www.endometriozisdernegi.com
www.endometriozis.org

Optimal management of Endometriosis associated infertility

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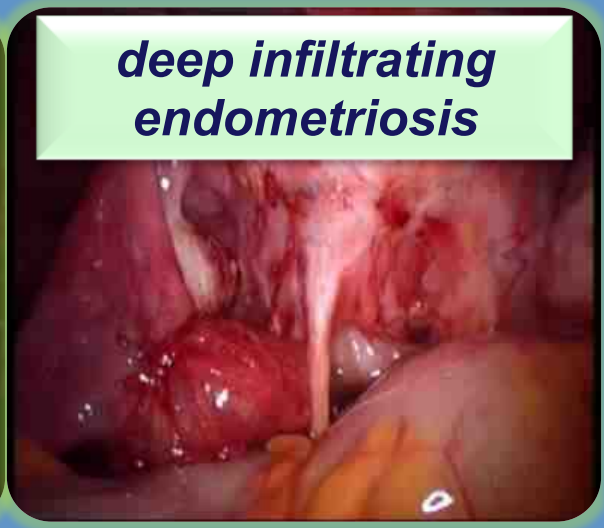
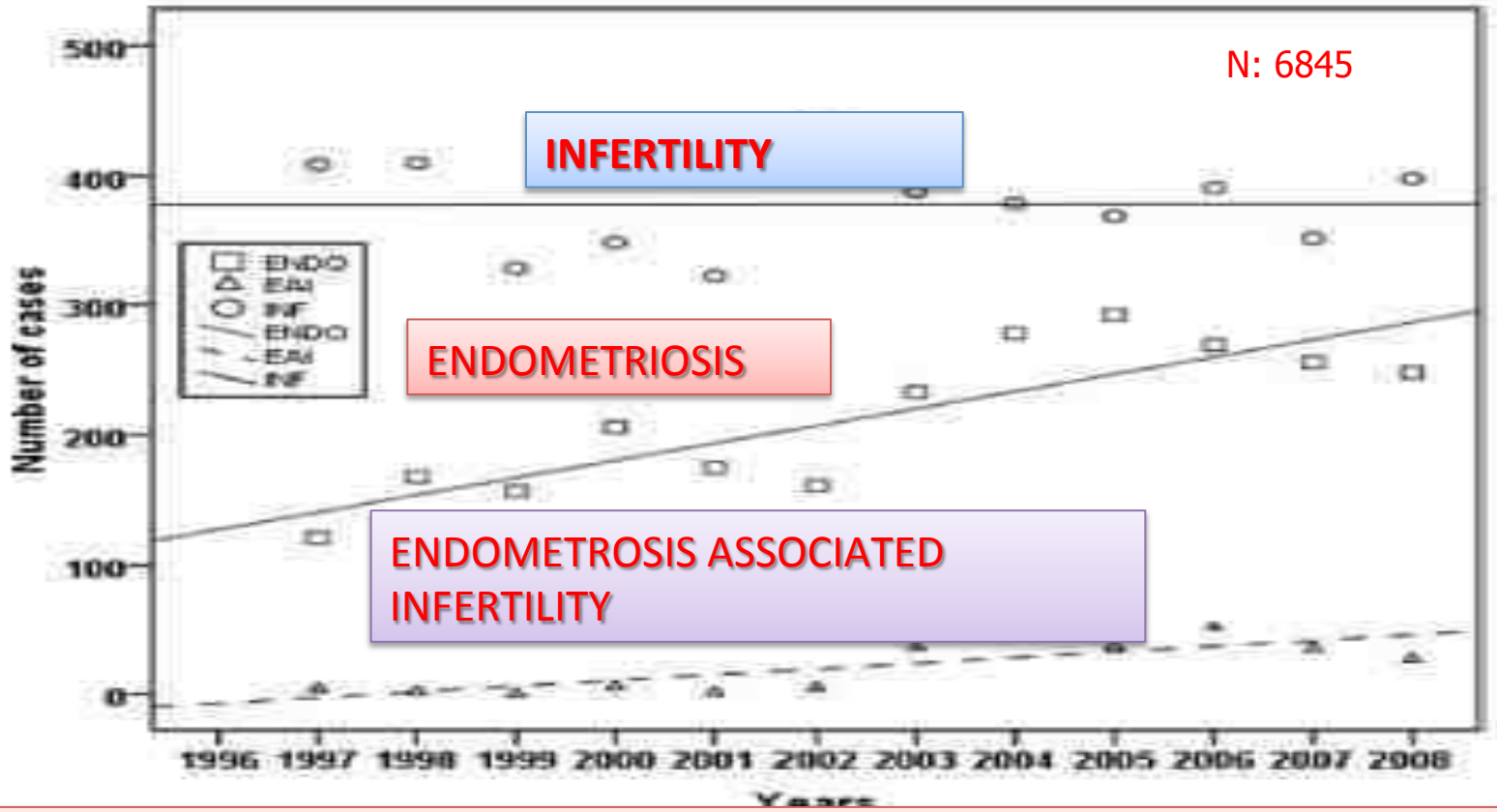
Endometriosis



Endometriosis-associated infertility: a decade's trend study of women from the Estrie Region of Quebec, Canada



Endometriosis associated Infertility has been increased through past 10 years

$p = 0.987$).

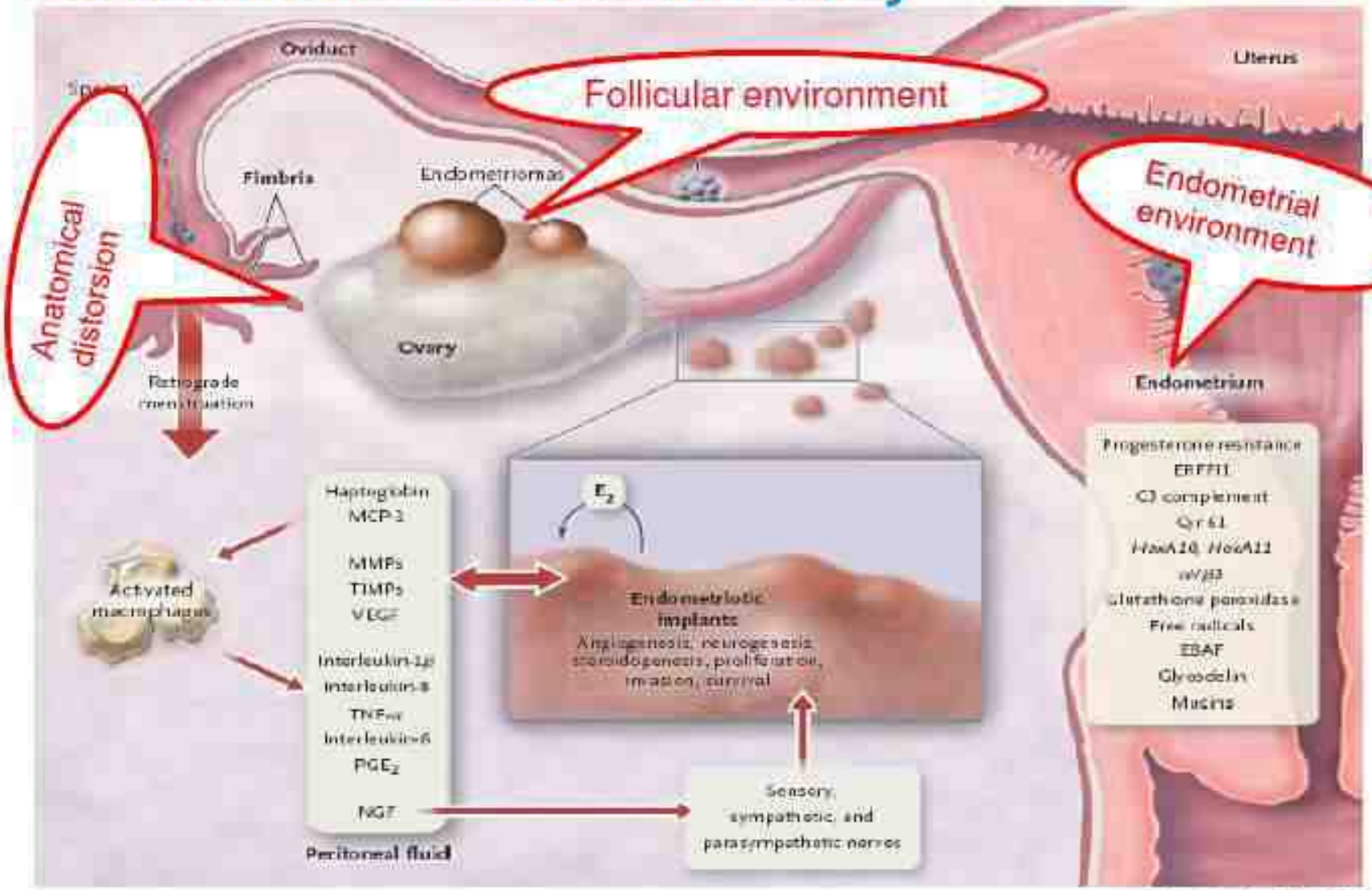
Krystel parıs & Azız arıs, 2010

What is known about the association between endometriosis and fertility ?

- Some papers report 30–40% of women with endometriosis experience infertility and that they have a reduced fecundity rate of 2–10%
- All women with endometriosis can experience infertility but those with severe physical disease may be more likely to
- Endometriosis may cause infertility where endometrial lesions have changed the pelvic anatomy . Little is known about other possible mechanisms.

	MONTHLY FECUNDITY RATES
First three months of attempting conception	**30%**
After 1 year	**4%**
Women with endometriosis	**2-10%**

Endometriosis and Infertility



2010

Treatment of infertility in patients with endometrioma

- Expectant

vs

- Surgery

vs

- IUI/IVF

Table IV. Pregnancy rate in the untreated control groups participating in endometriosis trials

	No. of patients	No. pregnant	%
Thomas and Cooke (1987)	17	4	23.5
Bayer *et al.* (1988)	36	17	47.2
Telimaa *et al.* (1987)	14	6	42.9
Fedele *et al.* (1992a)	36	17	47.2
Fedele *et al.* (1992b)	25	6	24.0
Marcoux *et al.* (1997)	169	37	21.9
GISE (1999)	47	13	27.7
Mahmood and Templeton (1990)	20	4	20.0
Overton *et al.* (1994)	18	7	38.9
Tummon *et al.* (1997)	50	4	8.0
Total	462	115	24.9

Pregnancy chances on an IVF/ICSI waiting list: a national prospective cohort study

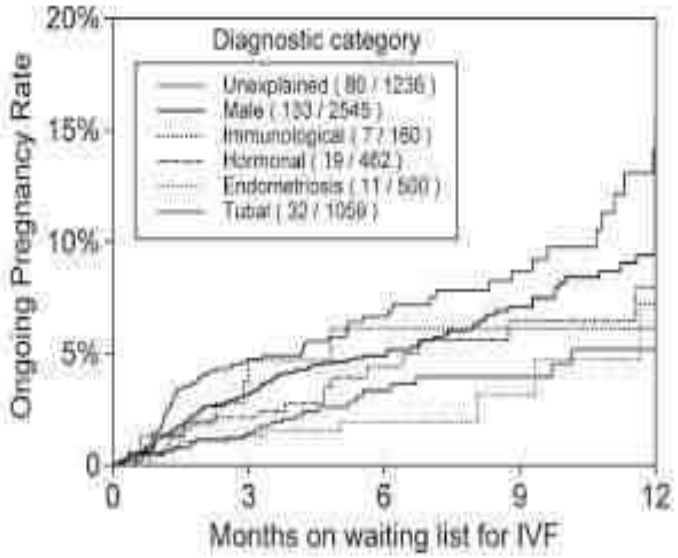


Figure 4: Cumulative chance of an ongoing treatment-free pregnancy, against time since registration on the waiting list for IVF or ICSI, separately for diagnostic categories.
Kaplan–Meier estimates, censoring for start of treatment and for termination of the active childwish.

Table II. HR for ongoing pregnancy without treatment of 5962 patients on the waiting list for IVF.

