (%)      | n (%)        | p value |
| 0.3                                 | 20 (46.5)  | 61 (54)      | 0.00    |
| 0.4                                 | 6 (14)     | 11 (9.7)     | 0.22    |
| 0.5                                 | 17 (39.5)  | 41 (36.3)    | 0.002   |
| * Parentheses indicate percentages  |            |              |         |

## ORIGINAL ARTICLE

**Effect of total motile sperm count in intra-uterine insemination on ongoing pregnancy rate**M. Kleppe<sup>1,2</sup>, M. H. van Hooff<sup>3</sup> & J. P. Rhemrev<sup>2</sup>

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Andrologia 2014, xx, 1–6

Total motile sperm count and IUI in humans

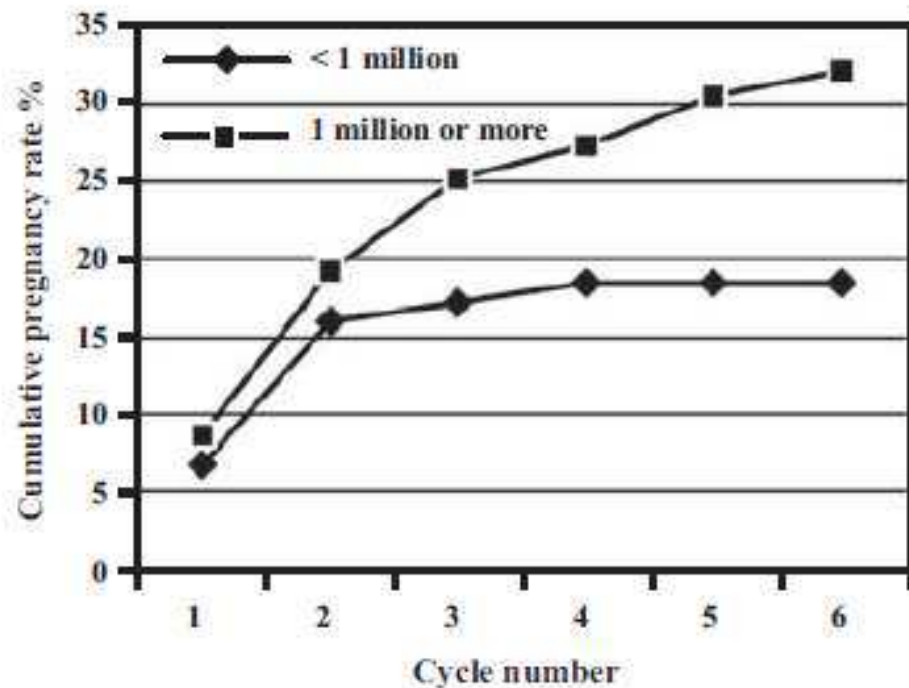


Fig. 2 Cumulative pregnancy rate.

- Total motil sperm sayısının 4 IUI siklusundan sonra kümülatif gebelik oranlarına belirgin etkisi yok
- Düşük total motil sperm sayısı olan çiftler de IUI dan yararlanabilir.
- 4 sikludan sonra <1 milyon TMS olan çiftlerde kümülatif gebelik oranı %17,3
- >1 milyon olan çiftlerde ise %25,5



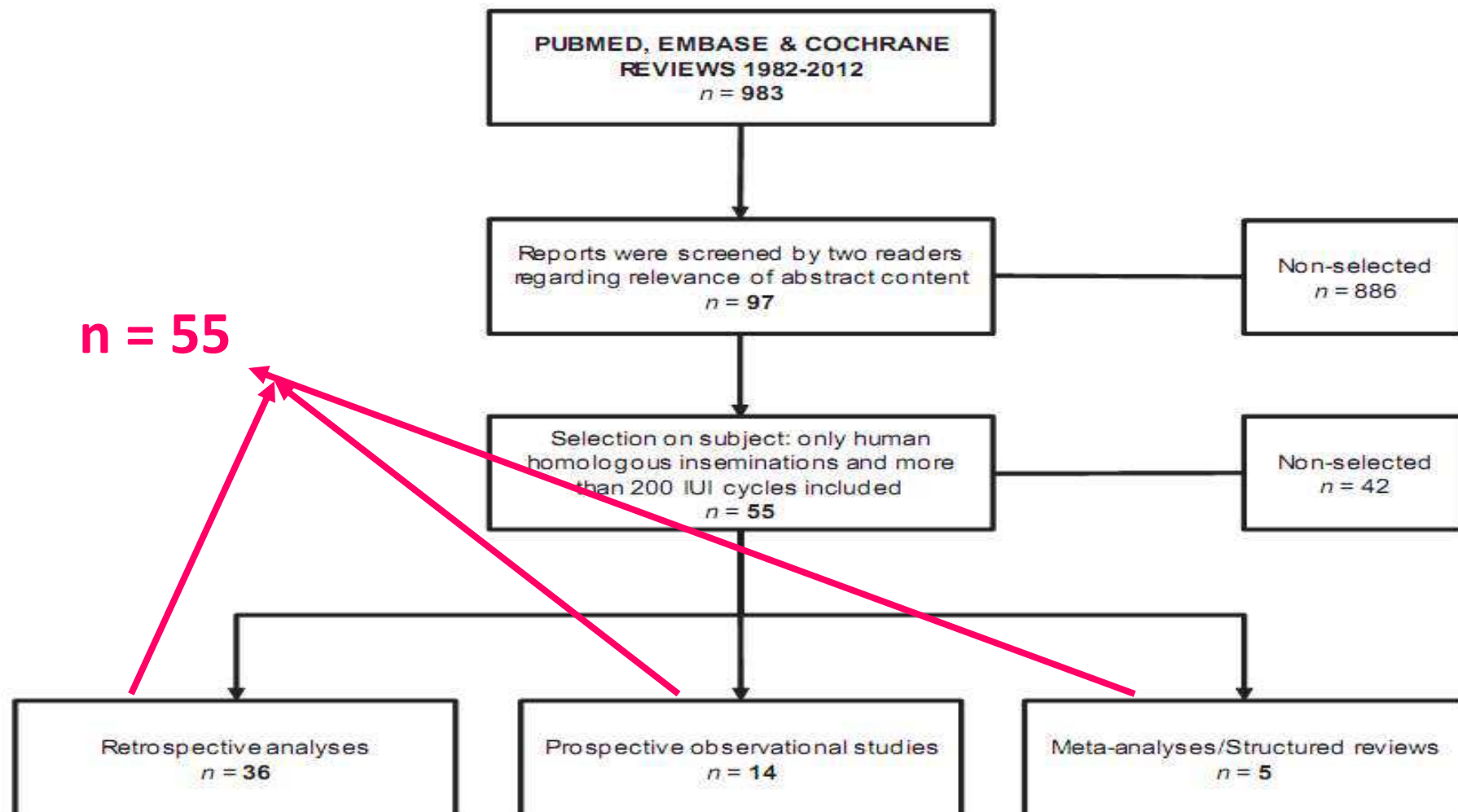


## MINI-REVIEW

# Semen quality and prediction of IUI success in male subfertility: a systematic review



Willem Ombelet <sup>a,b,\*</sup>, Nathalie Dhont <sup>a</sup>, Annelies Thijssen <sup>a,b</sup>, Eugene Bosmans <sup>a</sup>, Thinus Kruger <sup>c</sup>



## Semen parametreleri - IUI başarısı

- $IMC > 1 \times 10^6$  ise IUI da kabul edilebilir gebelik.
- $IMC < 1 \times 10^6$  ise morfoloji önem kazanır.
- 3x IUI ,  $IMC < 1 \times 10^6$ : kümülatif LBR %13.6
- 3x IUI ,  $IMC < 1 \times 10^6$ , morfoloji  $> \%4$  : kümülatif LBR %21.9
- 3x IUI ,  $IMC > 1 \times 10^6$ : kümülatif LBR %22.4

Immobilization after IUI  
Catheter washing before IUI

Duration of infertility  
Female age

IUI Sati  
• Fre  
• Spli  
• Diff  
• Wa

Semen  
• Swi  
• Gra  
• Wa  
• Oth

Time in  
and IU  
• 10~

Timin  
• Ba  
• LH  
• UI

In conclusion, the literature did not reveal level 1 evidence on the relationship between sperm quality and IUI success. Although more prospective observational cohort studies and well-organized retrospective analyses are urgently needed, this structured review indicates that IMC >1 million with IUI is probably the best cost-effective treatment before starting IVF, irrespective of sperm morphology. More answers to the question as to when to perform IUI in male factor infertility cases will never be obtained until more multicentre prospective trials according to standard protocols are organized. Despite the current ongoing debate concerning cost-effectiveness of IUI versus IVF in moderate male factor infertility, other factors might be important, such as the well-known differences between both strategies in risk profile and patient satisfaction.

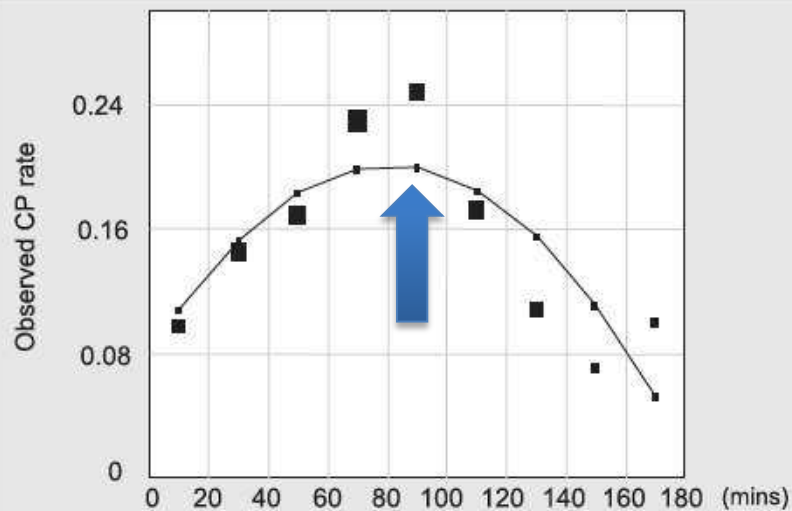
## The effect of IUI (intrauterine insemination) time on semen parameters

Elvan Koyun (OK)<sup>1</sup>, Recep Emre Okyay, Ömer Erbil Doğan<sup>1</sup>, Müge Kovalı<sup>1</sup>,  
Sultan Seda Doğan<sup>1</sup>, Bülent Gülekli<sup>1</sup>

**Table 2.** Marginal means (mean±SD) of post wash semen parameters in different periods.

| Semen parameters<br>(mean± min SD)           | Groups    |             |           |        |         |
|----------------------------------------------|-----------|-------------|-----------|--------|---------|
|                                              | 30 min    | 60 min      | 120 min   | F      | P value |
| Sperm count<br>(x10 <sup>6</sup> /ml)        | 30,2±25,5 | 30,8±29,0   | 21.5±19,1 | 13,065 | 0,000   |
| Total progressive motility (%)               | 96,8±8,3  | 95,2.5±10,4 | 87.5±21.9 | 20,128 | 0,000   |
| Total motile sperm count (x10 <sup>6</sup> ) | 8,8±7,5   | 9,2±10,9    | 5,4±4,8   | 11,454 | 0,000   |

# Clinical success of intrauterine insemination cycles is affected by the sperm preparation time



Dependence between the time interval from the end of sperm preparation to intrauterine insemination and observed clinical pregnancy (CP) rate. Points are observed CP rates associated with groups of cycles with intervals from 0 to 180 minutes by steps of 20 minutes and estimated with the use of polynomial quadratic regression.

