

Recent Developments in the Transmission of Human Life

19-21 January 2023

Berlin, Germany

Welcome to all Participants



Faculty Disclosure

I received grants, contracts, honoraria or consultation fees from:

IBSA
Ferring
Merck AG

I have no potential conflict of interest to declare

Endometriosis: a New ART Indication

Four recent new features

- 1. New approaches for **diagnosing** endometriosis
- 2. *Toxic-pelvic* condition on oocytes and embryos
- 3. Effects of endometriosis on the **eutopic endometrium**
- 4. Effects of surgery on **ovarian reserve**

Endometriosis: a New ART Indication

➤ 1. New approaches for diagnosing endometriosis

Diagnostic laparoscopy is not part of routine infertility workups because

- ART efficacy has tremendously improved
- Women seek infertility treatment at an older age

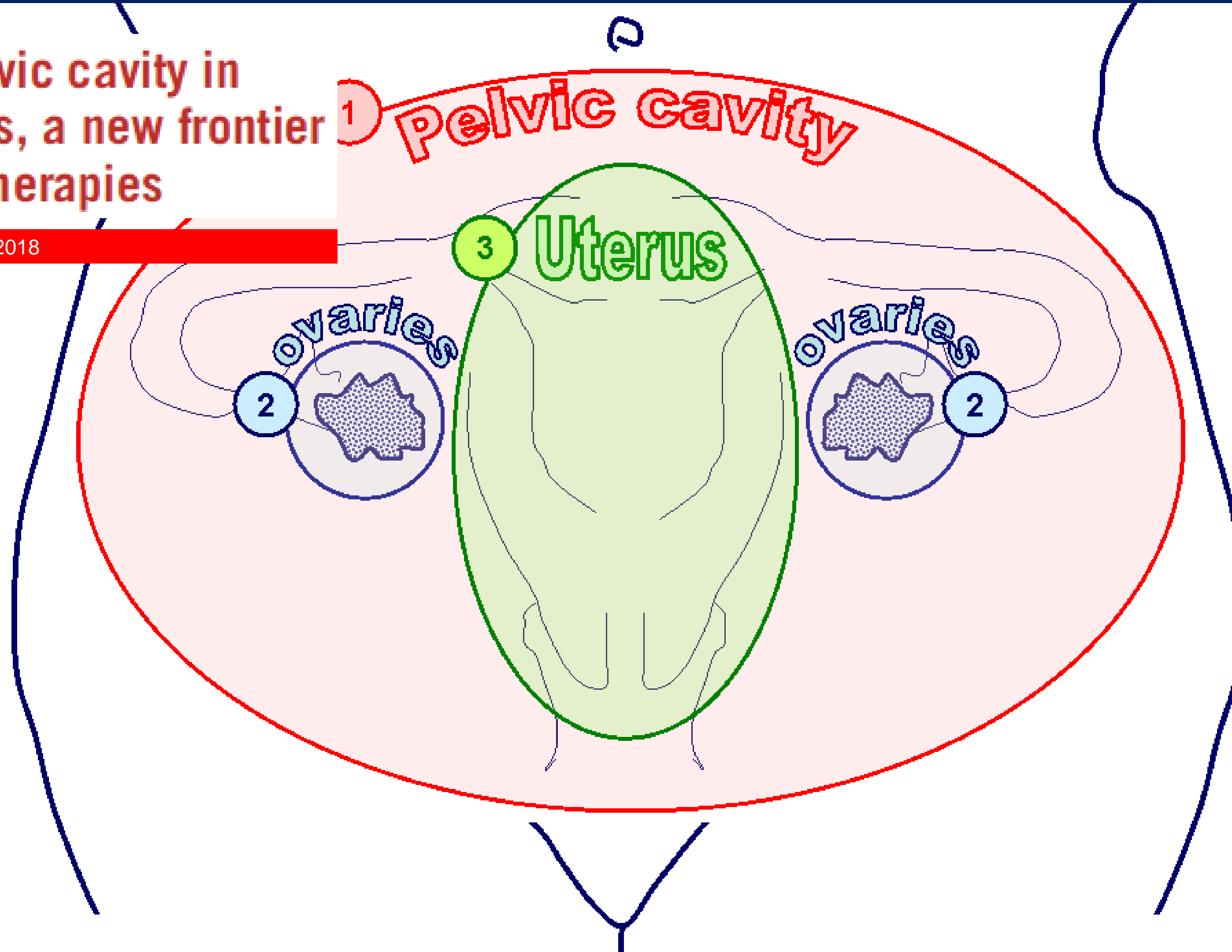
Imaging based approaches for diagnosing endometriosis are necessary, calling for systematic reading of:

- Ultrasound
- MRI

➤ 2. Toxic-pelvic condition on oocytes and embryos

The toxic pelvic cavity in endometriosis, a new frontier for medical therapies

de Ziegler et al. Fertil Steril 2018

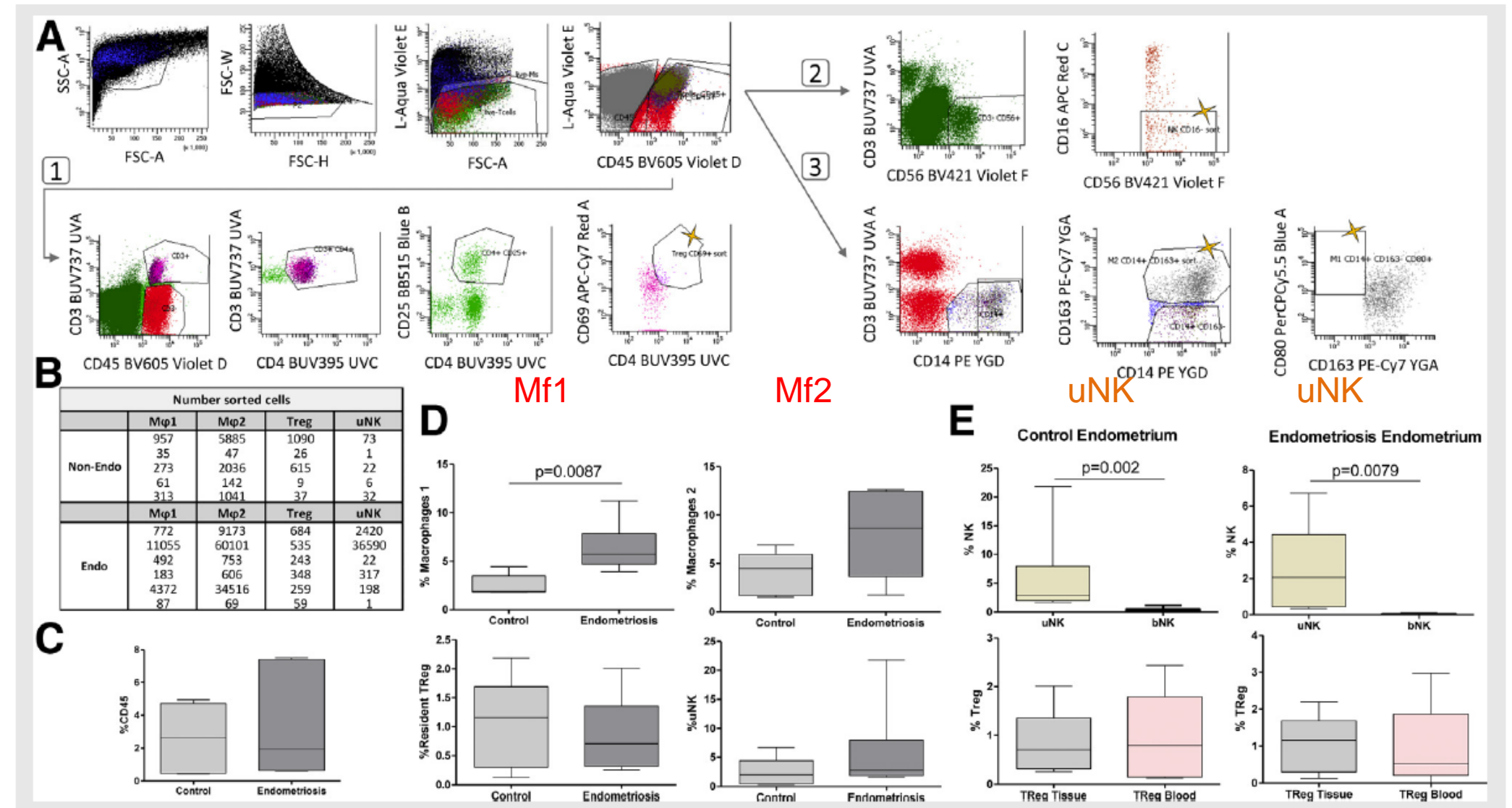


➤ 3. Effects of endometriosis on the eutopic endometrium & receptivity

Eutopic endometrium

In women with endometriosis, endometrial Mf1 are more proinflammatory
Mf2 paradoxically have a proinflammatory phenotype.