	HR	95% confidence interval lower–upper
Age (per year)	0.95	0.93–0.98
Duration of infertility (per year)	0.85	0.79–0.91
Indication		
Tubal pathology	1*	—
Endometriosis	0.73	0.37–1.46
Male	1.57	1.06–2.32
Hormonal	1.19	0.67–2.11
Unexplained	2.64	1.75–3.98
Immunological	1.69	0.75–3.84
Primary versus secondary infertility	0.71	0.56–0.90

Eijkemans et al., 2008

COH + IUI

SUGGESTED FOR;

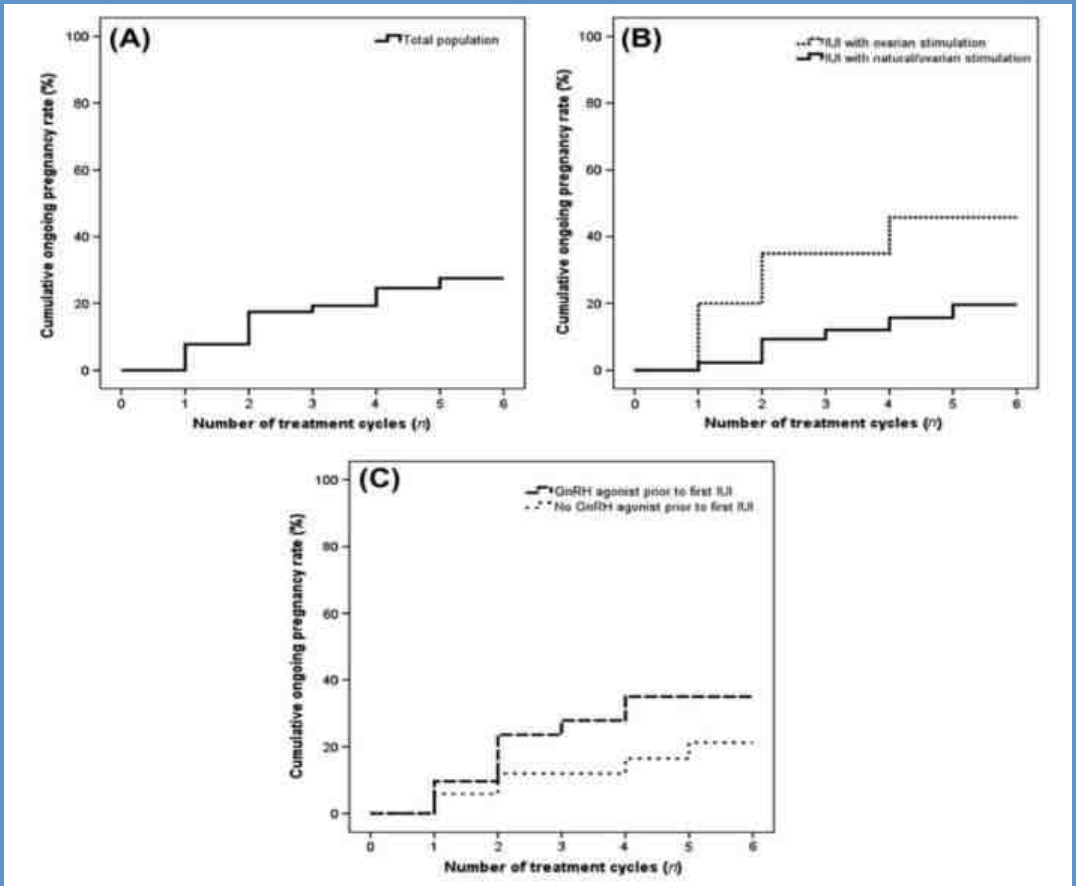
- Stage I or II endometriosis
- Surgically diagnosed and absent anatomic distortion

- Not in patients with ‘severe endometriosis’.

ML Macer, Obstet Gynecol Clin North Am. 2012

IUI for moderate/severe endometriosis

PR/cycle



IUI might be a valuable treatment in moderate-to-severe endometriosis patients and IUI with ovarian stimulation should be offered over IUI with natural/ovarian stimulation. Preceding long-term pituitary down-regulation might positively influence the ongoing pregnancy rate and can be considered.

From Van der Houven et al. RBM Online 2014

IUI
After Surgery?

- Retrospective cohort study

Stage I/II (n = 67) 1 year spontaneous or COH+IUI

Stage III/IV (n=29) 1 year spontaneous or COH + IUI

- COH with letrozole, clomiphene, or gonadotropins, with or without IUI.

Gandhi AR, JMIG, 2014

IUI
After Surgery?

12 months cumulative pregnancy rate

- Stage I/II : spontaneous 45%
  COH+IUI 42%
- Stage III/IV: spontaneous 20%
  COH+IUI 10%

NS

COH+IUI does not improve pregnancy rates in any stage of endometriosis

Stage III/IV → IVF

Gandhi AR, JMIG, 2014

Endometriosis-IVF Indications

- DOR
- Female age >37
- Infetility duration > 5 years
- Failed COS/IUI cycle
- Recurrent endometrioma
- Bilateral endometrioma
- With Adenomyosis
- Bilateral Tubal Factor
- Male Factor

Questions

- Does Endometriosis Affect IVF Outcome?
- Does Endometriosis Severity Affect IVF Outcome?

Do women with endometriosis have the same chances of success as women without endometriosis?

Endometriosis and Assisted Reproductive Technology: United States Trends and Outcomes 2000–2011

2015

Jennifer F. Kawwass, M.D.,[a,b] Sara Crawford, Ph.D.,[b] Donna R. Session, M.D.,[a] Dmitry M. Kissin, M.D., M.P.H.,[a,b] and Denise J. Jamieson, M.D., M.P.H.,[a,b] for the National ART Surveillance System Group

[a] Division of Reproductive Endocrinology and Infertility, Department of Gynecology and Obstetrics, Emory University School of Medicine; and [b] Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

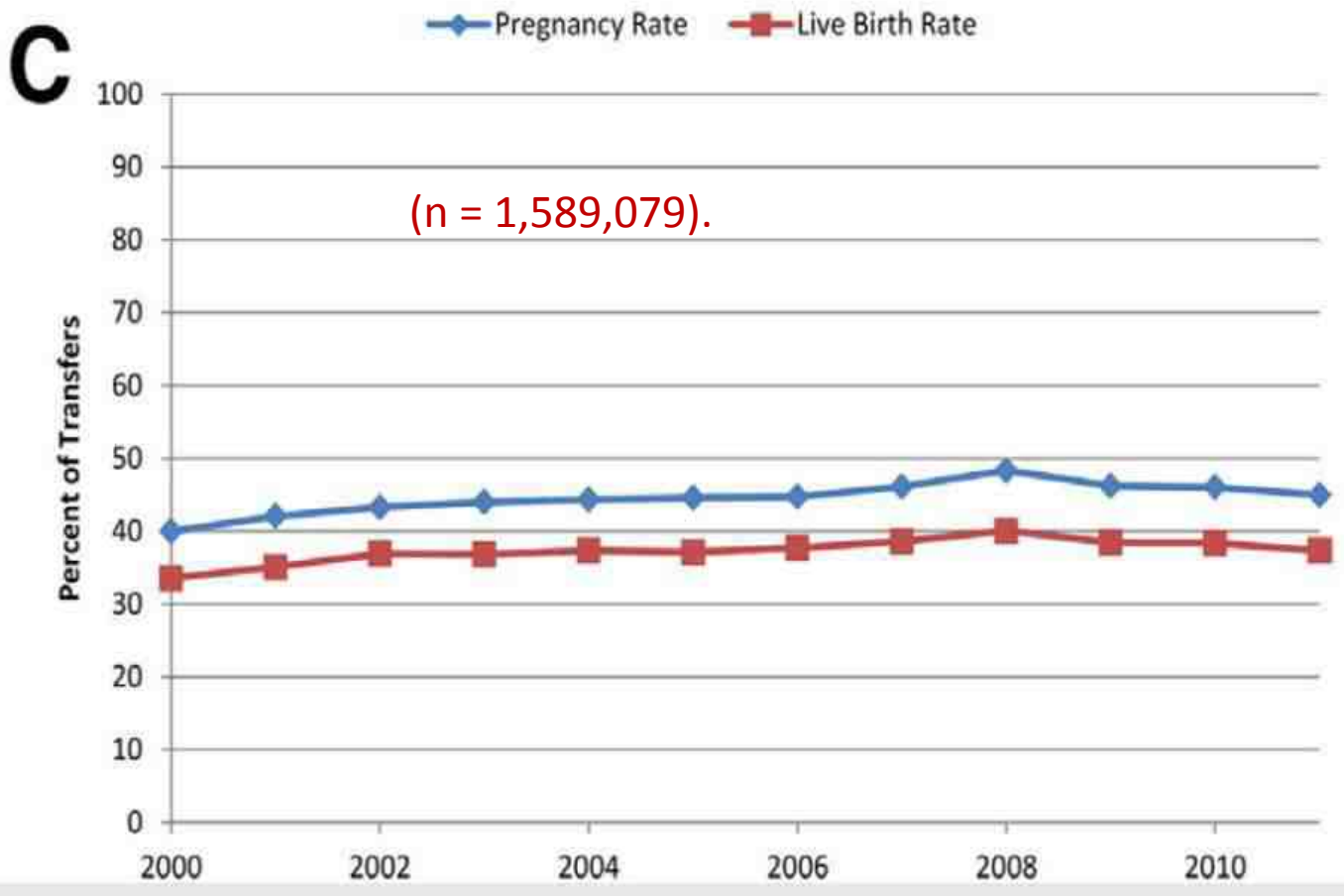


TABLE 3

Outcomes among fresh nondonor IVF cycles, endometriosis vs. male factor infertility 2000–2011.

Outcome	Endometriosis, n (%)	Male factor, n (%)	RR (95% CI)	aRR (95% CI)
Hyperstimulation[a]	1,187 (1.06)	4,929 (1.31)	0.80 (0.72–0.90)	0.82 (0.74–0.9
Hospitalization[a]	337 (0.3)	1,175 (0.31)	0.96 (0.83–1.11)	0.97 (0.84–1.1
Cancellation[a]	14,474 (12.87)	37,936 (10.10)	1.27 (1.22–1.33)	1.30 (1.25–1.3
Pregnancy[b]	40,085 (43.74)	140,835 (44.81)	0.98 (0.96–0.99)	0.96 (0.95–0.9
Live birth (≥20 wk)[b]	Tubal: 5,781 (33.80)	Tubal: 10,177 (32.57)	Tubal: 1.04 (1.002–1.08)	Tubal: 1.00 (0.97–1.0
	No tubal: 27,694 (37.15)	No tubal: 106,366 (37.58)	No tubal: 0.99 (0.97–1.01)	No tubal: 0.96 (0.94–0.9
Miscarriage (<20 wk)[b]	5,323 (5.83)	19,793 (6.32)	0.92 (0.89–0.96)	0.93 (0.89–0.9
Implantation[b,c]	25.28 (34.80)	26.30 (35.51)	0.98 (0.95–1.0008)	0.96 (0.94–0.9

[a] Per cycle start.

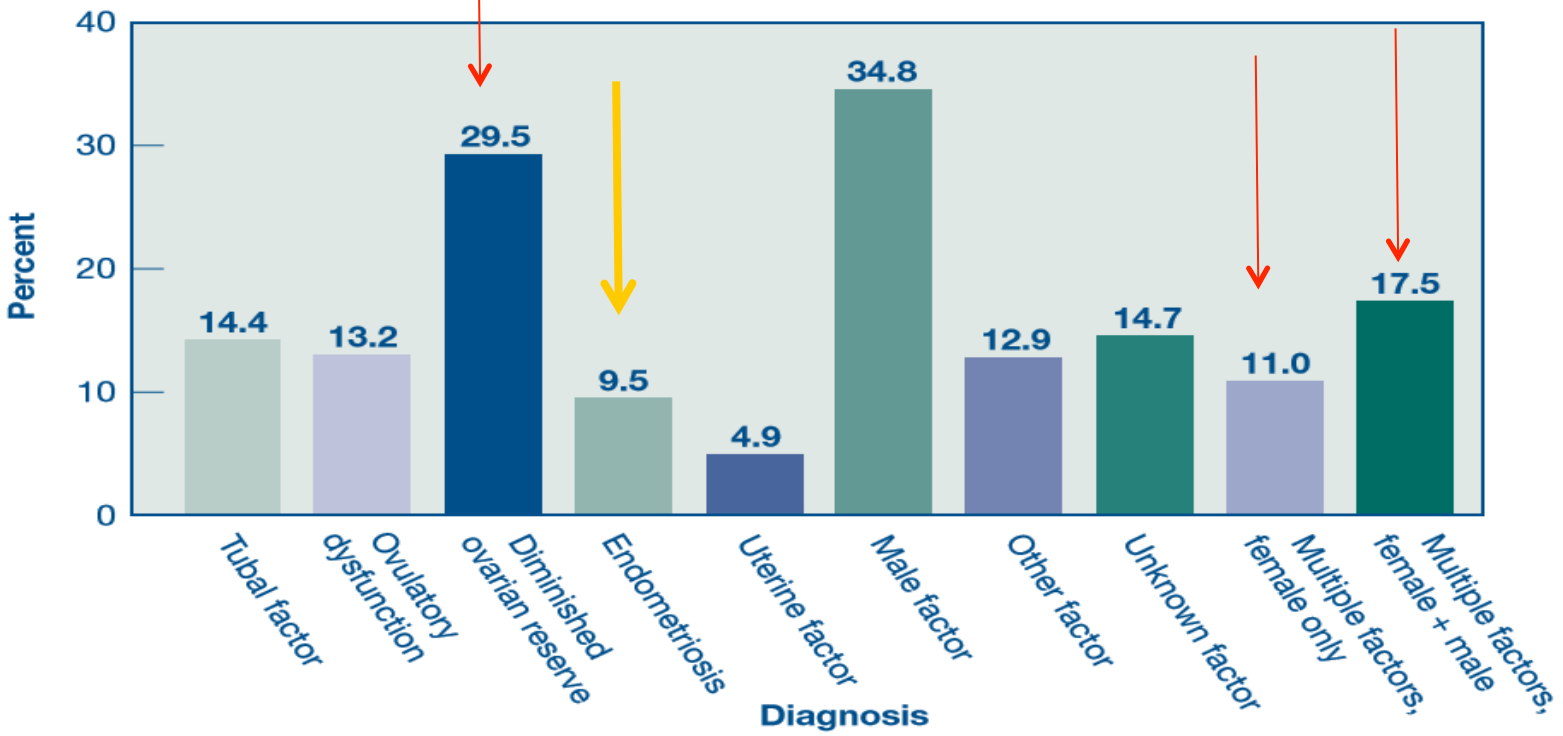
[b] Per noncancelled cycles for which a transfer was performed.