Fauque. Timing from sperm preparation to IUI. *Fertil Steril* 2014.

## Multivariate predictive model.

|                                                  | RR   | 95% CI    | OR   | 95% CI    | P value |
|--------------------------------------------------|------|-----------|------|-----------|---------|
| Maternal age (y)                                 | 0.92 | 0.89–0.94 | 0.88 | 0.84–0.92 | <.001   |
| TMSC outside interval of $1-11 \times 10^6$ unit | 0.31 | 0.18–0.53 | 0.19 | 0.09–0.38 | <.001   |
| Unexplained infertility                          | 0.32 | 0.21–0.47 | 0.20 | 0.11–0.34 | <.001   |
| TSP in interval 40–80 min                        | 3.11 | 2.34–4.13 | 5.36 | 3.49–8.23 | <.001   |

Note: The referent population was defined as women 25 years old, within TMSC optimal

Fauque et al *Fertil Steril* 2014



## Sperm DNA and chromatin integrity in semen samples used for intrauterine insemination

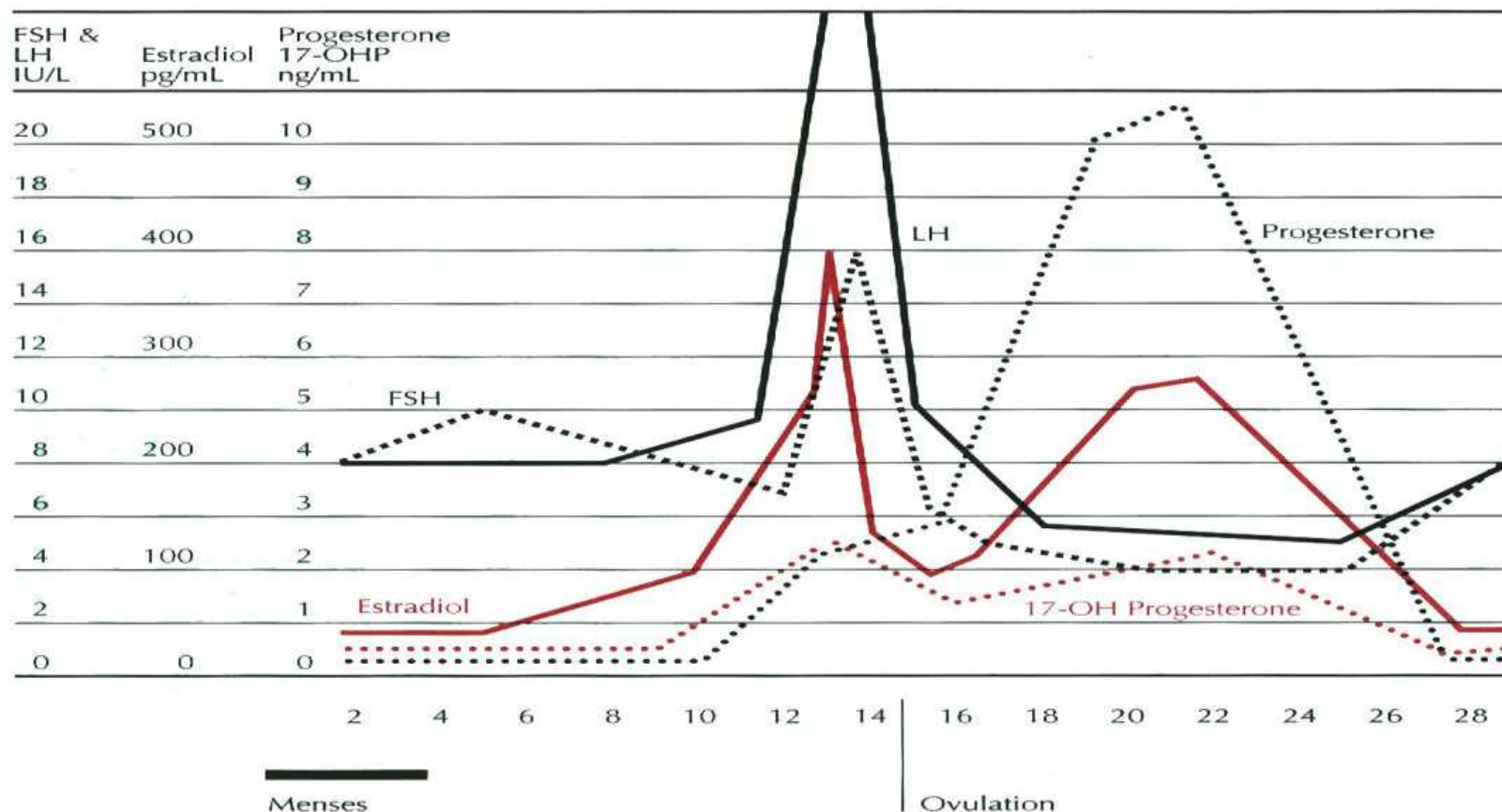
**Table 1** Mean ( $\pm$ SD) sperm %AB staining, %IAF fluorescence, %DFI, and %HDS in the IUI patients and controls

| Subgroup                   | IUI         | Ctl           | p-value <sup>a</sup> |
|----------------------------|-------------|---------------|----------------------|
| <i>n</i>                   | 102         | 15            |                      |
| Concentration (million/ml) | 76 $\pm$ 59 | 176 $\pm$ 228 | 0.0011               |
| Progressive motility (%)   | 55 $\pm$ 23 | 64 $\pm$ 11   | >0.05                |
| %AB staining               | 17 $\pm$ 10 | 12 $\pm$ 9    | >0.05                |
| %IAF fluorescence          | 17 $\pm$ 10 | 8 $\pm$ 6     | 0.0009               |
| %DFI                       | 10 $\pm$ 7  | 6 $\pm$ 3     | >0.05                |
| %HDS                       | 5 $\pm$ 3   | 6 $\pm$ 3     | >0.05                |

Sperm kromatin bütünlüğü ve DNA fragmentasyon indexi bozuk

**Conclusions** The data indicate that sperm chromatin integrity may be abnormal in men enrolled in IUI treatment cycles, despite the fact that most of these men are normozoospermic.

**hCG zamanlaması ?**



In stimulated cycles, ovulation usually occurs 36 hours after hCG administration.

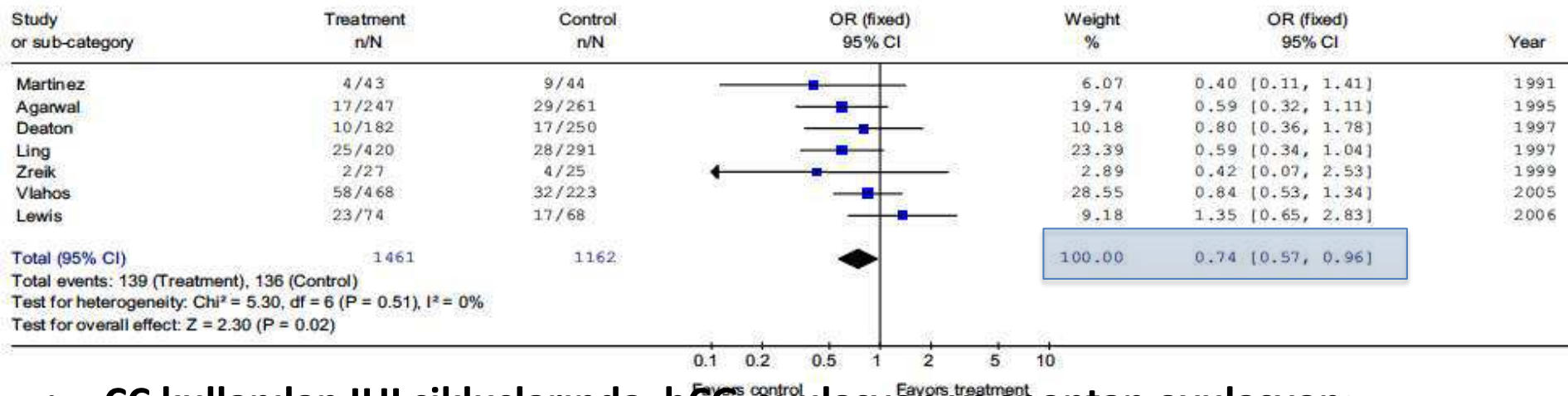
— Edwards & Steptoe. Proc R Soc Med 1974



# Human chorionic gonadotropin administration vs. luteinizing monitoring for intrauterine insemination timing, after administration of clomiphene citrate: a meta-analysis

*Ioannis P. Kosmas, M.D.,<sup>a</sup> Athina Tatsioni, M.D., Ph.D.,<sup>b</sup> Human Musavi Fatemi, M.D.,<sup>a</sup> Efstratios M. Kolibianakis, M.D., Ph.D.,<sup>a</sup> Herman Tournaye, M.D., Ph.D.,<sup>a</sup> and Paul Devroey, M.D., Ph.D.<sup>a</sup>*

Review: Clomiphene plus hCG versus Clomiphene plus LH  
Comparison: 01 clomiphene + hcg vs clomiphene +Lh overall  
Outcome: 01 clomiphene + hCG VS clomiphene + LH



- CC kullanılan IUI sikluslarında, hCG-ovulasyon vs spontan ovulasyon: Gebelikler anlamsız olmak koşulu ile spontan ovulasyon lehine (OR 0,74)
- Sadece ovulatuar disfonksiyon olanlarda hCG daha iyi gebelikler sunuyor..