Vallve-Juanico J. et al. FS 2019

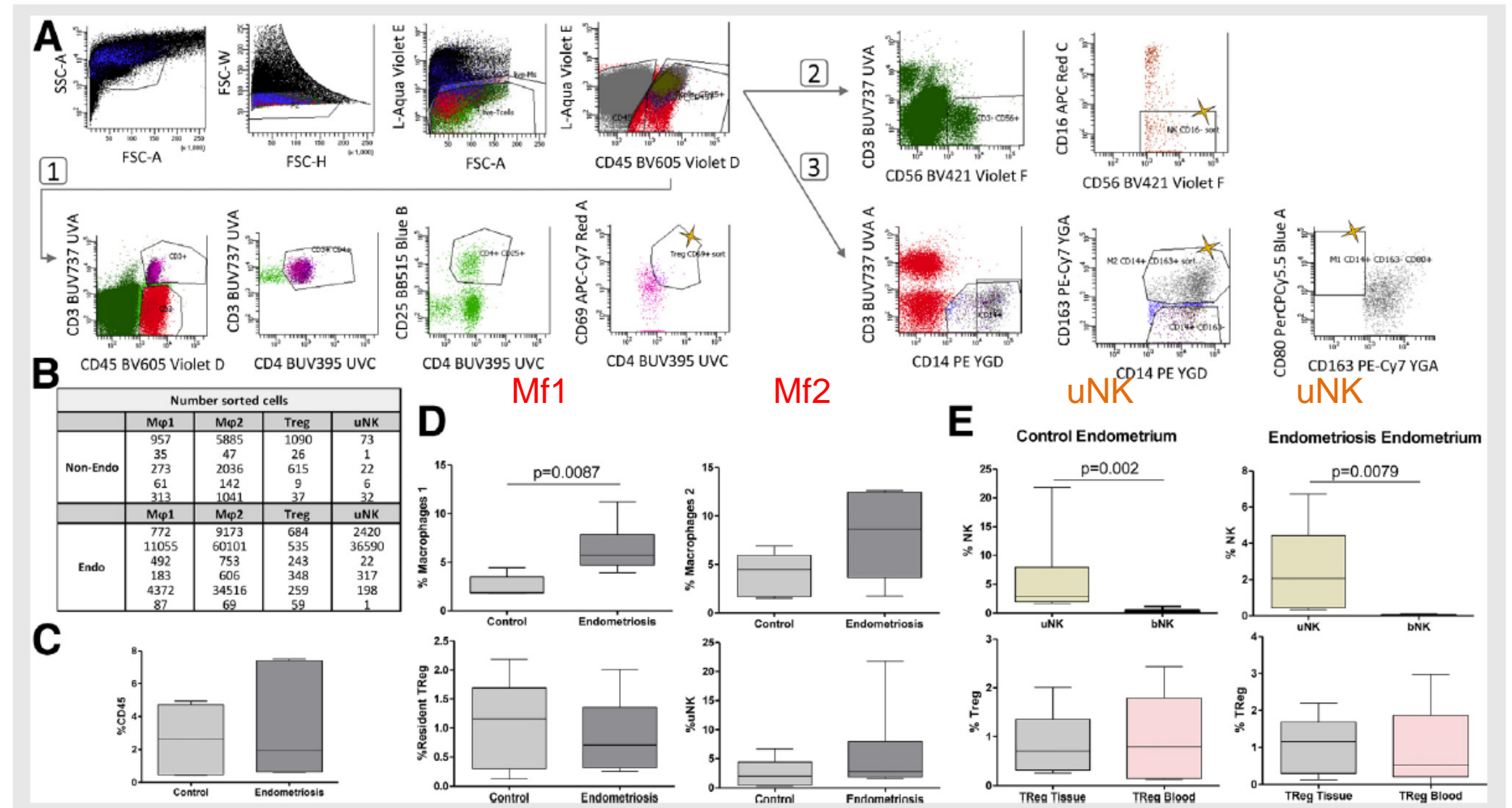


➤ 3. Effects of endometriosis on the eutopic endometrium & receptivity

Eutopic endometrium

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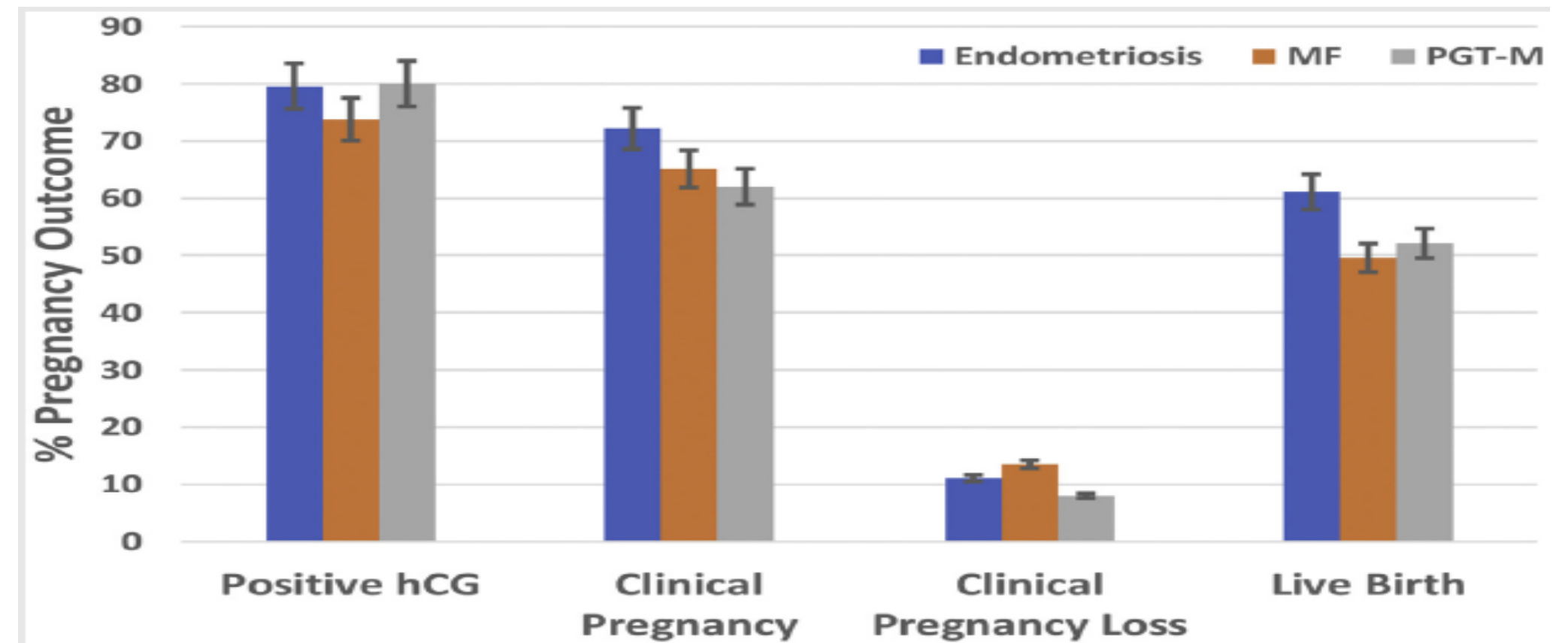
Vallve-Juanico J. et al. FS 2019



Endmetrial receptivity

In women with endometriosis, similar outcome following euploid blastocyst transfers.

Lauren Bishop et al. FS 2020



➤ 4. Effects of surgery on ovarian reserve

Effects of endometriosis – including endometriomas – on ovarian reserve is milder than originally envisioned.

Surgery for endometriosis – particularly, ovarian endometriomas – is more harmful than the disease itself.

As surgery does not improve ART outcome. Hence, no surgery before ART.