[c] Implantation is defined as the maximum of the total number of heartbeats on first ultrasound or number of infants born divided by the number of embryos transferred times 100. Implantation r is calculated per cycle; table reflects mean implantation rates for all cycles in each group.

Kawwass. Endometriosis: ART trends and outcomes. Fertil Steril 2015.

SART 2013

Figure 18
Percentages of ART Cycles Using Fresh Nondonor Eggs or Embryos, by Infertility Diagnosis,* 2013



* Total percentages are greater than 100% because more than one diagnosis can be reported for each cycle.

For more information on how to interpret the statistics in this table, see pages 11–20 in the *2013 Assisted Reproductive Technology Fertility Clinic Success Rates Report.*

2013 ART CYCLE PROFILE

Type of ART and Procedural Factors[a]

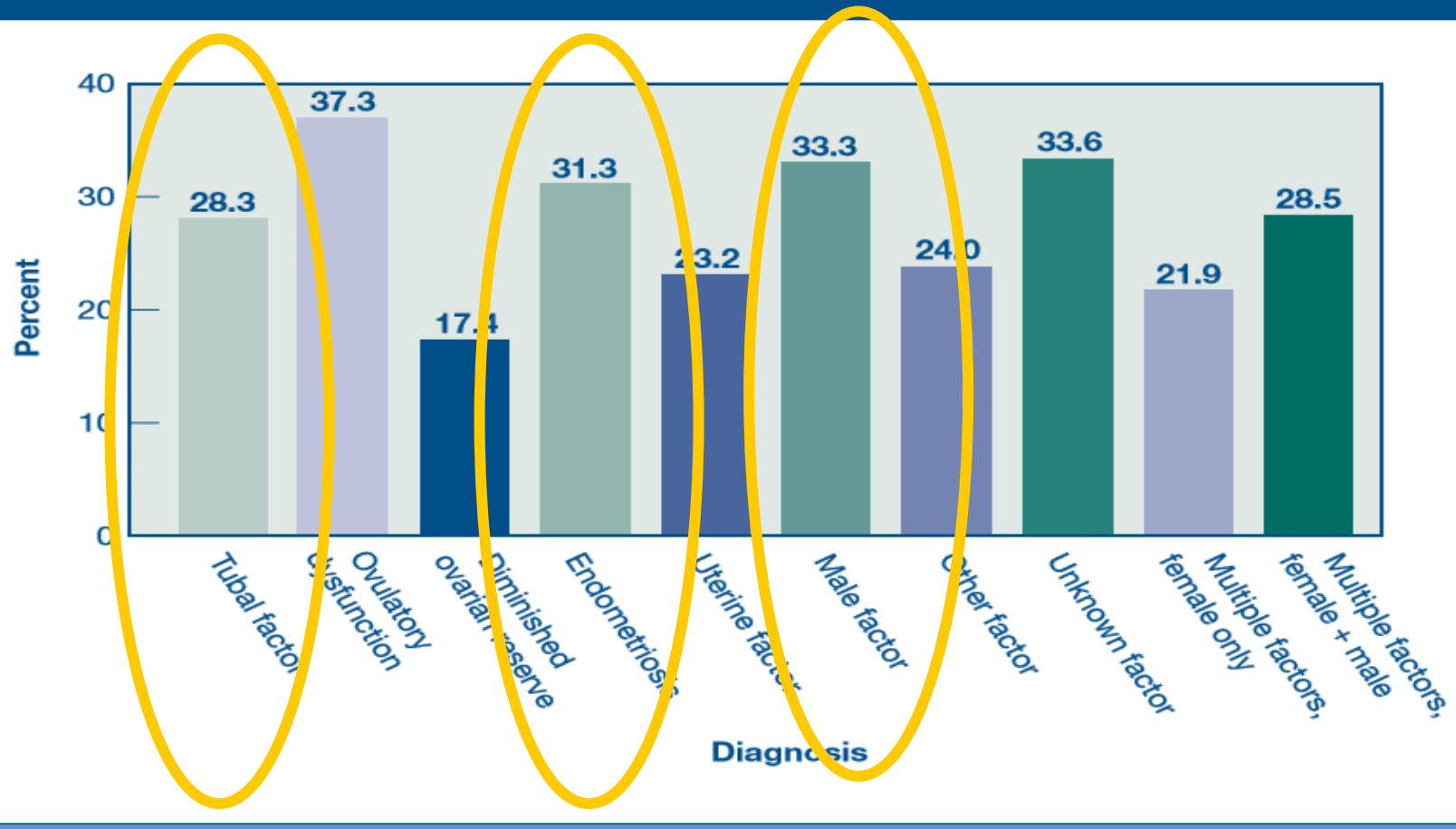
IVF	>99%	With ICSI	69%
Unstimulated	1%	Used PGD	6%
Used gestational carrier	<1%		

Patient Diagnosis[b]

Tubal factor	13%	Uterine factor	5%	*Multiple Factors:*	
Ovulatory dysfunction	14%	Male factor	33%	Female factors only	12%
Diminished ovarian reserve	32%	Other factor	15%	Female & male factors	17%
Endometriosis	9%	Unknown factor	13%		

SART 2013

Figure 19
Percentages of ART Cycles Using Fresh Nondonor Eggs or Embryos That Resulted in Live Births, by Infertility Diagnosis, 2013

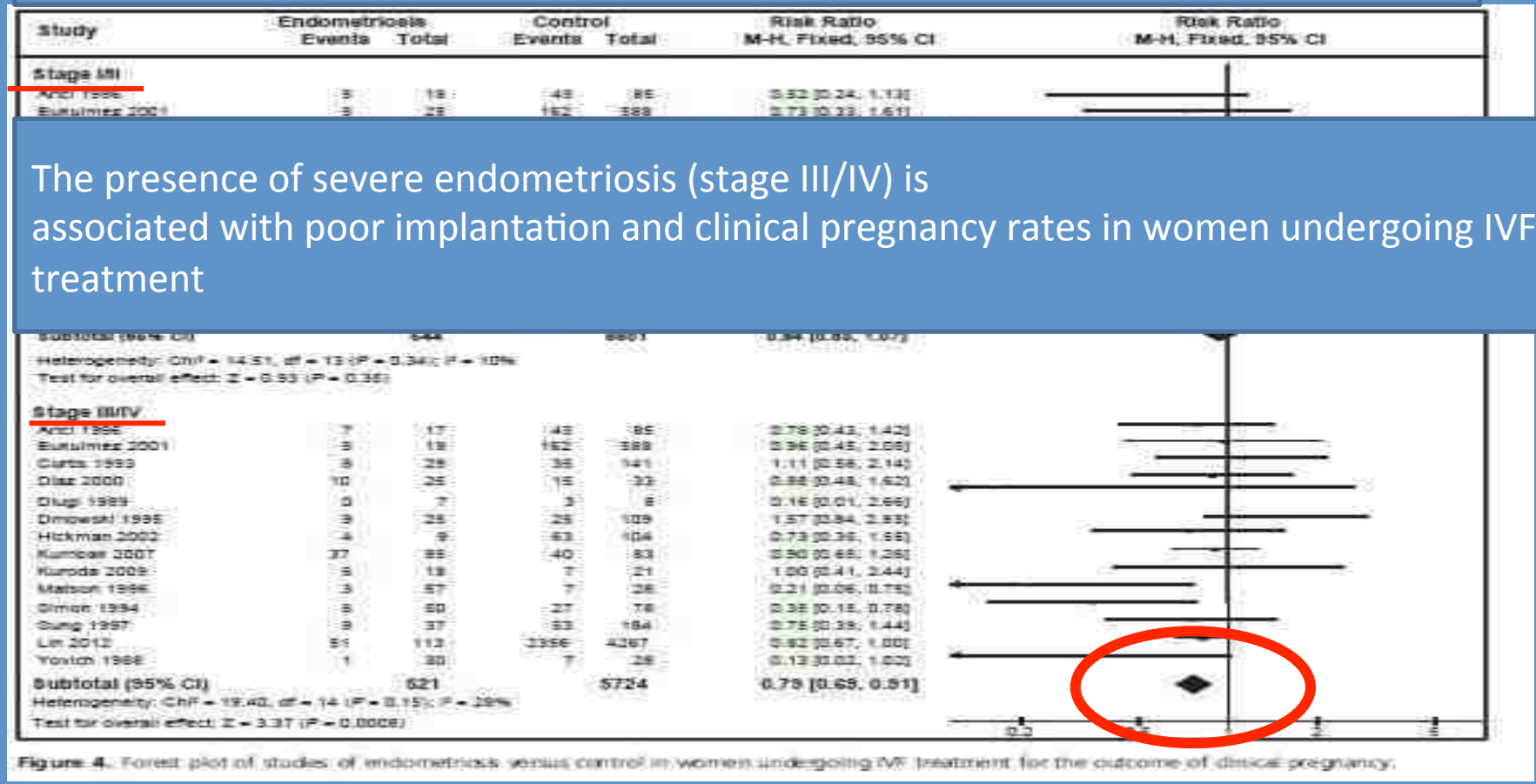


The effect of endometriosis on *in vitro* fertilisation outcome: a systematic review and meta-analysis

2013

HM Harb,[a] ID Gallos,[a] J Chu,[a] M Harb,[b] A Coomarasamy[a]

Twenty-seven observational studies were included, comprising 8984 women



The presence of severe endometriosis (stage III/IV) is associated with poor implantation and clinical pregnancy rates in women undergoing IVF treatment

Figure 4. Forest plot of studies of endometriosis versus control in women undergoing IVF treatment for the outcome of clinical pregnancy.

Ultrasound Obstet Gynecol 2014; 44: 261–278
Published online 13 August 2014 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.13366

Impact of endometriosis and its staging on assisted reproduction outcome: systematic review and meta-analysis

2014

M. A. P. BARBOSA*, D. M. TEIXEIRA*, P. A. A. S. NAVARRO*, R. A. FERRIANI*, C. O. NASTRI*† and W. P. MARTINS*†

**Department of Obstetrics and Gynecology, Medical School of Ribeirao Preto, University of Sao Paulo (FMRP-USP), Ribeirao Preto, Brazil; †Ultrasonography and Retraining Medical School of Ribeirao Preto (EURP), Ribeirao Preto, Brazil*

- *We included 92 studies in the review and 78 in the meta-analysis:*
- *20 167 women with endometriosis were compared with*
- *121 931 women without endometriosis, and*
- *1703 women with Stage-III/IV endometriosis were compared with*
- *2227 women with Stage-I/II endometriosis.*

- *The following results were observed for the comparison of women with endometriosis* vs *women without endometriosis:*
- *live birth, RR = 0.99 (95% CI, 0.92–1.06);*
- *clinical pregnancy, RR = 0.95 (95% CI, 0.89–1.02);*
- ***miscarriage, RR = 1.31 (95% CI,1.07–1.59);***
- ***number of oocytes retrieved, MD = –1.56 (95% CI, –2.05 to –1.08).***
- *The following results were observed for the comparison of women with Stage-III/IV* vs *Stage-I/II endometriosis:*
- *live birth, RR = 0.94 (95% CI, 0.80–1.11);*
- *clinical pregnancy, RR = 0.90 (95% CI, 0.82–1.00);*
- *miscarriage, RR = 0.99 (95% CI,0.73–1.36);*
- ***number of oocytes retrieved, MD = –1.03 (95% CI, –1.67 to –0.39).***

Review

Influence of Endometriosis on Assisted Reproductive Technology Outcomes

A Systematic Review and Meta-analysis

2015

Mukhri Hamdan, MObGyn, Siti Z. Omar, MObGyn, Gerard Dunselman, MD, PhD, and Ying Cheong, MD, MRCOG

Women with more severe disease (American Society for Reproductive Medicine III–IV) have a lower live birth rate, clinical pregnancy rate, and mean number of oocytes retrieved when compared with women with no endometriosis

intracytoplasmic sperm injection **have a similar live birth rate per woman** (odds ratio [OR] 0.94, 95% confidence interval [CI] 0.84–1.06, 13 studies, 12,682 patients, I2535%), **a lower clinical pregnancy rate per woman** (OR 0.78, 95% CI 0.65–0.94), 24 studies, 20,757 patients, I2566%), **a lower mean number of oocyte retrieved** per cycle (mean difference 21.98, 95% CI 22.87 to 21.09, 17 studies, 17,593 cycles, I2597%), and a **similar miscarriage rate per woman** (OR 1.26, 95% CI (0.92–1.70, nine studies, 1,259 patients, I250%).