# The effects of timing of intrauterine insemination in relation to ovulation and the number of inseminations on cycle pregnancy rate in common infertility etiologies

Mohamad E. Ghanem<sup>1,\*</sup>, Nagwa I. Bakre<sup>2</sup>, Mohamad A. Emam<sup>1</sup>, Laila A. Al Boghdady<sup>1</sup>, Adel S. Helal<sup>1</sup>, Abdel Gawad Elmetwally<sup>1</sup>, Mohamad Hassan<sup>3</sup>, Ibrahim A. Albahlol<sup>3</sup>, and Mostafa M. Elzayat<sup>1</sup>

**Table 1** Cycle outcome related to occurrence of ovulation at IUI 36 ± 2 h post-hCG.

| Parameter                                                                       | All cycles         | Male              | Non-male           |                    |                    |
|---------------------------------------------------------------------------------|--------------------|-------------------|--------------------|--------------------|--------------------|
|                                                                                 |                    |                   | Total              | Anovulation        | Unexplained        |
| Cycle outcome known                                                             | 1146               | 428               | 718                | 226                | 492                |
| Ovulation status known                                                          | 1114               | 422               | 692                | 212                | 480                |
| Ovulation present (n) <sup>a</sup>                                              | 816                | 322               | 494                | 146                | 348                |
| Ovulation absent (n) <sup>a</sup>                                               | 298                | 100               | 198                | 66                 | 132                |
| Ovulation rate (%)                                                              | 73.2               | 76.3              | 71.3               | 68.3               | 72.5               |
| All cycles with clinical pregnancy (n) <sup>a</sup>                             | 116                | 30                | 86                 | 34                 | 52                 |
| Overall CPR <sup>b</sup> (%)                                                    | 10.1               | 7.1               | 12.4               | 16.1               | 10.8               |
| Pregnancies in positive ovulation cycles (n) <sup>a</sup>                       | 96                 | 24                | 72                 | 28                 | 44                 |
| CPR <sup>b</sup> in cycles with positive ovulation (%)                          | 11.7               | 7.4               | 14.6               | 19.1               | 12.6               |
| Pregnancies in negative ovulation cycles (n) <sup>a</sup>                       | 20                 | 6                 | 14                 | 6                  | 8                  |
| CPR <sup>b</sup> with negative ovulation (%)                                    | 6.7                | 6                 | 7                  | 9.9                | 6                  |
| OR (95% CI) of pregnancy in positive ovulation versus negative ovulation cycles | 1.85 (1.12–3.06)   | 1.26 (0.52–2.95)  | 2.2 (1.23–4.08)    | 2.1 (0.91–4.85)    | 2.08 (1.01–4.31)   |
| P                                                                               | 0.015 <sup>c</sup> | 0.82 <sup>c</sup> | 0.007 <sup>c</sup> | 0.071 <sup>c</sup> | 0.047 <sup>c</sup> |

<sup>a</sup>Number.

<sup>b</sup>Cycle pregnancy rate.

<sup>c</sup>χ<sup>2</sup> test.

- Farklı endikasyonlarda IUI sikluları, hepsi 10.000 hCG ile tetiklenmiş, IUI günü usg ile ovulasyon delilleri araştırılmış

# The effects of timing of intrauterine insemination in relation to ovulation and the number of inseminations on cycle pregnancy rate in common infertility etiologies

Mohamad E. Ghanem<sup>1,\*</sup>, Nagwa I. Bakre<sup>2</sup>, Mohamad A. Emam<sup>1</sup>, Laila A. Al Boghdady<sup>1</sup>, Adel S. Helal<sup>1</sup>, Abdel Gawad Elmetwally<sup>1</sup>, Mohamad Hassan<sup>3</sup>, Ibrahim A. Albahlol<sup>3</sup>, and Mostafa M. Elzayat<sup>1</sup>

**Table II** Unruptured follicle cycles at  $36 \pm 2$  h randomized to single versus double IUI.

| Parameter                                            | All cycles        | Male               | Non-male           |                    |                    |
|------------------------------------------------------|-------------------|--------------------|--------------------|--------------------|--------------------|
|                                                      |                   |                    | Total              | Anovulation        | Unexplained        |
| <b>Total unruptured</b>                              | <b>298</b>        |                    | <b>Total</b>       | <b>Anovulation</b> | <b>Unexplained</b> |
| Single IUI (n) <sup>a</sup>                          | 192               | 70                 | 122                | 50                 | 72                 |
| Single IUI positive (n) <sup>a</sup>                 | 10                | 2                  | 8                  | 4                  | 4                  |
| Single IUI CPR <sup>b</sup> (%)                      | 5.05              | 2.8                | 6.6                | 8                  | 5.5                |
| Double IUI (n) <sup>a</sup>                          | 106               | 30                 | 76                 | 16                 | 60                 |
| Double IUI positive (n)                              | 10                | 4                  | 6                  | 2                  | 4                  |
| Double IUI CPR <sup>b</sup> (%)                      | 9.4               | 13.3               | 7.8                | 12.5               | 6.6                |
| OR (95% CI) of pregnancy in double versus single IUI | 1.90 (0.76–4.70)  | 4.66 (0.90–24.13)  | 1.20 (0.43–3.33)   | 1.56 (0.31–7.75)   | 1.23 (0.29–5.08)   |
| P                                                    | 0.22 <sup>c</sup> | 0.064 <sup>c</sup> | 0.779 <sup>c</sup> | 0.626 <sup>c</sup> | 1 <sup>c</sup>     |

<sup>a</sup>Number.

<sup>b</sup>Cycle pregnancy rate.

<sup>c</sup> $\chi^2$  test.



# A randomized study of simultaneous hCG administration with intrauterine insemination in stimulated cycles

Yunus Aydin<sup>\*</sup>, Hikmet Hassa, Tufan Oge, V. Yavuz Tokgoz

**Table 2**

Comparison of cycle characteristics and results in patients with different timing in hCG injection.

|                                         | IUI 34–36 h after hCG, n = 106<br>Mean ± SD<br>Median (25–75th) | IUI with hCG n = 98<br>Mean ± SD<br>Median (25–75th) | p and $\chi^2$ values     |
|-----------------------------------------|-----------------------------------------------------------------|------------------------------------------------------|---------------------------|
| Duration of stimulation, day            | 12.05 ± 2.67<br>11 (10–14)                                      | 12.75 ± 3.31<br>12 (11–14)                           | 0.169                     |
| Total rec-FSH dosage, IU                | 1008.84 ± 469.25<br>975 (675–1181.25)                           | 1035.67 ± 514.98<br>982 (775–1200.15)                | 0.648                     |
| Number of follicles <10 mm on hCG day   | 5.74 ± 4.70<br>5 (2–9)                                          | 7.53 ± 5.04<br>6 (3.50–11)                           | 0.012                     |
| Number of follicles 11–13 mm on hCG day | 1.29 ± 1.44<br>1 (0–2)                                          | 1.16 ± 1.31<br>1 (0–2)                               | 0.581                     |
| Number of follicles 14–16 mm on hCG day | 0.85 ± 0.95<br>1 (0–1)                                          | 0.95 ± 1.03<br>1 (0–2)                               | 0.509                     |
| Number of follicles >17 mm on hCG day   | 1.19 ± 0.55<br>1 (1–1)                                          | 1.13 ± 0.61<br>1 (1–1.25)                            | 0.580                     |
| Endometrial thickness on hCG day, mm    | 9.36 ± 2.57<br>9.10 (7.50–11.25)                                | 8.86 ± 2.54<br>8.70 (7.50–10.02)                     | 0.204                     |
| Biochemical pregnancy, n (%)            | 12 (11.3)                                                       | 13 (13.2)                                            | 0.641<br>$\chi^2 = 0.217$ |
| Clinical pregnancy, n (%)               | 10 (9.4)                                                        | 12 (12.2)                                            | 0.523<br>$\chi^2 = 0.408$ |

SD: standard deviation;  $\chi^2$ : Chi square. Variables were expressed by mean and standard deviation, median and 25–75th percentiles.  $\chi^2$  values were presented for categorical variables. p value less than 0.05 ( $p < 0.05$ ) was statistically significant.

# A comparison of pregnancy rate before and after the administration of HCG in intrauterine insemination

Razieh Dehghani-Firouzabai • Abbas Aflatoonian •  
Robab Davar • Maryam Farid-Mojtahedi

Arch Gynecol Obstet (2014) 289:429–432

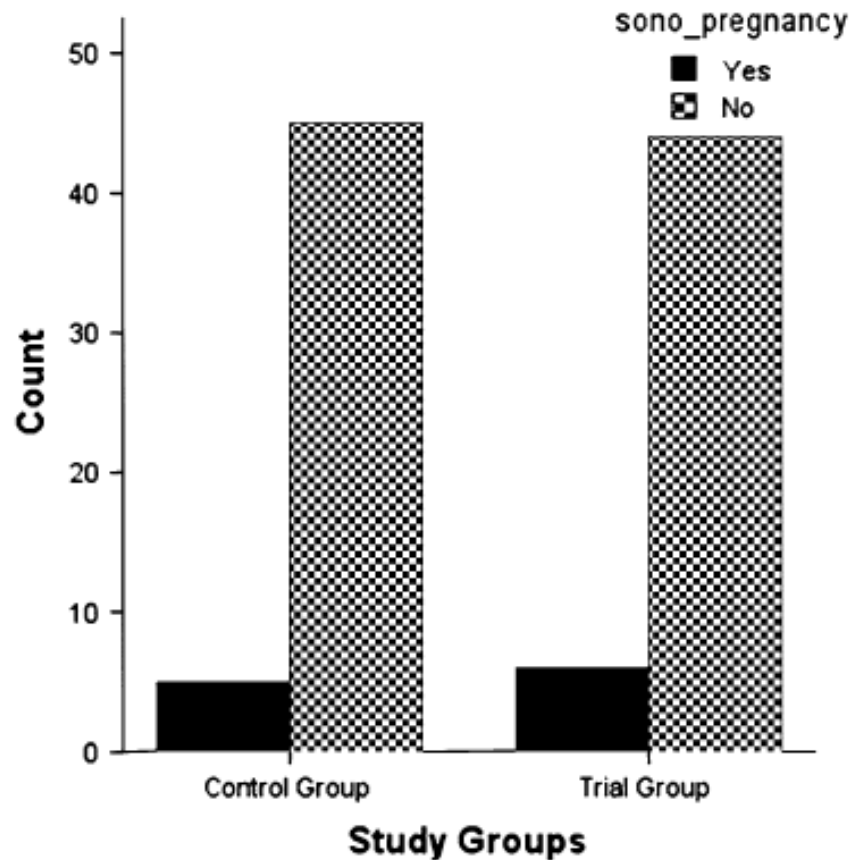


Fig. 1 Pregnancy rates in the two study groups

- >18 mm foll.  
Olduğunda
- Çalışma grubu:  
IUI'dan 3-5 dak  
sonra → HCG
- Kontrol grubu: HCG  
→ 24-36 h → IUI
- Gebelik oranları  
benzer bulunmuştur.