Human Reproduction Update, Vol.21, No.6 pp. 809–825, 2015
Advanced Access publication on July 12, 2015 doi:10.1093/humupd/dmv035

2015

human reproduction update

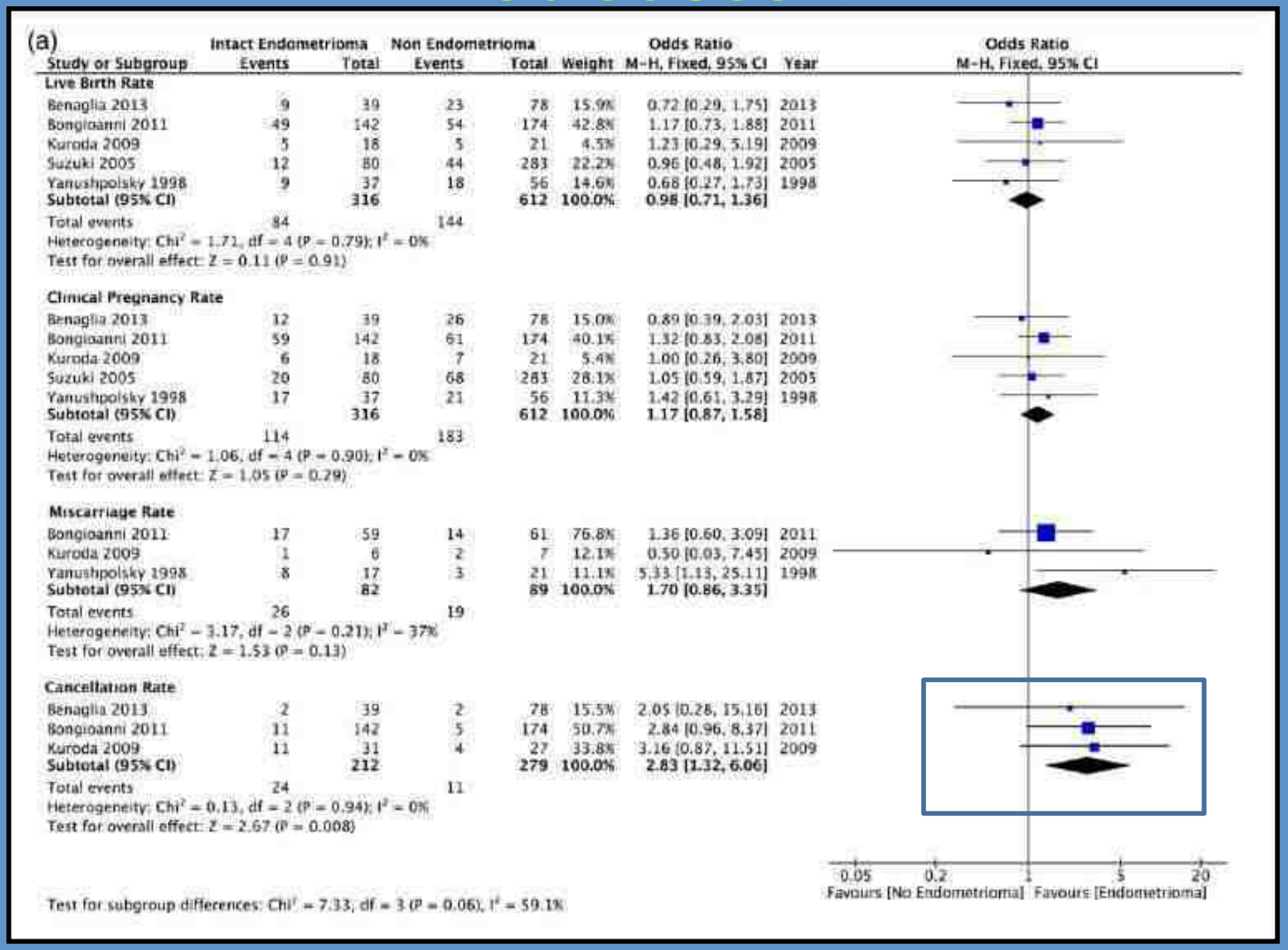
The impact of endometrioma on IVF/ICSI outcomes: a systematic review and meta-analysis

M. Hamdan[1,2,3], G. Dunselman[4], T.C. Li[5], and Y. Cheong[1,3,*]

[1]Human Development and Health Unit, Faculty of Medicine, University of Southampton, Southampton SO16 6YD, UK [2]Faculty of Medicine, Department of Obstetrics and Gynaecology, University of Malaya, Kuala Lumpur 50603, Malaysia [3]Complete Fertility Centre Southampton, Princess Anne Hospital, Coxford Road, Southampton SO16 5YD, UK [4]Department of Obstetrics and Gynaecology, Research Institute GROW, Maastricht University Medical Centre, Maastricht University, PO Box 616, 6200 MD Maastricht, The Netherlands [5]Faculty of Medicine, Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong, Hong Kong, Hong Kong

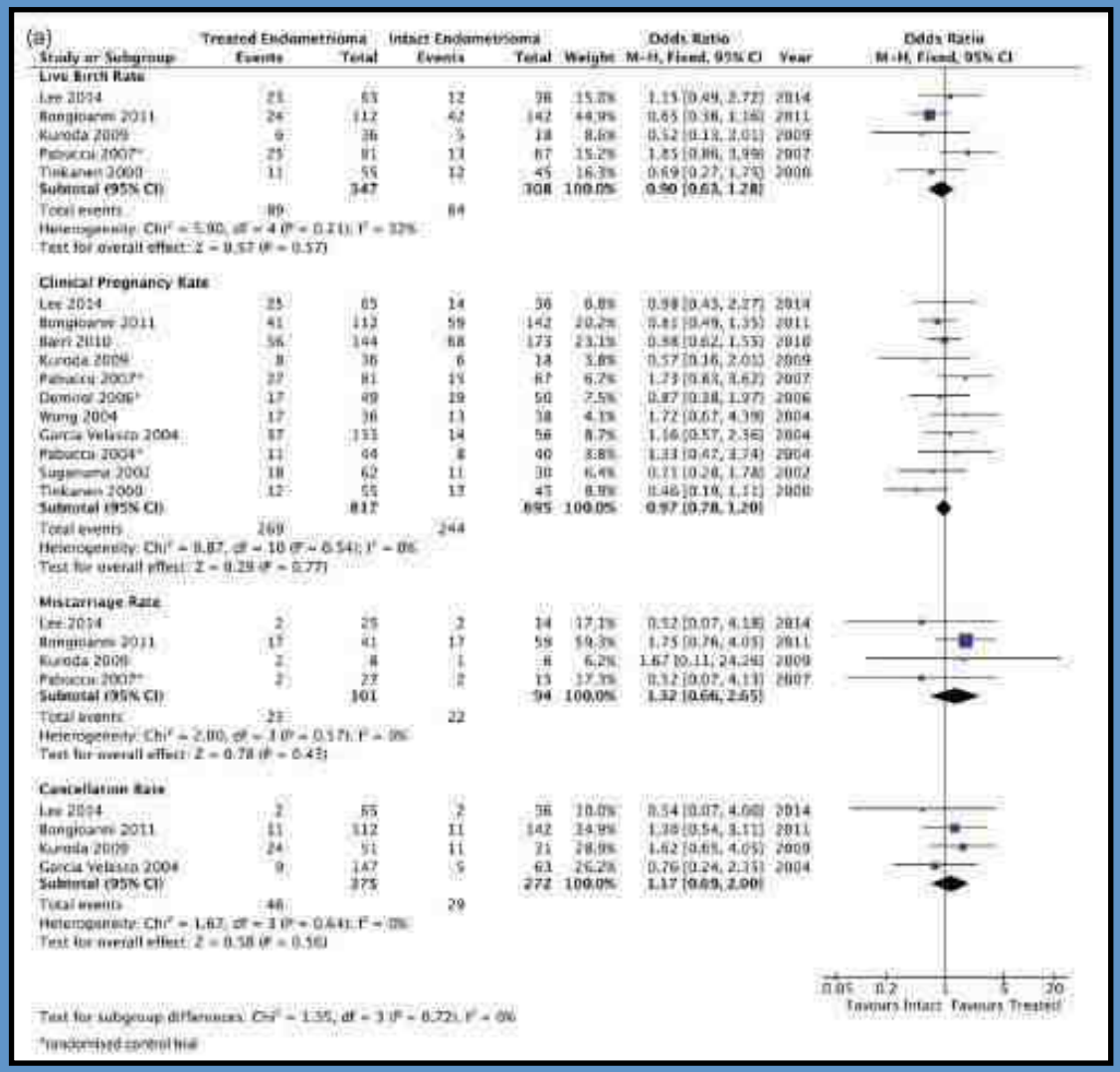
- We included 33 studies for the meta-analysis. The majority of the studies were retrospective (30/33), and three were RCTs.

Does endometrioma hamper ART success ?



Hamdan et al. HRU 2015

Does surgery improve ART success?



Hamdan et al. HRU 2015

Impact of endometriosis on in vitro fertilization outcomes: an evaluation of the Society for Assisted Reproductive Technologies Database

2016

Q9 Suneeta Senapati, M.D., M.S.C.E.,[a] Mary D. Sammel, Sc.D.,[b] Christopher Morse, M.D.,[c]
Q1 and Kurt T. Barnhart, M.D., M.S.C.E.[a,b]

A total of 347,185 autologous fresh and frozen assisted reproductive technology cycles from the period 2008–2010.

Although cycles of patients with endometriosis constituted 11% of the study sample, the majority (64%) reported a concomitant diagnosis, with male factor (42%), tubal factor (29%), and diminished ovarian reserve (22%) being the most common

SUPPLEMENTAL TABLE 1

Distribution of concomitant diagnoses associated with endometriosis.

Endometriosis + male factor	10,569 (41.8)
Endometriosis + tubal factor	7,401 (29.3)
Endometriosis + diminished ovarian reserve	5,558 (22.0)
Endometriosis + PCOS or ovulation disorder	3,686 (14.6)
Endometriosis + uterine factor	2,748 (10.9)
Endometriosis + noninfertile	632 (0.3)
Endometriosis + PGD	53 (0.2)
Endometriosis + other	6,115 (24.2)

Note: Values are number (percentage). PCOS = polycystic ovary disorder; preimplantation genetic diagnosis.

[a]Total percentages >100% owing to overlapping diagnoses.

Senapati. Endometriosis and IVF outcomes. Fertil Steril 2016.

- Endometriosis, when isolated or with concomitant diagnoses, was associated with lower oocyte yield compared with those with unexplained infertility, tubal factor, and all other infertility diagnoses combined.
- **Women with isolated endometriosis had similar or higher live birth rates compared with those in other diagnostic groups**.
- However, women with endometriosis with concomitant diagnoses had lower implantation rates and live birth rates compared with unexplained infertility, tubal factor, and all other diagnostic groups.

Is endometriosis per se associated with inferior pregnancy rates in IVF cycles?

ALL STAGES -------NO

III-IV------PROBABLY YES

Oocyte-Embryo quality

Oocyte Donation and Endometriosis: What Are the Lessons?

2013

Erik E. Hauzman, MD[1] Juan A. Garcia-Velasco, MD[1,2] Antonio Pellicer, MD[3,4]

[1] Division of Reproductive Endocrinology and Infertility IVI-Madrid
[2] Department of Obstetrics and Gynecology, Rey Juan Carlos University, Madrid, Spain
[3] Division of Reproductive Endocrinology and Infertility IVI-Valencia
[4] Department of Pediatrics, Obstetrics and Gynecology, Valencia University, Valencia, Spain

Address for correspondence and reprint requests Juan A. Garcia-Velasco, MD, IVI Madrid, Avda del Talgo 68-70, 28023 Madrid, Spain (e-mail: juan.garcia.velasco@ivi.es).

Semin Reprod Med 2013;31:173–177

Pateint with endometriosis, who received oocytes from healthy donors, show similar reproductive outcome as oocyte recipients without endometriosis

Conversely, the pregnancy rates were lower in subjects without endometriosis who received donor oocytes from subjects with endometriosis

		ted by endometri-
		es donated by ecipients without ot affected in sis with oocytes ut known
		affected by recip-
		s (i. e., proportion
Bodri et al[40]	Retrospective matched case-control study of cycles with discordant outcomes	No differences in indications (i.e., proportion of endometriosis patients)

PR, pregnancy rate; IR, implantation rate; MR, miscarriage rate; LBR, live-birth rate.

Studies on oocyte donation cycles have reinforced the role of oocyte quality in infertile patients with the disease

Targeting oxidative stress to treat endometriosis

Avi Harlev, Sajal Gupta & Ashok Agarwal PhD HCLD (ABB) EMB (ACE)

To cite this article: Avi Harlev, Sajal Gupta & Ashok Agarwal PhD HCLD (ABB) EMB (ACE) (2015) Targeting oxidative stress to treat endometriosis, Expert Opinion on Therapeutic Targets, 19:11, 1447-1464, DOI: 10.1517/14728222.2015.1077226

To link to this article: http://dx.doi.org/10.1517/14728222.2015.1077226

2015

Published online: 10 Aug 2015.

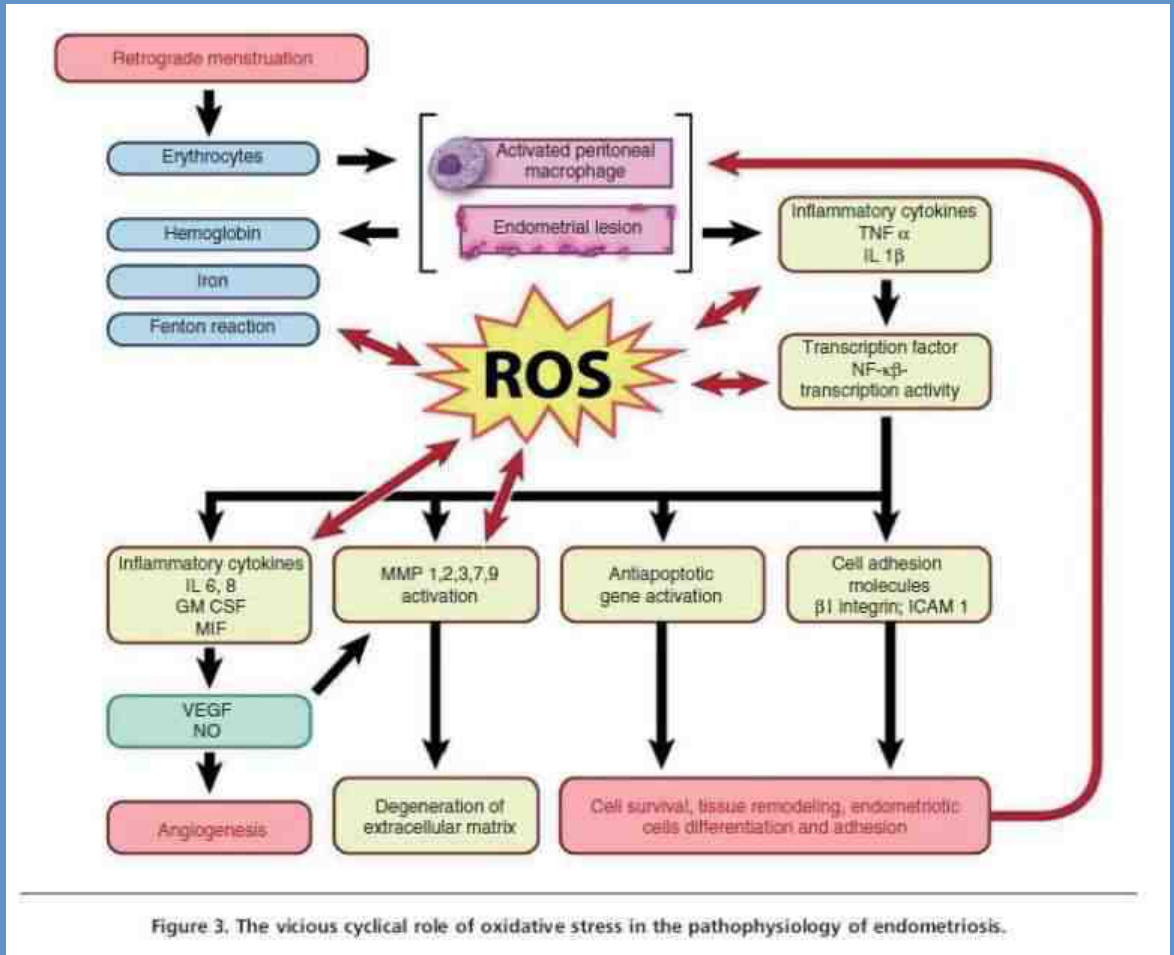


Figure 3. The vicious cyclical role of oxidative stress in the pathophysiology of endometriosis.

The role of antioxidative measures in the treatment of endometriosis

- Vitamins C and E
- Resveratrol
- Melatonin
- Xanthohumol
- Epigallocatechin-3-gallate

IVF/ICSI for Endometriosis
Oocyte Quality

- Detrimental effect
- *Saito H et, 2002*
- Barcelos ID et al.- 2009
- AK Singh et al. -2013
- Karuputhula et al. 2013
- Dib et al.- 2013
- Da Broi MG et al.- 2014
- PT Goud et al.-2014
- Xu B et al.-2015
- Choi YS et al.- 2015
- Barcelos ID et al. -2015

- No detrimental effect

IVF/ICSI for Endometriosis

Embryo Quality

- Detrimental effect
  - Yanushpolsky et al-1998
  - Pellicer et al-1995
  - Kumbak et al-2008
- No detrimental effect
  - Suzuki et al-2005
  - Tocci et al-2010
  - Tinkanen et al-2000
  - Reinblatt et al-2011
  - Filippi F-2014

Is endometriosis per se associated with decreased oocyte qualit in IVF cycles?

OOCYTE --------YES
EMBRYO-----PROBABLY NO

Does surgery affect IVF outcome ?

Second surgery for recurrent unilateral endometriomas and impact on ovarian reserve: a case-control study

2015

2015

TABLE 2

Comparison of ovarian reserve before second surgery in case subjects and at similar follow-up in control subjects.

Variable	Case (n = 18)	Control (n = 18)	*P* value
AMH (ng/mL), mean ± SD	2.7 ± 1.9	3.1 ± 1.9	.59
Basal FSH (mIU/mL), mean ± SD	8.7 ± 3.9	8.4 ± 3.7	.85
Total AFC (n), median (range)	8 (4–15)	9 (5–15)	.37
AFC in the healthy ovary (n), median (range)	5.5 (3–9)	6 (2–12)	.54
AFC in the affected ovary (n), median (range)	2 (1–6)	3 (1–5)	.24
Volume of the affected ovary in case subjects and of the previously operated ovary in control subjects (cm^3), mean ± SEM	95.0 ± 22.2	6.8 ± 0.4	< .001
Volume of the healthy ovary (cm^3), mean ± SEM	6.9 ± 0.3	6.6 ± 0.3	.44

Note: Abbreviations as in Table 1.

Ferrero. Ovarian reserve and recurrent surgery. Fertil Steril 2015.

Comparison of ovarian reserve before and after second surgery in case subjects.

Variable	Before second surgery (n = 18)	After second surgery (n = 18)	*P* value
AMH (ng/mL), mean ± SD	2.7 ± 1.9	1.2 ± 1.2	< .001
Basal FSH (mIU/mL), mean ± SD	8.7 ± 3.9	14.9 ± 6.6	< .001
Total AFC (n), median (range)	8 (4–15)	6.5 (4–13)	.34
AFC in the healthy ovary (n), median (range)	5.5 (3–9)	5.5 (4–12)	.65
AFC in the affected ovary (n), median (range)	2 (1–6)	1 (0–4)	.005
Volume of the affected ovary (cm^3), mean ± SEM	95.0 ± 22.2	4.7 ± 0.2	< .001
Volume of the healthy ovary (cm^3), mean ± SEM	6.9 ± 0.3	6.4 ± 0.2	.23

Note: Abbreviations as in Table 1.

Ferrero. Ovarian reserve and recurrent surgery. Fertil Steril 2015.

ASRM practice committee, Endometriosis and infertility Surgery 2012

- Benefits and risks to be balanced by the clinician
  - PRO
    - Prevention of rupture
    - Facilitate oocyte retrieval
    - Detection of occult malignancy
    - Avoidance of contamination of follicular fluid
    - Avoidance of progression of endometriosis
  - CONTRA
    - Surgical trauma
    - Surgical complications
    - Surgical costs
    - Potential decreased ovarian response
    - No proven benefit on ART outcome

- If no surgery
  - AVOID puncturing the cyst during egg aspiration
    - If you do: switch to clean needle, consider longer AB
  - Always under antibiotics
  - Inform patients on infection risks
    - Ovarian abscess !
  - Inform patients on not aspirating unaccessible follicles
  - Inform patients on possible evolution of the cyst in pregnancy

- If opting for surgery
  - Appropriate expertise, refer if necessary
  - Try to avoid repeat surgery
  - Treat other endometriosis lesions as well
    - Importance of preop work-up
- Patient preference

Treatment of infertility associated with deep endometriosis: definition of therapeutic balances

2015

Edgardo Somigliana, M.D., Ph.D.,[a] and Juan Antonio Garcia-Velasco, M.D., Ph.D.[b]

[a] Fondazione Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy; and [b] IVI-Madrid and Rey Juan Carlos University, Madrid, Spain

TABLE 2

Success rates of IVF in women with deep endometriosis.

Study (reference)	Study period	Country	Study design	Type of lesions	Data given	No. of patients	CP (%)	Live births (%)
Bianchi et al., 2009 (35)	2005–08	Brazil	Prospective	DE	Per cycle	105	24%	n.r.
Matthieu d'Argent et al., 2010 (36)	2007–08	France	Retrospective	Colorectal endometriosis	Per cycle	29	12 (41%)	8 (27%)
Ballester et al., 2012 (37)	2007–08	France	Retrospective	DE + endometrioma	Per patient	73	35 (48%)	n.r.
Ballester et al., 2012 (38)	2005–11	France	Prospective	Colorectal endometriosis	Per patient	75	32 (43%)	n.r.
Ballester et al., 2012 (39)	2007–10	France	Prospective	DE	Per patient	142	86 (61%)	n.r.
Papaleo et al., 2014 (40)	2008–09	Italy	Retrospective	DE	Per patient	24	7 (29%)	n.r.

Note: Literature review on studies specifically reporting on IVF results in women with deep endometriosis (January 2000 to June 2015). CP = clinical pregnancy; DE = deep endometriosis; n.r. = not recorded.

Original Article

Impact of Laparoscopic Surgical Management of Deep Endometriosis on Pregnancy Rate

N:115

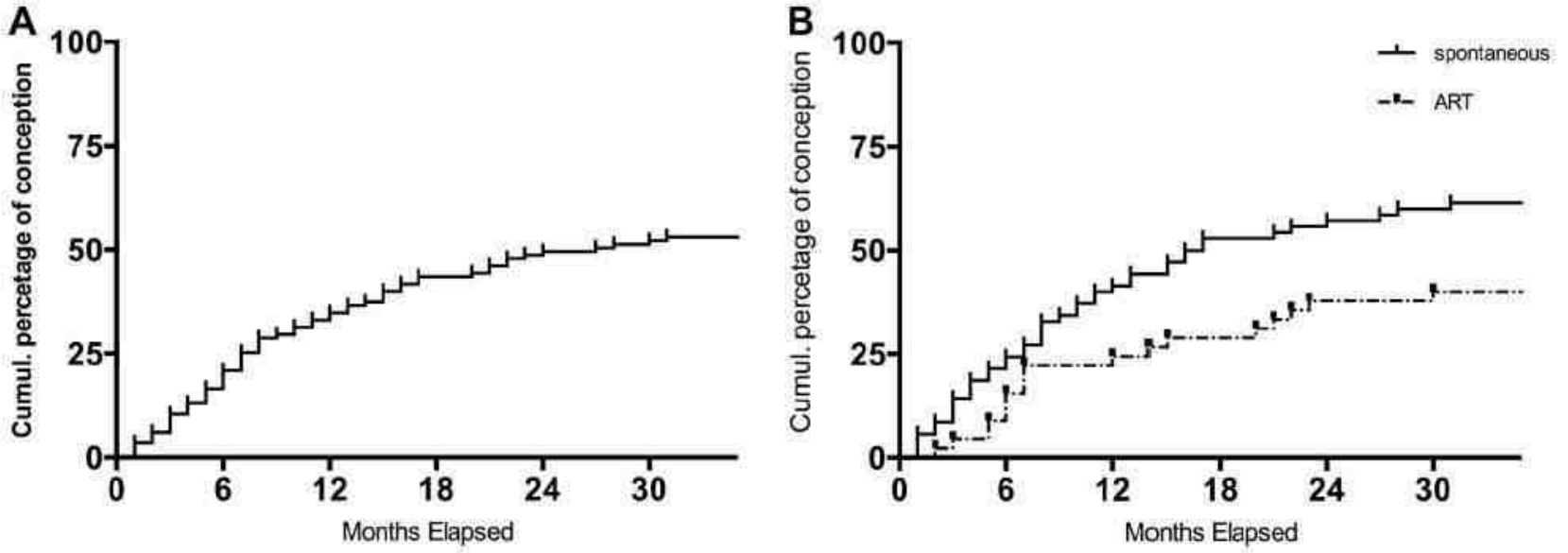
Gabriele Centini, MD, Karolina Afors, MD, Rouba Murtada, MD, István Máté Argay, MD, Lucia Lazzeri, MD, PhD, Cherif Youssef Akladios, MD, PhD, Errico Zupi, MD*, Felice Petraglia, MD, and Arnaud Wattiez, MD, PhD

From the IRCAD (Drs. Centini, Afors, Murtada, Argay, and Wattiez), Hopitaux Universitaires, Strasbourg, France, Department of Molecular and Developmental Medicine (Drs. Centini, Lazzeri, Zupi, and Petraglia), University of Siena, Siena, Italy, and CHRU de Strasbourg, Pôle de Gynécologie-Obstétrique (Dr. Akladios), Hôpital de Hautepierre, Strasbourg, France.