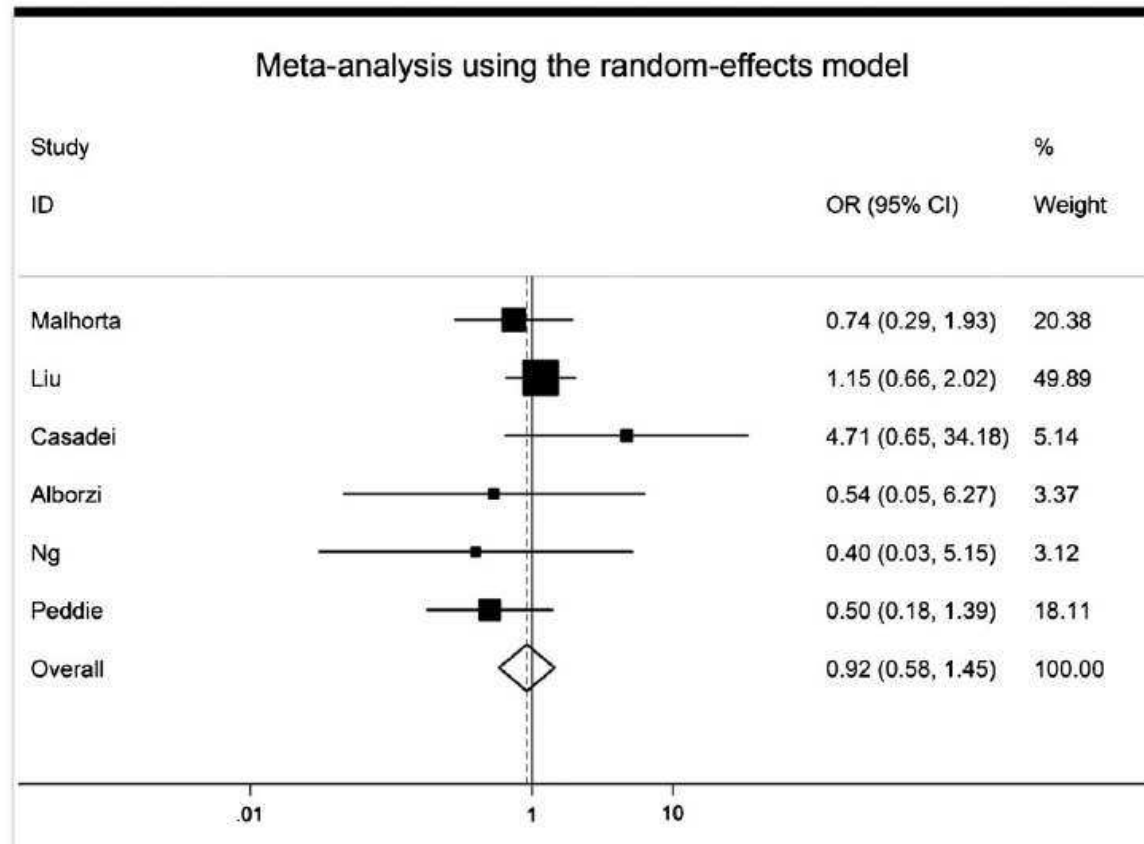


**IUI**

**Tek  
veya  
Çift??**

# Double versus single intrauterine insemination for unexplained infertility: a meta-analysis of randomized trials

Nikolaos P. Polyzos, M.D.,<sup>a</sup> Spyridon Tzioras, M.D., Ph.D.,<sup>a</sup> Davide Mauri, M.D., Ph.D.,<sup>a</sup> and Athina Tatsioni, M.D., Ph.D.<sup>b</sup>



ORIGINAL ARTICLE

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# Double versus single homologous intrauterine insemination for male factor infertility: a systematic review and meta-analysis

Asian Journal of Andrology (2013) 15, 533–538



# Double versus single homologous intrauterine insemination for male factor infertility: a systematic review and meta-analysis

Apostolos Zavos<sup>1</sup>, Alexandros Daponte<sup>1</sup>, Antonios Garas<sup>1</sup>, Christina Verykouki<sup>1</sup>, Evangelos Papanikolaou<sup>2</sup>, Georgios Anifandis<sup>1</sup> and Nikolaos P Polyzos<sup>3</sup>

Asian Journal of Andrology (2013) 15, 533–538

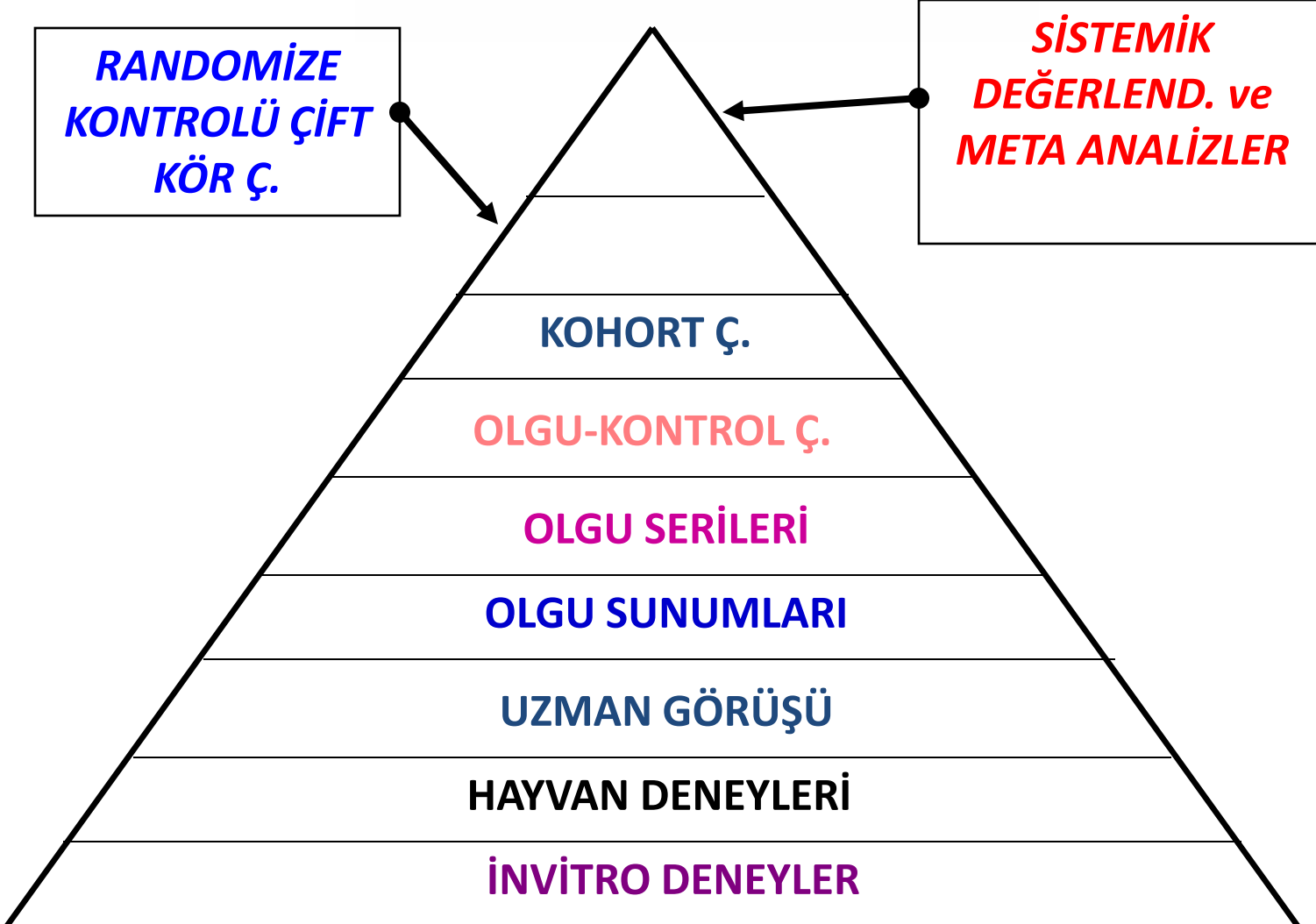
| Study or Subgroup                                                                                        | Single IUI |            | Double IUI |            | Weight        | Odds Ratio<br>M-H, Random, 95% CI | Odds Ratio<br>M-H, Random, 95% CI |
|----------------------------------------------------------------------------------------------------------|------------|------------|------------|------------|---------------|-----------------------------------|-----------------------------------|
|                                                                                                          | Events     | Total      | Events     | Total      |               |                                   |                                   |
| Ragni (1999) <sup>9</sup>                                                                                | 10         | 63         | 3          | 65         | 16.0%         | 3.90 [1.02, 14.91]                |                                   |
| Albrorzi (2003) <sup>12</sup>                                                                            | 1          | 25         | 2          | 27         | 5.9%          | 0.52 [0.04, 6.13]                 |                                   |
| Liu (2006) <sup>8</sup>                                                                                  | 95         | 381        | 44         | 386        | 48.2%         | 2.58 [1.75, 3.81]                 |                                   |
| Casadei (2006) <sup>13</sup>                                                                             | 3          | 11         | 4          | 35         | 11.3%         | 2.91 [0.54, 15.70]                |                                   |
| Bagis (2010) <sup>14</sup>                                                                               | 5          | 65         | 7          | 67         | 18.7%         | 0.71 [0.21, 2.38]                 |                                   |
| <b>Total (95% CI)</b>                                                                                    |            | <b>545</b> |            | <b>580</b> | <b>100.0%</b> | <b>2.00 [1.07, 3.75]</b>          |                                   |
| Total events                                                                                             | 114        |            | 60         |            |               |                                   |                                   |
| Heterogeneity: Tau <sup>2</sup> = 0.17; Chi <sup>2</sup> = 6.03, df = 4 (P = 0.20); I <sup>2</sup> = 34% |            |            |            |            |               |                                   |                                   |
| Test for overall effect: Z = 2.16 (P = 0.03)                                                             |            |            |            |            |               |                                   |                                   |

(OR: 2.00; 95% CI: 1.07–3.75;  $P < 0.03$ )

In conclusion, the current systematic review highlights the need for future trials and does not indicate a need to change clinical practice.