2016

Fig. 2

(A) Cumulative percentage of conception regardless of postoperative fertility treatment. (B) Cumulative percentage of conception according to the chance to conceive spontaneously. ART = patients referred directly to assisted reproduction; spontaneous = patients who tried to conceive spontaneously for 12 months before being referred to ART.



This study demonstrates that laparoscopic excision of deep endometriosis enhances pregnancy rate, by both spontaneous conception and ART.

DIE-Infertility

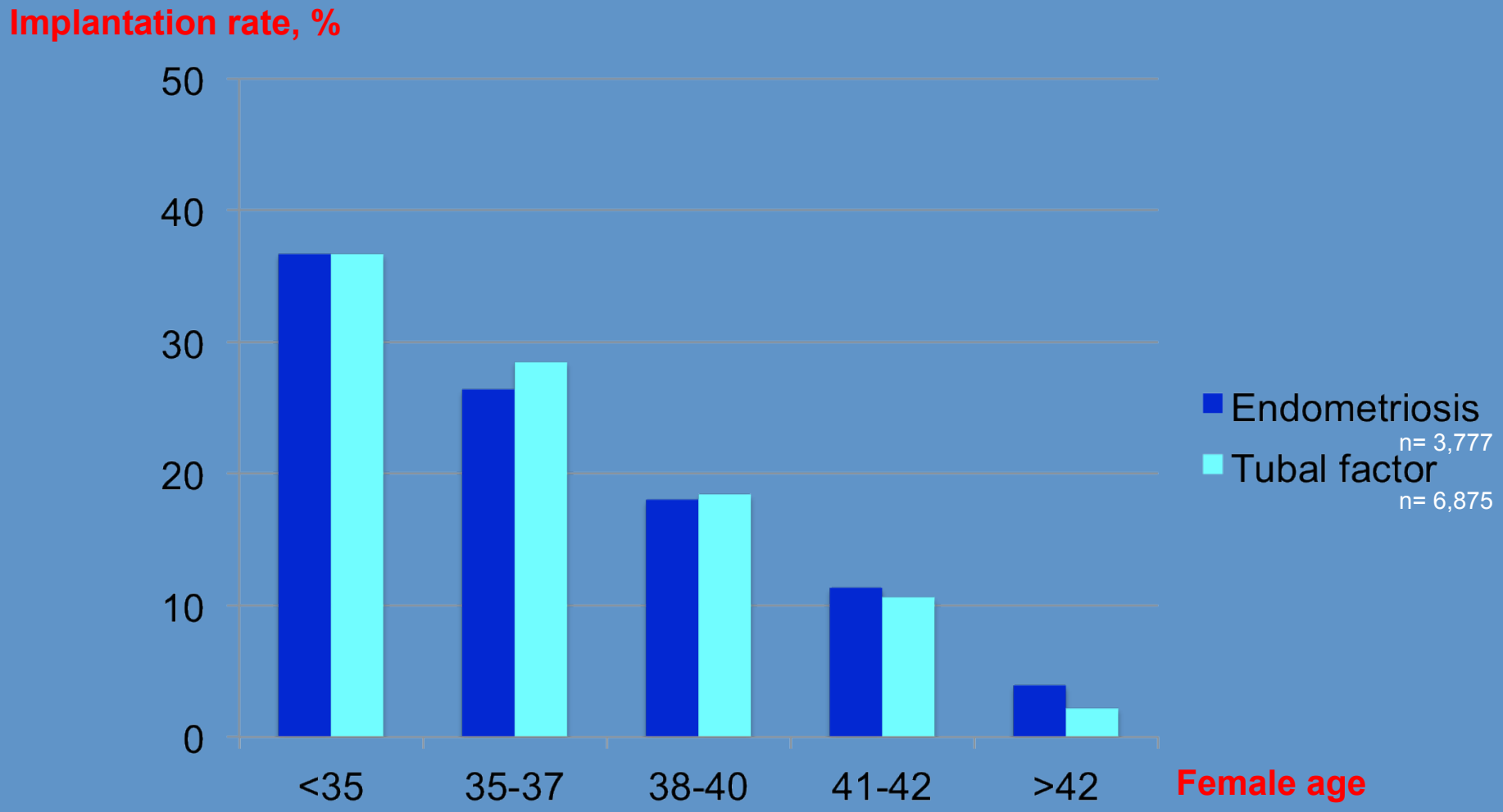
- Asymptomatic Cases----- ART
  - After 2 IVF failures, surgery should be considered
- Symptomatic (pain) cases
  - Both surgery and ART have satisfactory pregnancy rates
  - Shaving/discoid or segmental resection---best fertility result is not clear
  - No severe pain---- First ART
  - Severe pain ------- first surgery, wait for 6 mounths for spontan conception-----ART

WHİCH PATİENTS CAN HAVE GOOD RESULT WİTH ENDOMETRIOSIS SURGERY FOR PROMOTING FERTILITY ?

Surgery should be considered in patients younger than 35 years with good ovarian reserve and without male or tubal factors

Endometrial receptivity (Implantation)

SART-2010 (*n=146,693 cycles; 4% for Endometriosis)*



- The aim of this study was to assess the endometrial receptivity gene signature in patients with different stages of endometriosis by investigating transcriptomic modifications of their endometrium using the endometrial receptivity array (ERA) test.
- Gene expression microarray was used to diagnose the receptivity status by quantifying the expression of 238 specific genes directly related to human endometrial Receptivity
- None of the 238 genes present in the ERA array were significantly over- or under- expressed in any of different stages of the disease compared with controls.
- Endometrial receptivity gene signature during the implantation window does not vary significantly among patients with endometriosis even considering different stages compared with healthy women.

Is endometriosis per se associated with decreased implantation rate in IVF cycles?

PROBABLY NO

Prolonged GnRHa treatment prior to ART in women with endometriosis

- Limited evidence that 3 months of GnRH agonist use may improve chance of conception; live births were not assessed and there was little evidence of patient acceptability of side effects
- Is there a real benefit?
- Disadvantages
  - Cost
  - Difficult ovarian stimulation
- What are the mechanisms?
  - Suppression of endometriosis
  - Endometrial re-setting
- Can similar benefit be achieved by other means?
  - Other medical treatment options
  - Cryopreservation and FET

IVF/ICSI in patients with severe endometriosis

Table 2 Outcome parameters.

	Total group (n = 113)	*No long-term pituitary down-regulation (n = 45)*	*Long-term pituitary down-regulation (n = 68)*
Total oocytes	8.9 ± 6.2	9.0 ± 6.4	8.9 ± 6.2
Fertilization	0.57 ± 0.24	0.56 ± 0.25	0.58 ± 0.24
Total embryos	5.1 ± 4.1	5.2 ± 4.5	5.1 ± 3.8
Total cryopreserved embryos[a]	3.3 ± 3.4	3.2 ± 3.2	3.2 ± 3.6
Embryo transfer[b]			
Single-embryo transfer	86 (92.5)	35 (92.1)	51 (92.7)
Double-embryo transfer	7 (7.5)	3 (7.9)	4 (7.3)
Implantation[a,b]	0.29 ± 0.46	0.28 ± 0.45	0.30 ± 0.47
Clinical pregnancy	27 (23.9)	10 (22.2)	17 (25.0)
Miscarriage	5 (4.4)	1 (2.2)	4 (5.9)
Ongoing pregnancy	22 (19.5)	9 (20.0)[c]	13 (19.1)
Total cryopreserved ET cycles per woman[a]	1 (0–4)	2 (0–3)	1 (0–4)
Total cryopreserved embryos transferred[a,e]	1 (0–4)	2 (0–3)	1 (0–4)
Ongoing pregnancy after cryopreserved ET cycles[f]	12 (10.6)	1 (2.2)	11 (16.2)
Ongoing pregnancy fresh + cryopreserved ET cycles	34 (30.1)	10 (22.2)[c]	24 (35.3)
Patients with ≥1 cryopreserved embryo left[g]	11 (24.4)	3 (18.8)	8 (27.6)
Complication[b]	3 (2.7)	0	3 (4.4)
Recurrence	3 (2.7)	0	3 (4.4)

Values are mean ± SD, *n* (%) or median (range).

[a] Mann–Whitney test.

From Van der Houven et al. RBM Online 2014

Live birth rate in fresh and frozen embryo transfer cycles in women with endometriosis

Ahmed M.F. Mohamed [a,c,*], Spyridon Chouliaras [a], Carolyn J.P. Jones [b], Luciano G. Nardo [a,b]

Table 1
Characteristics of women with endometriosis and the control nonendometriosis atients.

	Endometriosis $n=415$	Non-endometriosis $n=6871$	χ^2 test P value	Mann-Whitney test P value
Age	34 (21–46)	34 (19–47)		NS
FSH	6.4 (1.5–13.8)	6.4 (1.5–13.8)		NS
BMI	23.7 (21.9–6.1)	24.1 (21.7–27.2)		NS
Ethnicity				
White	319 (77%)	5359 (78%)		
Asian	75 (18%)	1099 (16%)		NS
Black	4 (1%)	68 (1%)		
Other	17 (4%)	345 (5%)		
Embryo:				
Single	147 (35.4%)	2441 (35.5%)		
Two	258 (62.2%)	4284 (62.3%)	NS	
Three	10 (2.4%)	146 (2.1%)		

Fresh vs Frozen

- Long down-regulated (day 21) regimen with uFSH, recFSH or hMG
- Cryopreserved embryos were transferred in down-regulated hormonally controlled cycles

Mohamed, EJOG, 2011

Fresh vs Frozen

Table 4
Direct comparison of fresh and frozen ET cycles alone.

		Endometriosis	Non-endometriosis	χ^2 test *P* value
		n = 148	*n* = 3375	
Frozen *n* = 3523	LBR	25 (16.9%)	403 (11.9%)	0.07
	CPR	27 (18.2%)	428 (12.7%)	0.04
		n = 267	*n* = 3496	
Fresh *n* = 3763	LBR	52 (19.5%)	675 (19.3%)	NS
	CPR	54 (20.2%)	730 (20.9%)	NS

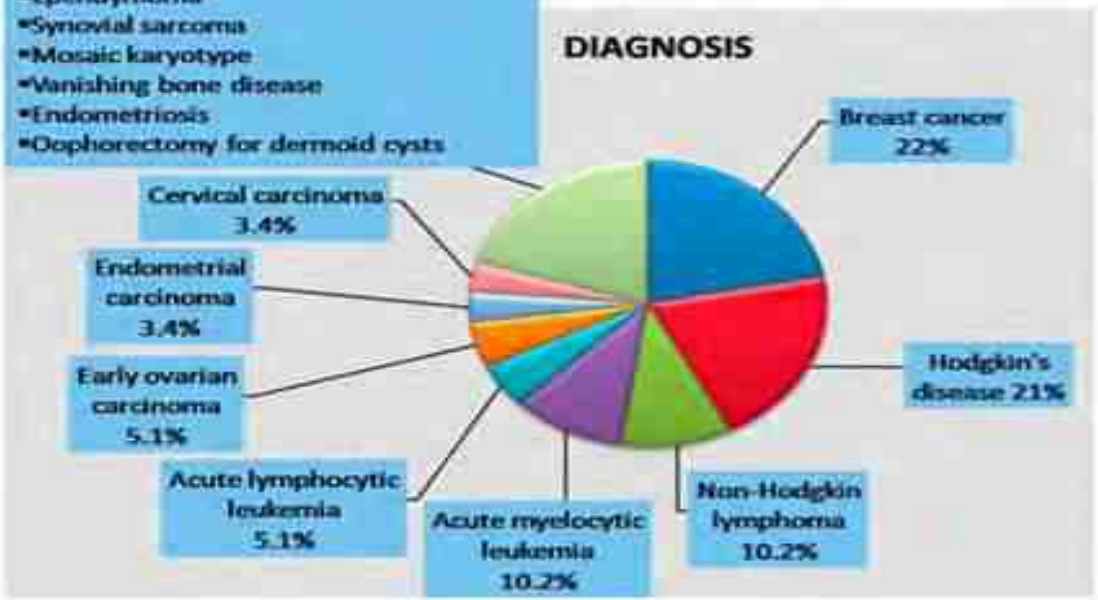
Unlike the general IVF population, in women with endometriosis frozen ET cycles result with higher LBR and CPR than frozen ET cycles in non-endometriosis group

Mohamed, EJOG, 2011

The role of fertility preservation in patients with endometriosis

Medical indications: numbers

OTHERS 20.3%
- Aplastic anemia
- Diamond-Blackfan Syndrome
- Myelodysplasia
- Thalassemia major
- Hemophagocytic lymphohistiocytosis
- Lupus nephritis
- Ependymoma
- Synovial sarcoma
- Mosaic karyotype
- Vanishing bone disease
- Endometriosis
- Oophorectomy for dermoid cysts



In ITALY:

61.000 women between 10-30 years at risk of premature ovarian failure *(ISTAT 2012)*

75.000 women suffering endometriosis *(Benaglia et al, 2010)*

2.500 women <40 years with diagnosis of breast cancer *(Globocan 2010)*

F.A.V.O.

Embryo/oocyte cryopreservation

PRO

- Documented results especially when embryos are frozen
- No risk of procedure-related ovarian reserve depletion
- The pick-up may avoid contact of the oocyte with the detrimental effect of the peritoneal fluid
- Patients suffering from endometriosis are frequent costumers of ART procedures

CONS

- Risk of infections related to oocyte retrieval and abscess formation
- Poor quality oocytes, embryos (controversial data)
- Need of ovarian stimulation that might cause the progression of the disease (controversial data)
- Need of repeated IVF cycles in order to collect an adequate number of oocytes that can be stored

What is the role of fertility preservation within endometriosis care?

- Fertility preservation in women with endometriosis: for all, for some, for none?
- There is insufficient evidence to support routine fertility preservation for women with endometriosis
- More clinical data and in-depth economic analysis are imperative prior to recommending its routine use.

Zheng et al. Reproductive Biology and Endocrinology (2015) 13:103
DOI 10.1186/s12958-015-0092-2

REPRODUCTIVE BIOLOGY AND ENDOCRINOLOGY

RESEARCH Open Access

Risk of endometrial polyps in women with endometriosis: a meta-analysis

Qiao-Mei Zheng[1†], Hong-luan Mao[1†], Yan-Jing Zhao[2], Jing Zhao[1], Xuan Wei[1] and Pei-Shu Liu[1*]

- Nine cohort studies and one case–control study including 2896 women were included in this meta-analysis.

The risk of EP increased in women with endometriosis compared with those without endometriosis (the pooled RR, 2.81; 95 % CI, 2.48–3.18).

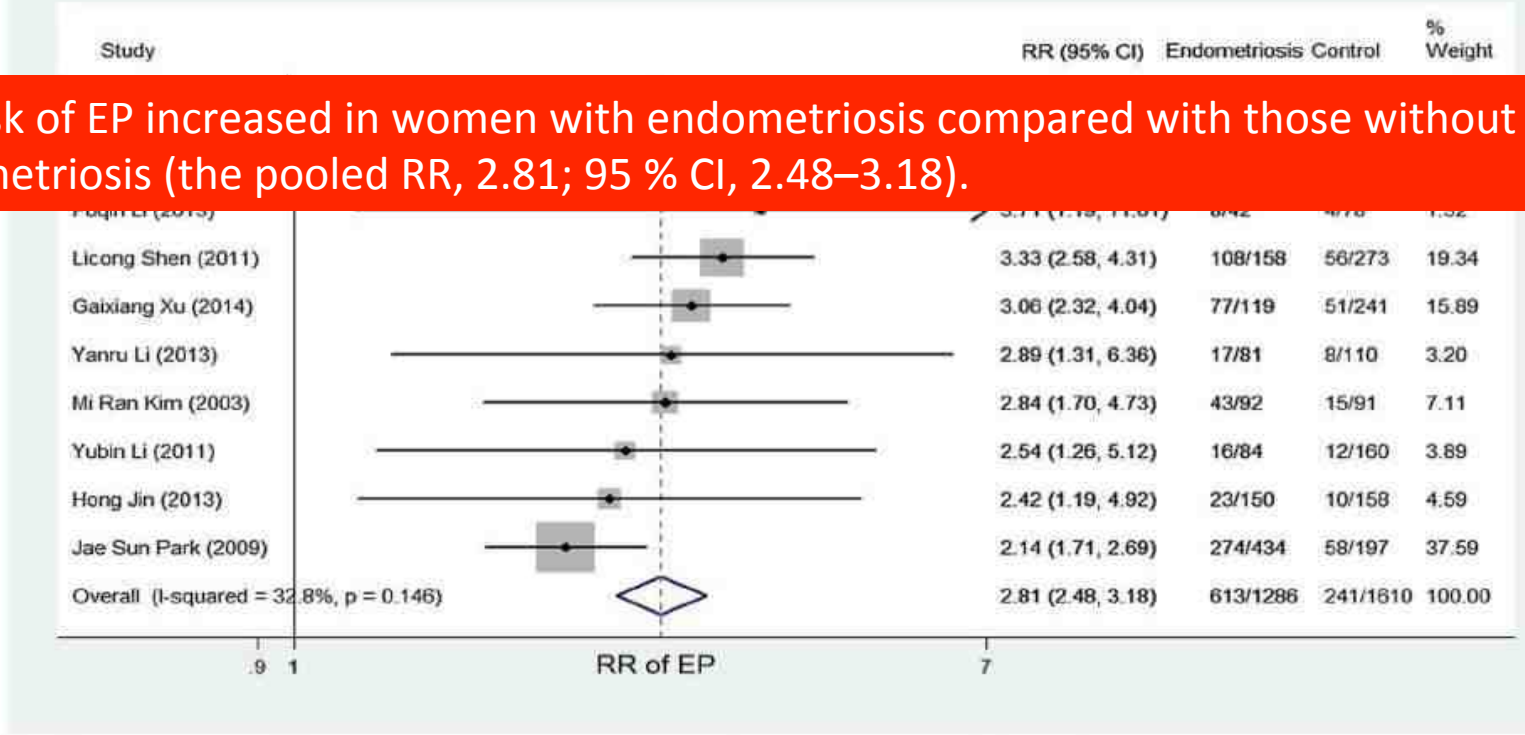


Fig. 2 Forest plot of the 10 included studies evaluating the association between endometriosis and EP

What is the effect of IVF on endometriosis (disease and symptoms)?

- Few studies have examined effect of IVF on endometriosis disease and symptoms; these have found there to be little effect

Endometriosis-related infertility: assisted reproductive technology has no adverse impact on pain or quality-of-life scores

Pietro Santulli, M.D., Ph.D.,[a,b] Mathilde Bourdon,[a] Marion Presse,[a] Vanessa Gayet, M.D.,[a] Louis Marcellin, M.D., Ph.D.,[a,b,c] Caroline Prunet,[d] Dominique de Ziegler, M.D.,[a] and Charles Chapron, M.D.[a,c]

2016

SUPPLEMENTAL TABLE 2

Impact of ART on severe pelvic pain symptoms in endometriosis and disease-free groups.

	Baseline			Synchronization			Stimulation			Postretrieval		
Groups	Disease-free (n = 104)	Endometriosis (n = 102)	*P* value	Disease-free (n = 104)	Endometriosis (n = 102)	*P* value	Disease-free (n = 104)	Endometriosis (n = 102)	*P* value	Disease-free (n = 104)	Endometriosis (n = 102)	*P* value
Dysmenorrhea	14 (13.5)	52 (51.0)	<.001[a]	3 (2.9)	4 (3.9)	.720[b]	NA	NA		18 (23.7)[f]	27 (38)[f]	.112[a]
Dyspareunia	2 (1.9)	11 (10.8)	.008[c]	1 (1.0)	8 (7.7)	.018[b]	1 (1.0)	5 (4.9)	.117[b]	5 (4.8)	2 (2.0)	.445[b]
Pelvic pain	2 (1.9)	8 (7.8)	.057[b]	0 (0.0)	3 (2.9)	.120[b]	7 (6.7)	14 (13.7)	.100[a]	6 (5.8)	11 (10.8)	.191[a]
GI symptoms	0 (0.0)	9 (8.8)	.001[b]	0 (0.0)	4 (3.9)	.058[b]	0 (0.0)	5 (4.9)	.028[b]	0 (0.0)	7 (6.9)	.007[b]
LUT symptoms	0 (0.0)	1 (1.0)	.495[b]	0 (0.0)	1 (1.0)	.495[b]	0 (0.0)	1 (1.0)	.495[b]	1 (1.0)	1 (1.0)	1.00[b]

Note. Data are mean ± n (%) unless otherwise specified. Severe pain is defined as visual analogic scale (VAS) ≥ 7. GI = gastrointestinal; LUT = low urinary tract; NA = not applicable. [a] Pearson's chi-square test. [b] Fisher's exact test. [c] Mean calculation in nonpregnant patients after IVF (76 in disease-free group, 71 in endometriosis group).

Santulli. Pain during ART in endometriosis. Fertil Steril 2016.

After multiple linear regression, no worsening of pain was observed in the endometriosis group as compared with disease-free group.

In addition subgroup analysis according to endometriosis phenotype failed to show any increase of pain.

TABLE 3

Fertility Quality of Life (FertiQoL) score in endometriosis and disease-free groups.

FertiQoL	Endometriosis group (n = 50)	Disease-free group (n = 75)	*P* value
Core FertiQoL			
Emotional	54.67 ± 17.24	58.94 ± 21.99	.249[a]
Relational	72.28 ± 18.75	71.28 ± 16.16	.582[a]
Mind–Body	60.46 ± 22.71	69.17 ± 21.40	.031[a]
Social	60.46 ± 18.55	66.89 ± 20.20	.072[a]
Total Core FertiQoL	61.04 ± 15.85	66.57 ± 17.81	.132[a]
Treatment FertiQoL			
Treatment environment	66.42 ± 13.88	63.91 ± 16.50	.374[a]
Treatment tolerability	57.60 ± 22.20	59.93 ± 19.40	.536[a]
Total Treatment FertiQoL	61.68 ± 16.90	60.36 ± 17.48	.671[a]
Total FertiQoL	61.23 ± 12.57	64.13 ± 15.30	.261[a]

Note: Data are mean ± standard error unless otherwise specified. All items reversed or scored so that higher scores indicate a more favorable quality of life. Scaled scores are computed to achieve a range of 0–100.

[a] Student's *t* test.

Santulli. Pain during ART in endometriosis. Fertil Steril 2016.

Minerva Ginecol. 2016 Jan 29. [Epub ahead of print]

Surgical evaluation of endometriosis progression after IVF as compared to controls who did not have ovarian stimulation. A retrospective cohort study.

2016

Crochet P[1], Lathi RB, Dahan MH, Ocampo J, Nutis M, Nezhat C.

Author information

Abstract

BACKGROUND: To examine the surgical findings at repeated surgeries for endometriosis and to compare disease progression in patients after IVF to those without interval fertility treatments.

METHODS: A Retrospective case-control study set at the referral center for gynecologic endoscopy at Stanford University. Women who had two surgeries for treatment of symptomatic endometriosis since 1997 were searched in the database. Twenty-one women were identified who underwent IVF treatment between the two procedures (IVF group), and compared to 36 women who did not receive any fertility treatment (controls). The main outcomes were time to recurrence and surgical findings including rASRM score. The presence and size of endometrioma, rectovaginal and para-rectal spaces location of endometriosis were also compared between the two surgical procedures.

RESULTS: Demographics in the two groups were similar. The change in rASRM score between surgeries was not significantly different (P=0.80) between the two groups. There was no difference between the two groups in the size and number of pathology proven endometriomas as well as no difference in the presence of rectovaginal and pararectal endometriosis.

CONCLUSION: No significant difference was found in the two groups, suggesting that IVF treatment does not lead to an accelerated progression of endometriosis in patients with recurrence.

Hum. Reprod. Advance Access published March 9, 2016
Human Reproduction, Vol.0, No.0 pp. 1–10, 2016
doi:10.1093/humrep/dew035

human reproduction ORIGINAL ARTICLE *Gynaecology*

Increased rate of spontaneous miscarriages in endometriosis-affected women

2016

Pietro Santulli[1,2,3,*], Louis Marcellin[1,2,3], Sophie Menard[1], Thibault Thubert[1], Babak Khoshnood[4], Vanessa Gayet[1], Francois Goffinet[4,5], Pierre-Yves Ancel[4,†], and Charles Chapron[1,2,3,†]

Table III Incidence rate ratio of previous miscarriage results from the random-effects Poisson regression analysis.