There seems to be a trend towards better outcomes with an increase in the frequency of IUIs per treatment cycle when the cause of infertility is an isolated male factor. However, this must first be validated by large and well-designed randomized trials.

# KANIT PİRAMİDİ



# Intra-uterine insemination for unexplained subfertility (Review)



THE COCHRANE  
COLLABORATION®

2012, Issue 9

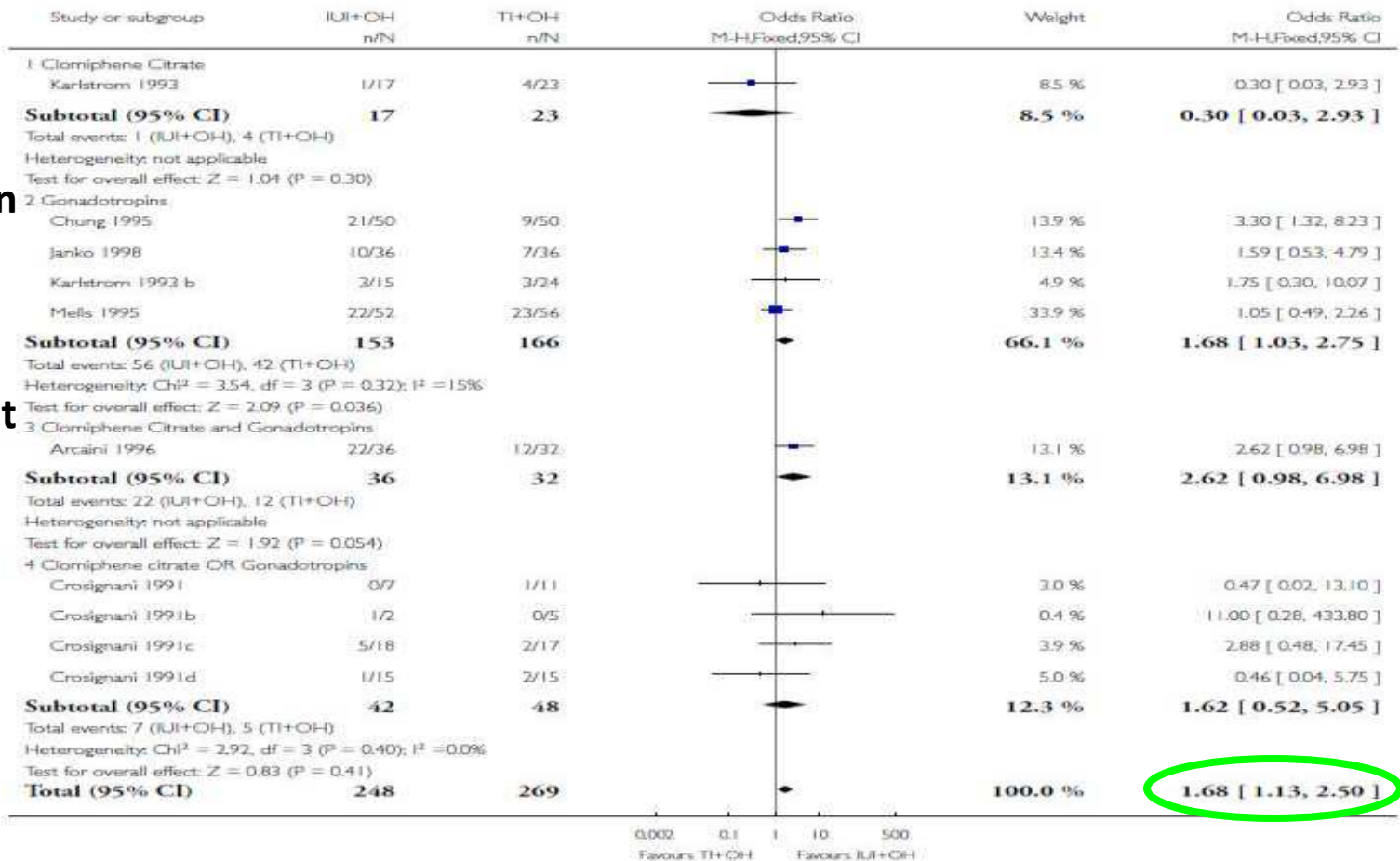
Veltman-Verhulst SM, Cohlen BJ, Hughes E, Heineman MJ

**Analysis 2.2. Comparison 2 IUI versus TI both in stimulated cycle, Outcome 2 Pregnancy rate per couple (all cycles).**

Review: Intra-uterine insemination for unexplained subfertility

Comparison: 2 IUI versus TI both in stimulated cycle

Outcome: 2 Pregnancy rate per couple (all cycles)



GENEL  
SONUÇLAR  
Açıklanamayan  
infertilite-IUI:  
Stimule  
sikluslarda IUI  
vs Zamanlı Koit



THE COCHRANE  
COLLABORATION

2012, Issue 9

### Analysis 3.2. Comparison 3 IUI in natural cycle versus IUI in stimulated cycle, Outcome 2 Pregnancy rate per couple (all cycles).

Review: Intra-uterine insemination for unexplained subfertility

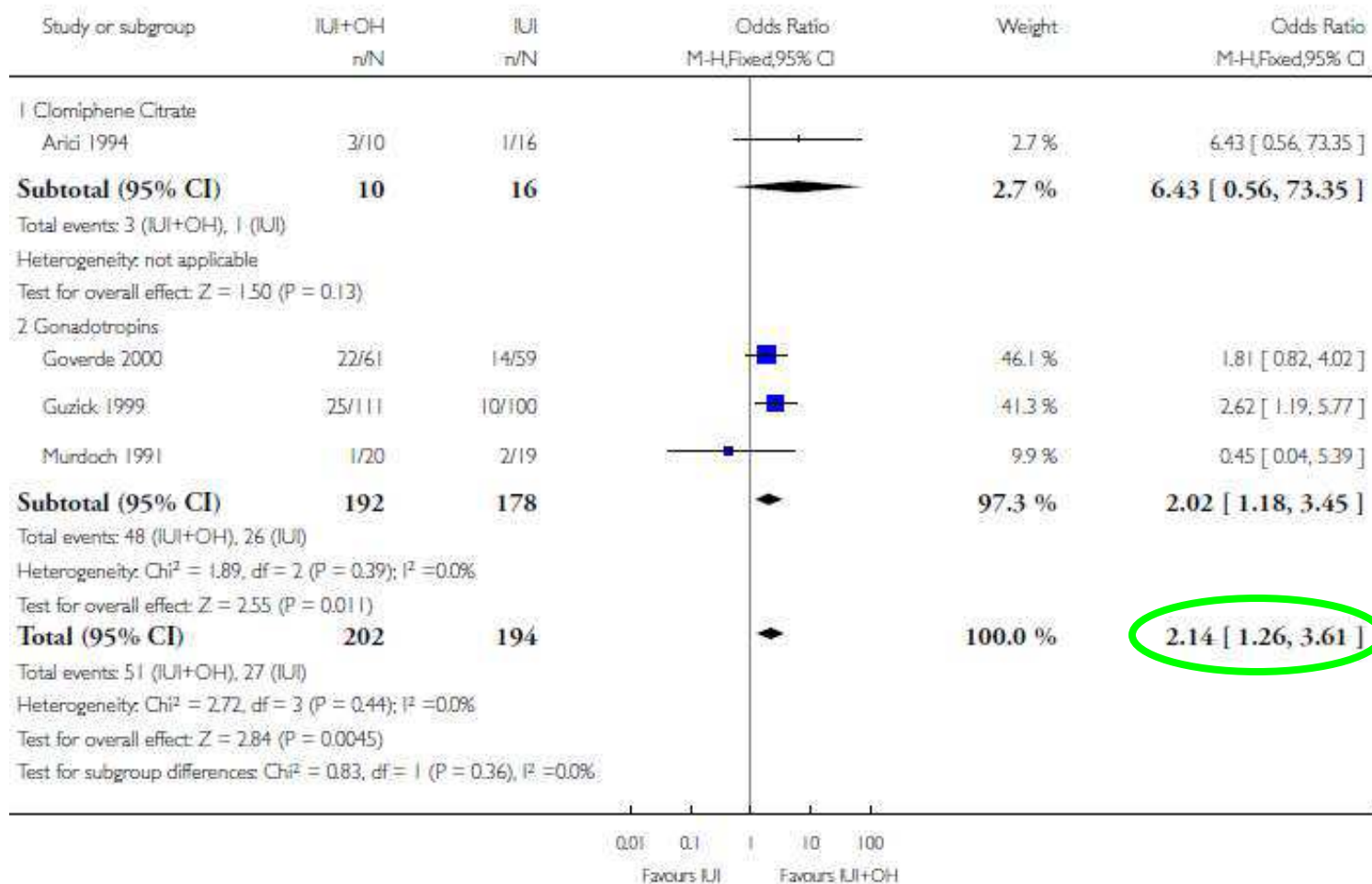
Comparison: 3 IUI in natural cycle versus IUI in stimulated cycle

Outcome: 2 Pregnancy rate per couple (all cycles)

## GENEL SONUÇLAR-devam

## Açıklanamayan infertilite-IUI:

## Stimule sikluslarda IUI vs Naturel siklus IUI





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2012, Issue 9

### Analysis 3.1. Comparison 3 IUI in natural cycle versus IUI in stimulated cycle, Outcome

Live birth rate

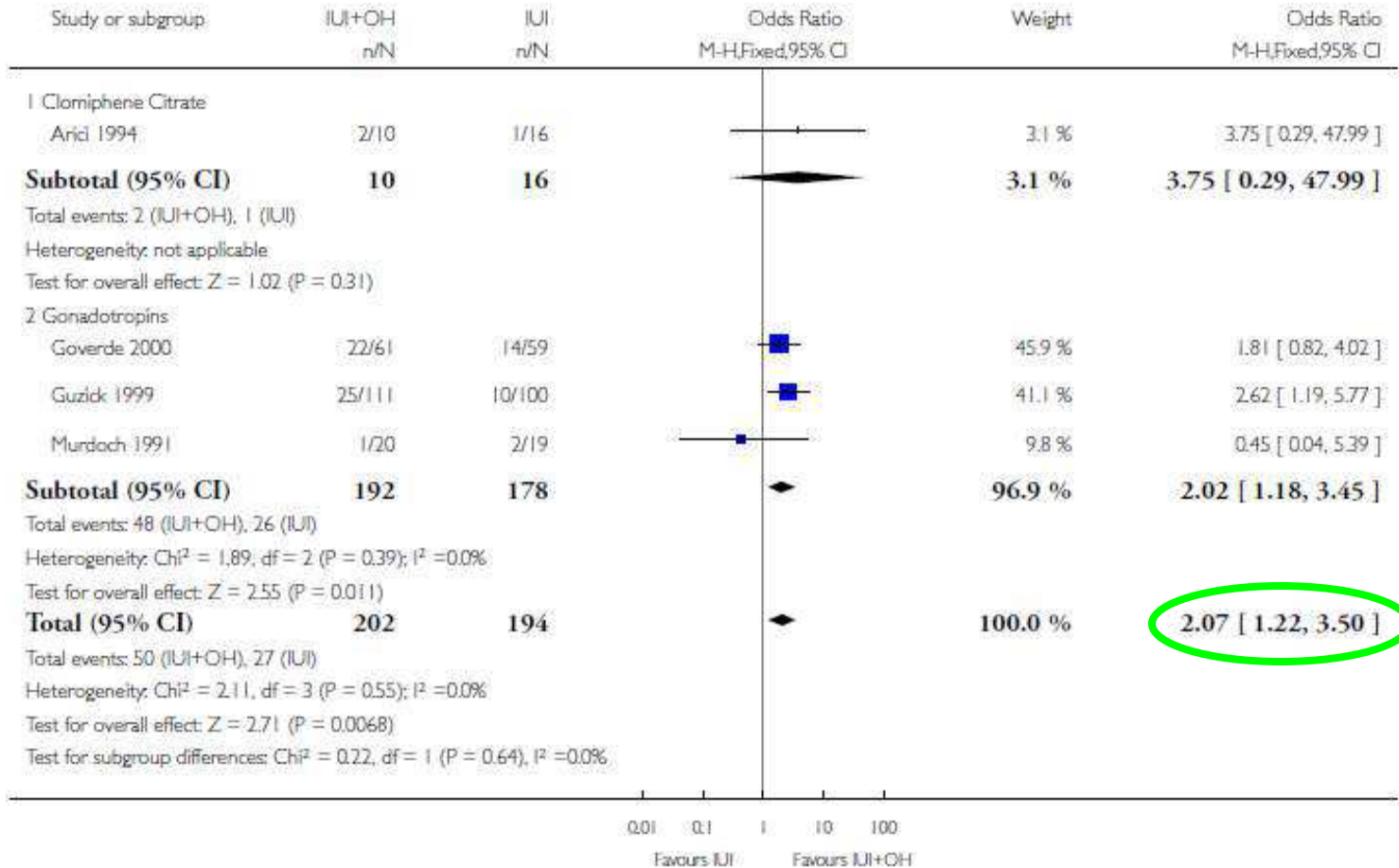
Review: Intra-uterine insemination for unexplained subfertility

Comparison: 3 IUI in natural cycle versus IUI in stimulated cycle

Outcome: 1 Live birth rate per couple (all cycles)

## GENEL SONUÇLAR-devam

## Açıklanamayan infertilite-IUI-canlı doğum sonuçları Stimule sikluslarda IUI vs Naturel IUI





# Intra-uterine insemination for male subfertility (Review)



THE COCHRANE  
COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in 2008, Issue 1

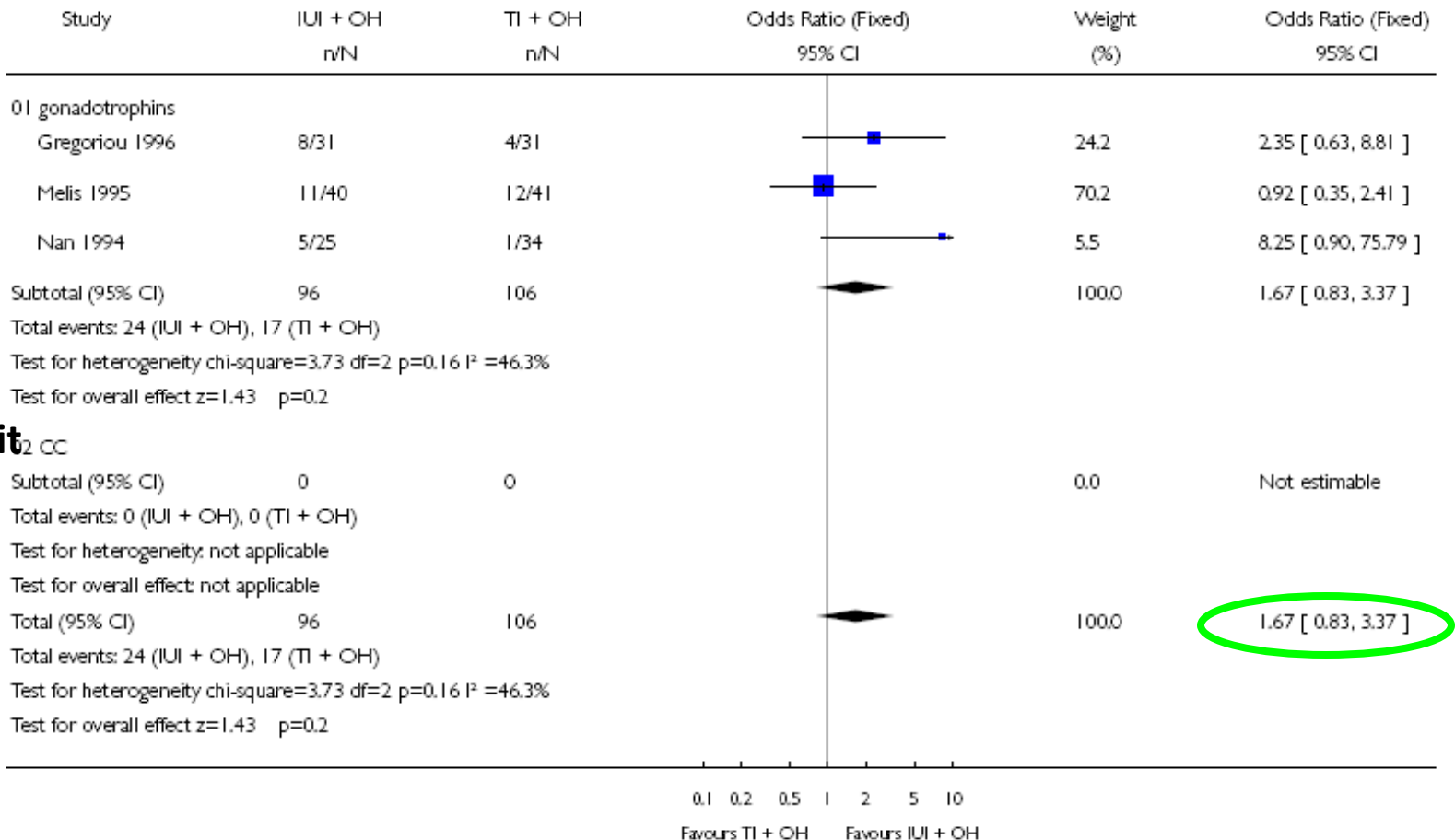
**Analysis 02.03. Comparison 02 IUI versus TI both in stimulated cycles, Outcome 03 Pregnancy rate per couple (all cycles)**

Review: Intra-uterine insemination for male subfertility

Comparison: 02 IUI versus TI both in stimulated cycles

Outcome: 03 Pregnancy rate per couple (all cycles)

**GENEL  
SONUÇLAR  
Erkek  
subfertilitesi-  
IUI:  
Stimule  
sikluslarda IUI  
vs Zamanlı Koit**



## Analysis 05.02. Comparison 05 IUI in stimulated cycles versus IUI in natural cycles, Outcome 02 Ongoing pregnancy rate per couple (all cycles)

Review: Intra-uterine insemination for male subfertility

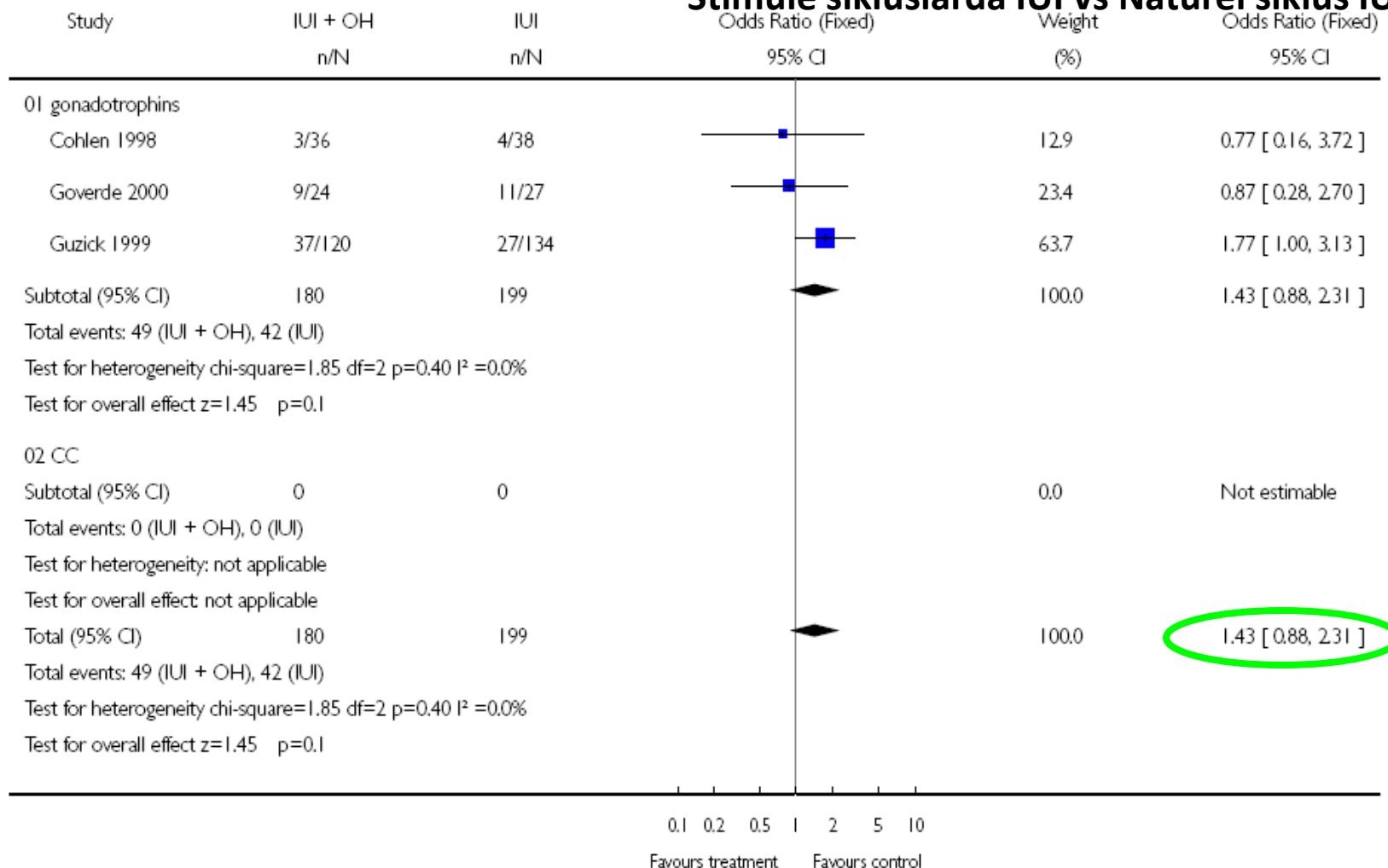
Comparison: 05 IUI in stimulated cycles versus IUI in natural cycles