	IRR (95% CI)	*P*-value	Adjusted IRR[a] (95% CI)	*P*-values
Control patients	1	0.002	1	<0.001
Endometriosis-affected patients	1.47 (1.16–1.84)		1.64 (1.29–2.09)	
Control patients	1		1	
Superficial endometriosis	1.90 (1.27–2.85)	0.002	1.78 (1.20–2.65)	0.004
Endometrioma	1.38 (0.91–2.11)	0.130	1.77 (1.16–2.68)	0.008
DIE	1.36 (1.03–1.81)	0.030	1.55 (1.16–2.06)	0.003

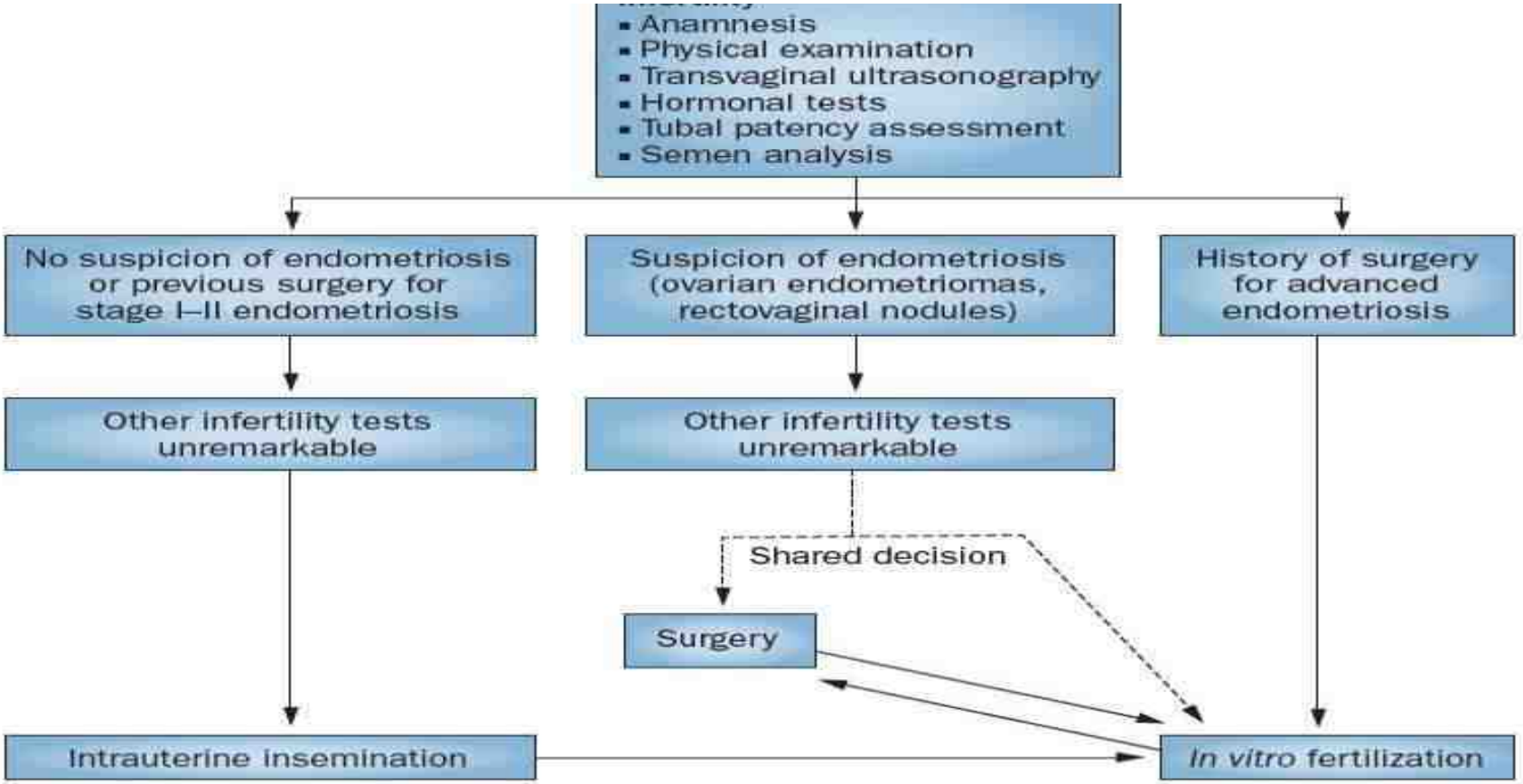
n, number of pregnancies.
[a]Adjusted for age, BMI, fertility status, previous infertility treatment and smoking habits.

After using a random-effects Poisson regression and adjusting for confounding factors, we found a significantly increased incidence rate ratio (IRR) for miscarriages in women with endometriosis (adjusted IRR: 1.70, 95% confidence interval: 1.34–2.16).

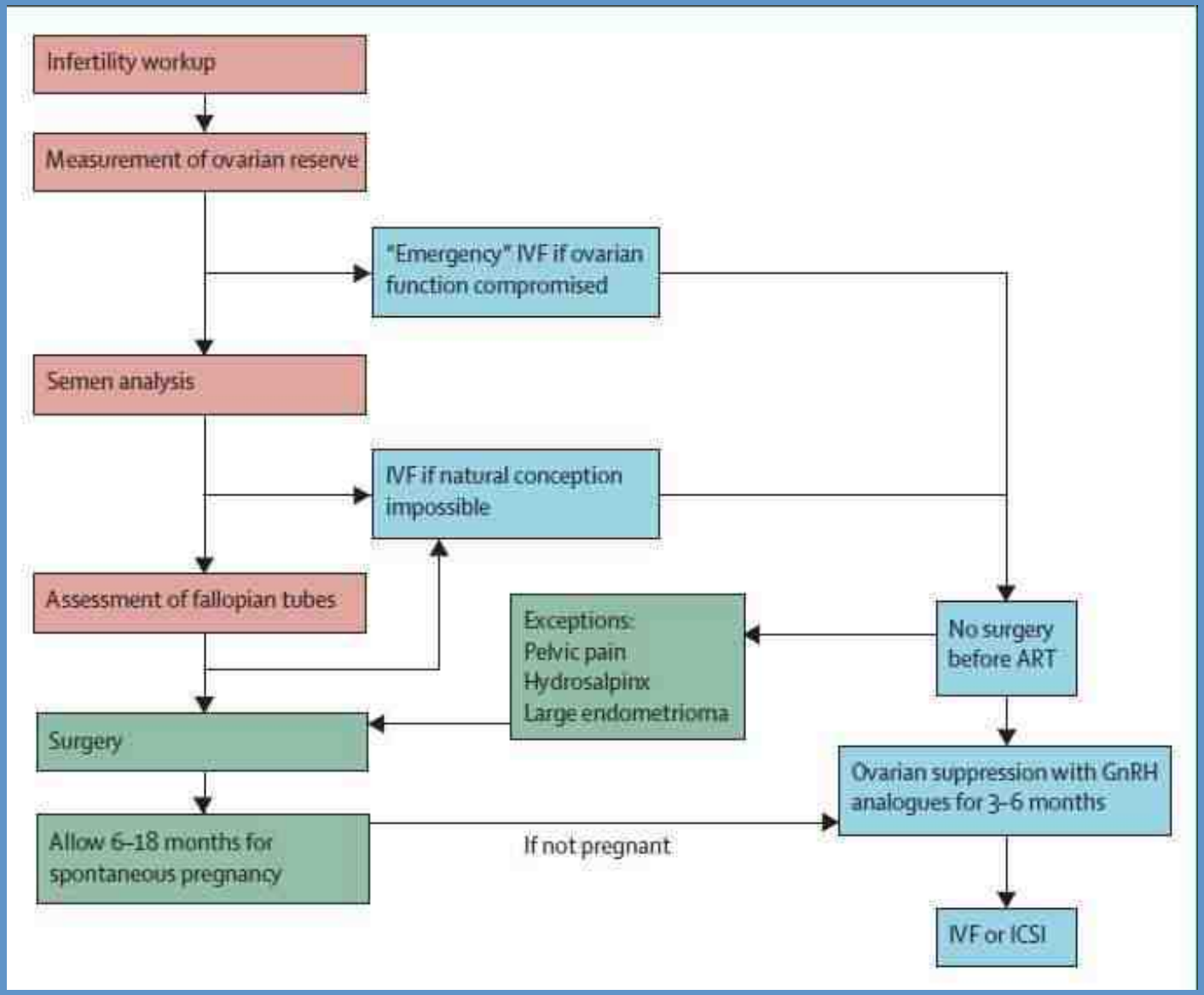
Vercellini, P. *et al. Nat. Rev. Endocrinol.* 10, 261–275 (2014); published online 24 December 2013

Endometriosis: pathogenesis and treatment

Paolo Vercellini, Paola Viganò, Edgardo Somigliana and Luigi Fedele



Algorithm for management of infertility associated with endometriosis



Dominique de Ziegler, 2010

THE JOURNAL OF OBSTETRICS AND GYNECOLOGY OF INDIA

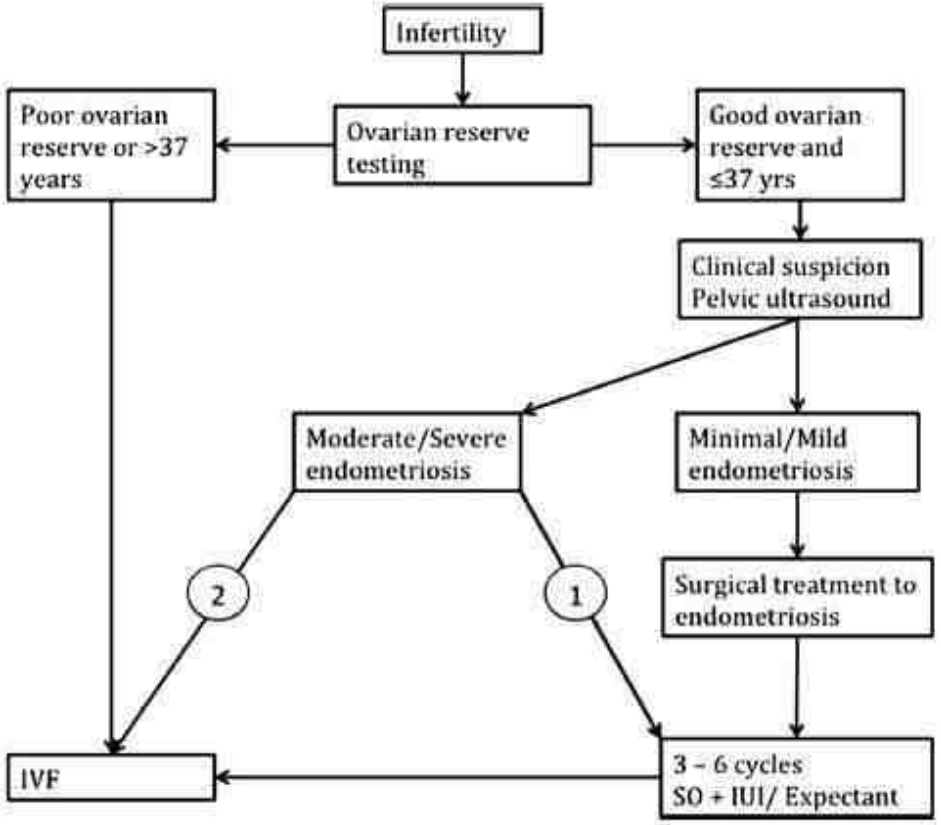
The Journal of Obstetrics and Gynecology of India (January–February 2015) 65(1):11–16
DOI 10.1007/s13224-014-0652-y

INVITED MINI REVIEW

Treatment of Endometriosis in Women Desiring Fertility

Mavrelos D. · Saridogan E.

Fig. 1 Algorithm for diagnosis and treatment of patients with endometriosis desiring fertility. / If the pelvic anatomy is restored and Fallopian tubes are found to be patent during laparoscopy 2 if pelvic anatomy is significantly distorted and/or Fallopian tubes found to be affected at laparoscopy



Conclusions

- COH/IUI improves pregnancy rates especially in early stages
- ART in women with endometriosis may be challenging due to reduced ovarian reserve
- Clinical pregnancy rates may not be different than other causes of infertility
- Live birth rates are the same as for other causes of infertility
- Medical treatment does not improve pregnancy rates but, adjunctive medical treatment requires further research
- Surgery for endometrioma prior to ART reduces ovarian reserve without improving pregnancy rates
- Surgical treatment of early stage endometriosis improves pregnancy rates
- Surgical treatment of advanced endometriosis improves pregnancy rates when tubal patency is restored