Outcome: 02 Ongoing pregnancy rate per couple (all cycles)

### GENEL SONUÇLAR

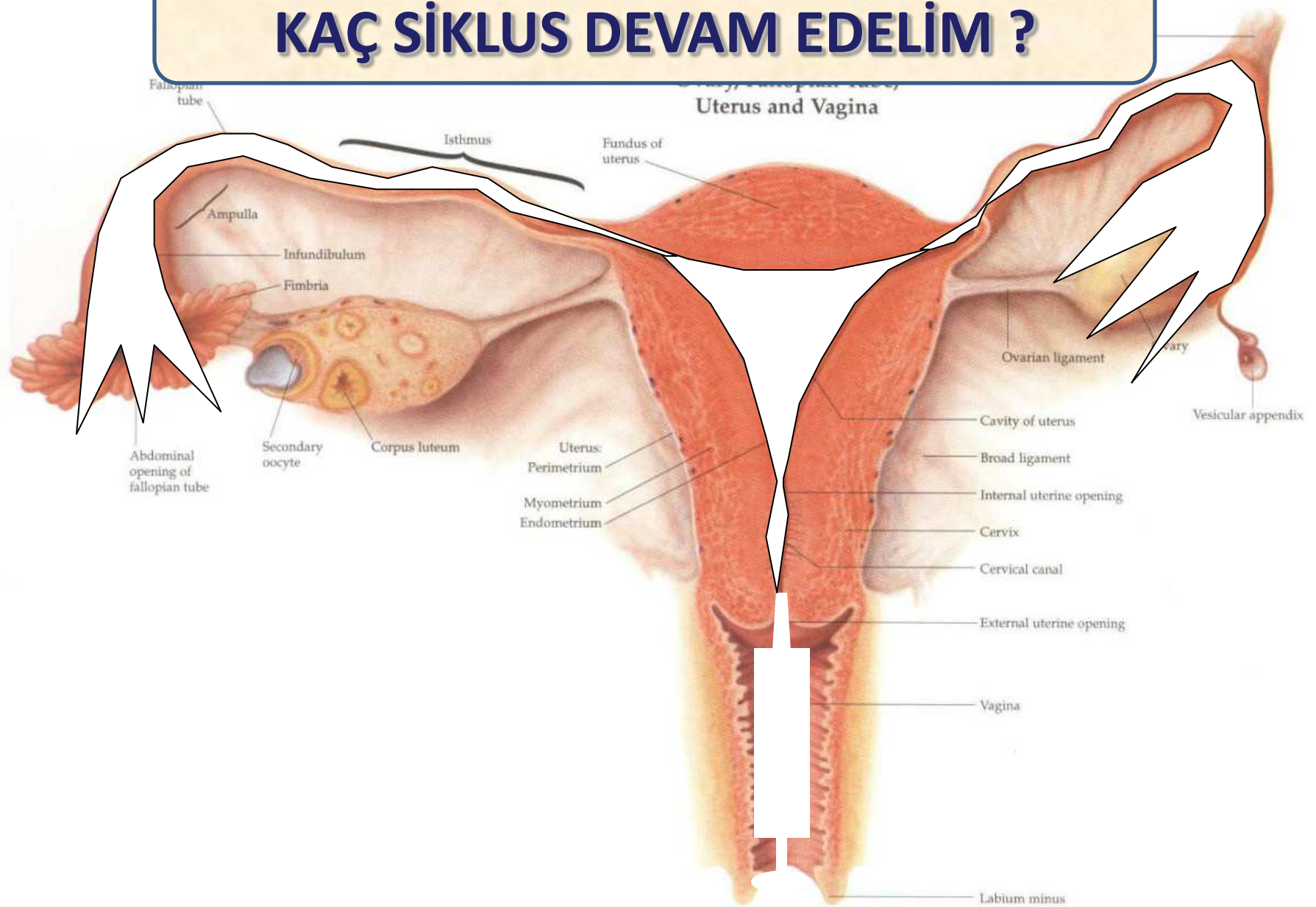
### Erkek subfertilitesi-IUI:

### Stimule sikluslarda IUI vs Naturel siklus IUI





# KAÇ SIKLUS DEVAM EDELİM ?



- IUI sonrası oluşacak gebelikler ilk tedavi sikluslarında gerçekleşir.
- Gebeliklerin 71%’i ilk 2 siklusda oluşur (*Friedman et al, 1990*).
- IUI gebeliklerinin 85%’i ise ilk dört siklusedir (*Isaksson & Titinen, 1997*). Bundan sonra IUI’a devam etmek önerilmez (*Kirby et al, 1991*)

# Controlled ovarian hyperstimulation and intrauterine insemination for treatment of **unexplained infertility** should be limited to a maximum of three trials

FERTILITY AND STERILITY®  
VOL. 75, NO. 1, JANUARY 2001

*Mohamed Aboulghar, M.D., Ragaa Mansour, M.D., Gamal Serour, M.D.,  
Ashraf Abdrazek, M.D., Yehia Amin, M.D., and Catharine Rhodes, M.R.C.O.G.*

|         | Patients<br>(n) | Treatment            | Pregnancy<br>(n) | Overall<br>cycle<br>fecundity | Cumulative<br>pregnancy<br>rate |
|---------|-----------------|----------------------|------------------|-------------------------------|---------------------------------|
| Group A | 594             | 1-3 cycle<br>COH+IUI | 182              | 16.4%                         | %39.2                           |
| Group B | 91              | 4-6 cycle<br>COH+IUI | 9                | 5.6%                          | %48.5<br>(%9.3)                 |
| Group C | 131             | 1 cycle<br>IVF-ICSI  | 48               | 36.6%                         |                                 |

# Intrauterine insemination: how many cycles should we perform?<sup>†</sup>

Human Reproduction Vol.23, No.4 pp. 885–888, 2008

Inge M. Custers<sup>1,7</sup>, Pieter Steures<sup>1</sup>, Peter Hompes<sup>2</sup>, Paul Flierman<sup>3</sup>, Yvonne van Kasteren<sup>4</sup>, Peter A. van Dop<sup>5</sup>, Fulco van der Veen<sup>1</sup> and Ben W.J. Mol<sup>1,6</sup>

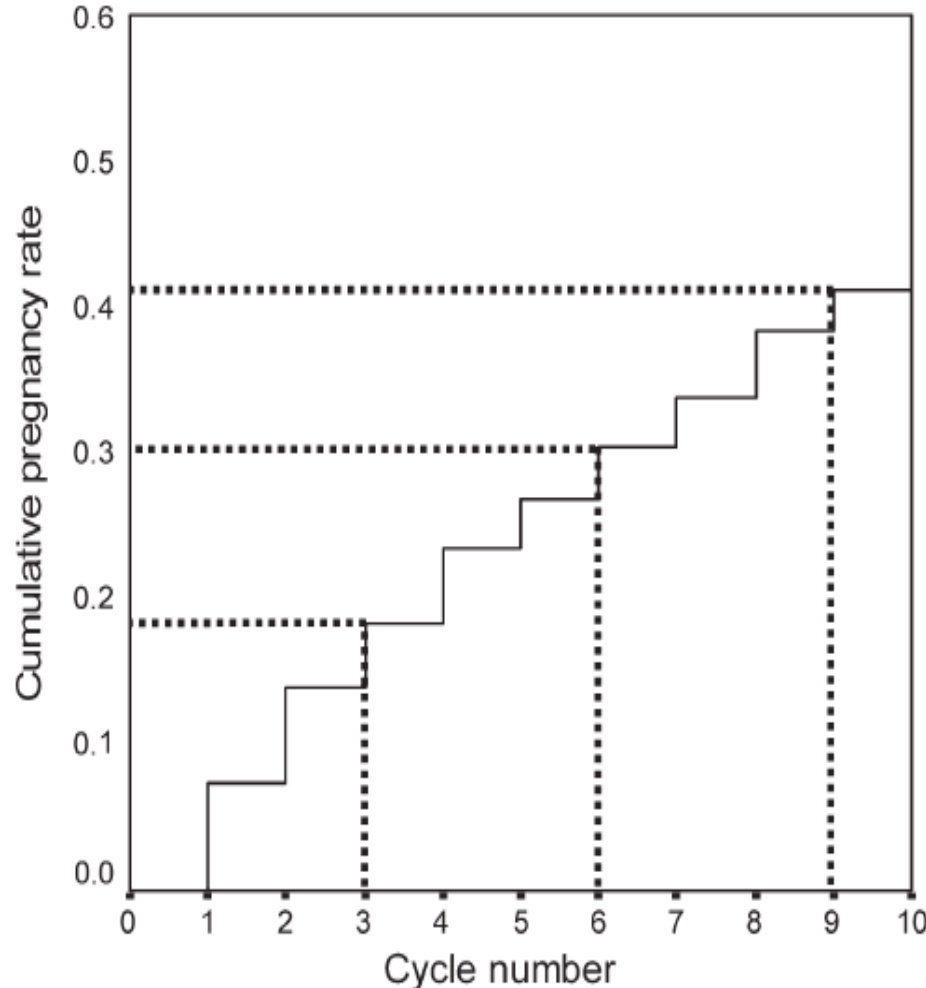


Figure 1: Cumulative OPRs from first to ninth IUI treatment cycle

- 3714 çift/15303 siklus
- multicenter, retrospektif kohort *“very mild stimulation”* (%51 CC; %19 gt)
- Ort OPR/siklus % 5.6  
(VII. % 5.1 VIII. %6.7 IX. % 4.6)
- 3.cyc. COPR:%18  
6.cyc. COPR:%30  
9.cyc. COPR:%41
  - 35 yaşından genç hastalara
  - 6 siklus başarısız inseminasyon sonrası IVF’e geçmeden önce
  - IUI uygulamasını bir seçenek

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

Richard H. Reindollar, M.D.,<sup>a</sup> Meredith M. Regan, Sc.D.,<sup>b</sup> Peter J. Neumann, Sc.D.,<sup>c</sup> Bat-Sheva Levine,

**TABLE 2**

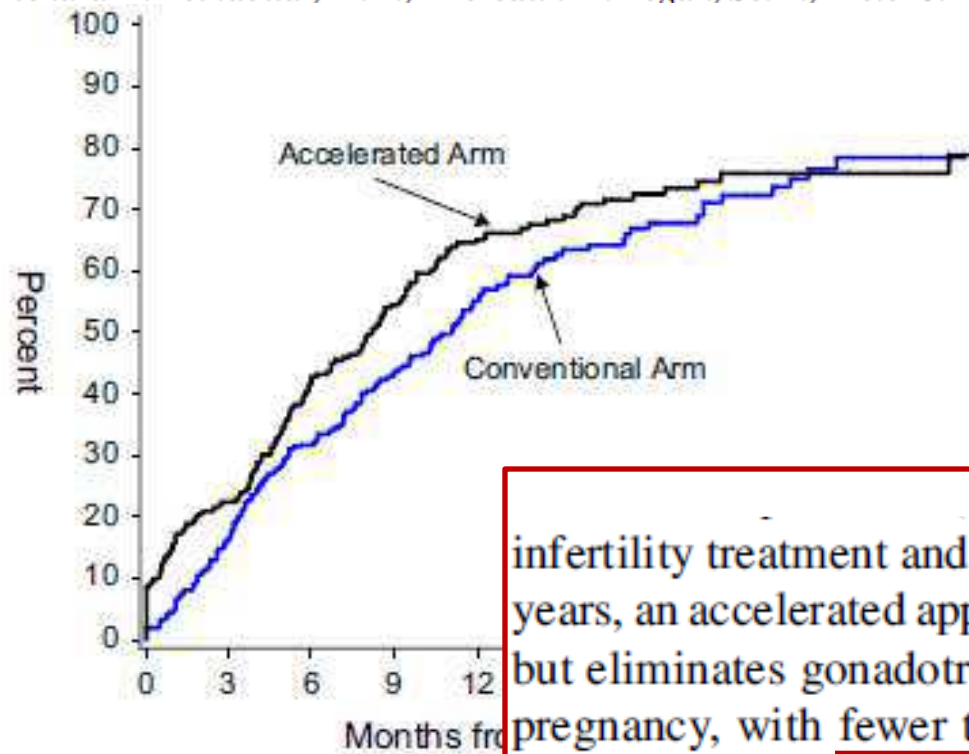
Number of couples initiating treatment cycles, total number of cycles initiated, and pregnancy rates by treatment group as of April 30, 2006.

|                                        | 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 <sup>a</sup>    | 361 <sup>a</sup>    | 622                 | 1346                | 1009                |
| No. of pregnancies                     |                                           |                     |                     |                     |                     |                     |                     |                     |                     |
| Total <sup>b</sup>                     | 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 <sup>c</sup>     | 28 <sup>c</sup>     |
| Live birth                             | 41                                        | 51                  | 92                  | 37                  | 58                  | 100                 | 158                 | 150 <sup>c</sup>    | 171 <sup>c</sup>    |
| Pregnancy rates (live birth + ongoing) |                                           |                     |                     |                     |                     |                     |                     |                     |                     |
| Per initiated cycle                    | 7.0<br>(4.8-10.0)                         | 8.2<br>(5.8-11.4)   | 7.6<br>(6.2-9.2)    | 9.8<br>(6.8-14.0)   | 28.0<br>(21.8-35.2) | 32.7<br>(27.0-38.9) | 30.7<br>(27.1-34.5) |                     |                     |
| Per couple                             | 19.3<br>(14.5-25.0)                       | 21.9<br>(16.9-27.7) | 20.6<br>(17.1-24.6) | 25.4<br>(19.1-32.7) | 65.8<br>(56.2-74.5) | 68.6<br>(61.1-75.5) | 67.5<br>(61.7-72.9) | 74.9<br>(69.0-80.2) | 77.7<br>(72.1-82.7) |



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

Richard H. Reindollar, M.D.,<sup>a</sup> Meredith M. Regan, Sc.D.,<sup>b</sup> Peter J. Neumann, Sc.D.,<sup>c</sup> Bat-Sheva Levine,



3xCC+IUI

3xFSH+IUI

6xIVF

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.

|              |     |     |     |     |    |    |    |    |    |    |   |
|--------------|-----|-----|-----|-----|----|----|----|----|----|----|---|
| Conventional | 247 | 199 | 154 | 118 | 79 | 50 | 36 | 23 | 14 | 11 | 8 |
| Accelerated  | 256 | 195 | 135 | 98  | 63 | 47 | 31 | 19 | 14 | 10 | 5 |

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

*Richard H. Reindollar, M.D.,<sup>a</sup> Meredith M. Regan, Sc.D.,<sup>b</sup> Peter J. Neumann, Sc.D.,<sup>c</sup> Bat-Sheva Levine,*

- 40 yaş altı
- CC-IUI ile başlanıp, 2 siklus sonrasında FSH-IUI aşaması atlanması ve IVF'e geçilmesi ile:
- Kısa sürede
- Az maliyetle
- Etkin gebelik



# 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.,<sup>a,b</sup> Kim L. Thornton, M.D.,<sup>c</sup> David Ryley, M.D.,<sup>c</sup> Michael M. Alper, M.D.,<sup>c</sup>

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

| Randomized treatment arm | No. of couples (%) | First two treatment cycles                                  |                                               | Duration of study                                         |                                                  |
|--------------------------|--------------------|-------------------------------------------------------------|-----------------------------------------------|-----------------------------------------------------------|--------------------------------------------------|
|                          |                    | No. of clinical pregnancies <sup>a,b</sup><br>(%, 97.5% CI) | No. of live births <sup>c</sup> (%, 97.5% CI) | No. of clinical pregnancies <sup>d</sup><br>(%, 97.5% CI) | No. of live births <sup>d</sup><br>(%, 97.5% CI) |
| CC/IUI                   | 51 (33.1)          | 1 (21.6, 10.2–37.3)                                         | 1 (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)                                        | 18 (31.4, 17.7–47.9)                          | 38 (74.5, 58.4–86.9)                                      | 24 (47.1, 31.2–63.4)                             |
| Total <sup>e</sup>       | 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.

<sup>a</sup> Number of clinical pregnancies includes all ultrasound-confirmed pregnancies, including pregnancy losses.

<sup>b</sup> 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.

<sup>c</sup> 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.

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

<sup>e</sup> 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)

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

Marlene B. Goldman, Sc.D.,<sup>a,b</sup> Kim L. Thornton, M.D.,<sup>c</sup> David Ryley, M.D.,<sup>c</sup> Michael M. Alper, M.D.,<sup>c</sup>

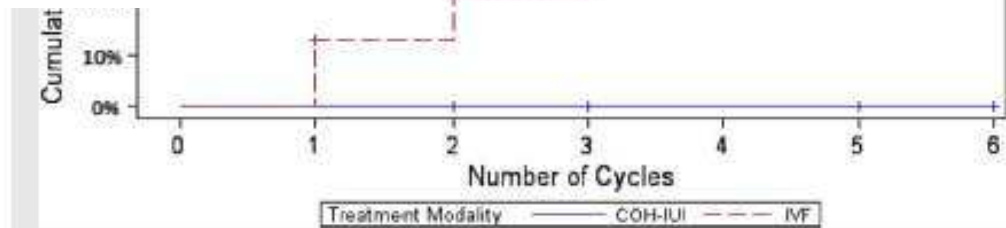
- >38-42 yaş
- Hemen IVF
- 2 siklus CC veya FSH-IUI grubuna kıyasla..
- Yüksek gebelik ve canlı doğum oranları

# 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.,<sup>a</sup> Marlene B. Goldman, Sc.D.,<sup>b,c</sup> June L. Fung, Ph.D.,<sup>b</sup> Michael M. Alper, M.D.,<sup>d,e</sup>  
and Richard H. Reindollar, M.D.<sup>b</sup>

YAŞ bağımsız  
FSH 10-15  
E2>40



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<sub>2</sub> > 100 pg/mL) are shown in Figure 2. **That no live births occurred among**

(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.

# ÖZET

## **FASTT**

- Açıklanamayan infertilite
- 40 yaşa kadar
- CC-IUI (3 siklus?)
- Sonuç yoksa direkt IVF

## **FORT-T**

- Açıklanamayan infertilite
- 40 yaş üstü
- COH-IUI yapılmaksızın direkt IVF

# Fertility

Assessment and treatment for people with  
fertility problems

**NICE clinical guideline 156**

[guidance.nice.org.uk/cg156](http://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]**

# SONUÇ

## IUI KIME, NE ZAMAN, KAÇ DEFA ?

- İzah edilemeyen infertilite
- Erkek faktörlü infertilite?
- < 40 y ; < 5 yıllık infertilite
- hCG zamanlaması ?
- Gonadotropin + IUI
- 3 (max 4) siklus
- Sadece erkek infertilitesinde double ?

TESCHENMÄRTER