Diagnosis of endometriosis

Pathophysiology of endometriosis: oocyte quality

Endometriosis through women's age

Endometrial receptivity

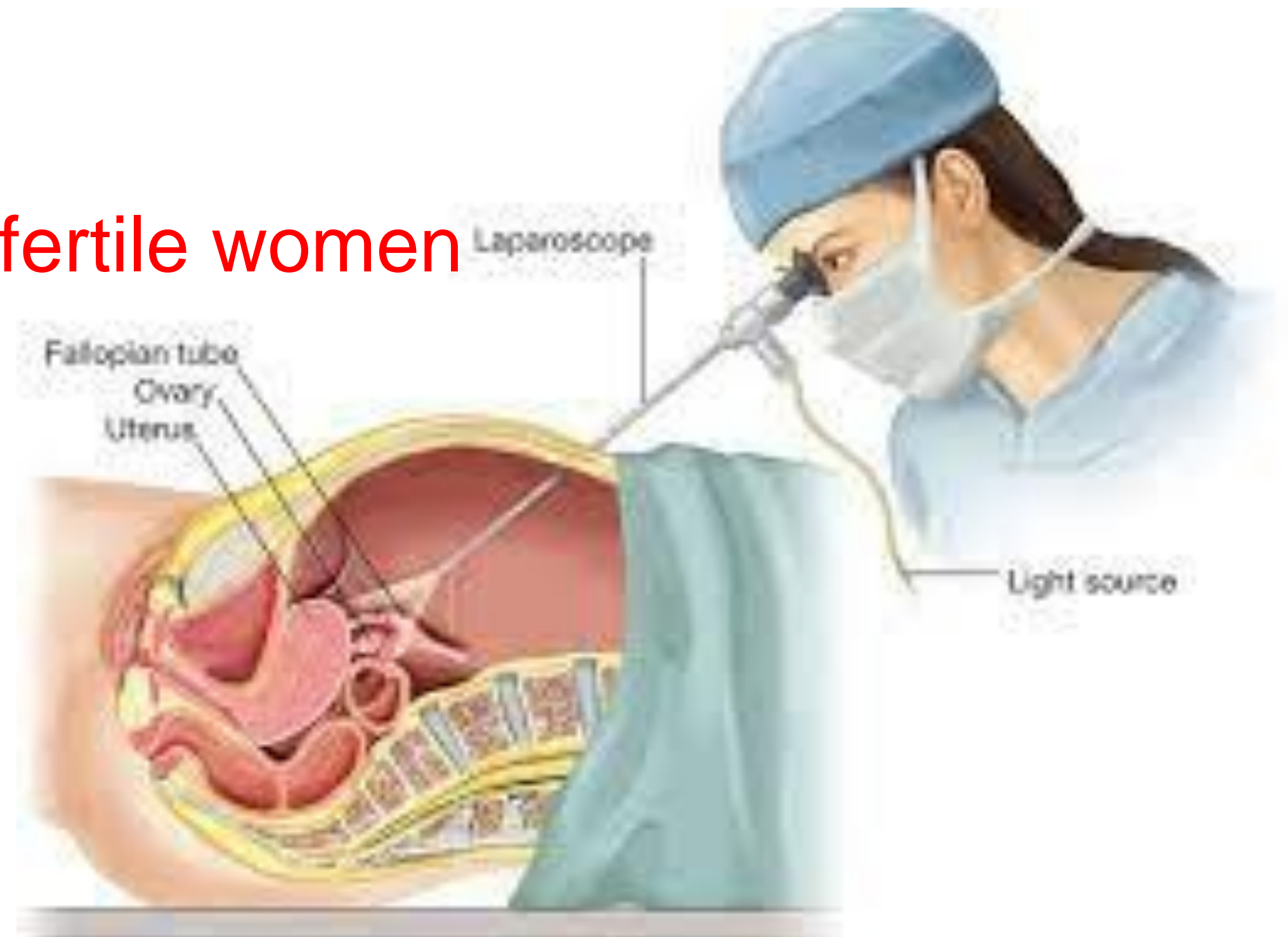
Surgery more harmful on ovarian reserve than endometriosis itself

Practical management

Routine diagnostic laparoscopies in Infertility

Practically abandoned because:

- High efficacy of ART
- Ever-increasing age of infertile women



Routine diagnostic laparoscopies in Infertility

Prevalence of endometriosis in infertile women

~10% of women in their reproductive years – 176 million women worldwide – 176 Millions worldwide

Zondervan KT, et al. Endometriosis. *Nat Rev Dis Primers* 2018; 4(1): 9.

25% - 50% of infertile have endometriosis

Missmer SA, et al. Incidence of laparoscopically confirmed endometriosis by demographic, anthropometric, and lifestyle factors. *Am J Epidemiol* 2004; **160**(8): 784-96.

Practice Committee of the American Society for Reproductive M. Endometriosis and infertility: a committee opinion. *Fertil Steril* 2012; **98**(3): 591-8.

Evans MB, Decherney AH. Fertility and Endometriosis. *Clin Obstet Gynecol* 2017; **60**(3): 497-502.

Routine diagnostic laparoscopies in Infertility

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

Fertil Steril 2016

- 400,059 cycles reported during 2008–2010,
- 347,185 cycles after excluding donor, gestational carrier, and banking cycles.

➤ **39,356 initiated cycles with endometriosis, (11%)**

- Of these, 14,053 cycles (4%) isolated endometriosis (Endometriosis Only),
- 25,303 cycles (7%) in endometriosis and additional diagnosis (Endometriosis Plus).

Routine diagnostic laparoscopies in Infertility

The abandon of routine diagnostic laparoscopies:

- Created a void for diagnosing endometriosis
- Causes a false impression of decreased prevalence
- Requires replacement diagnostic option

Endometriosis: Surgery or ART?

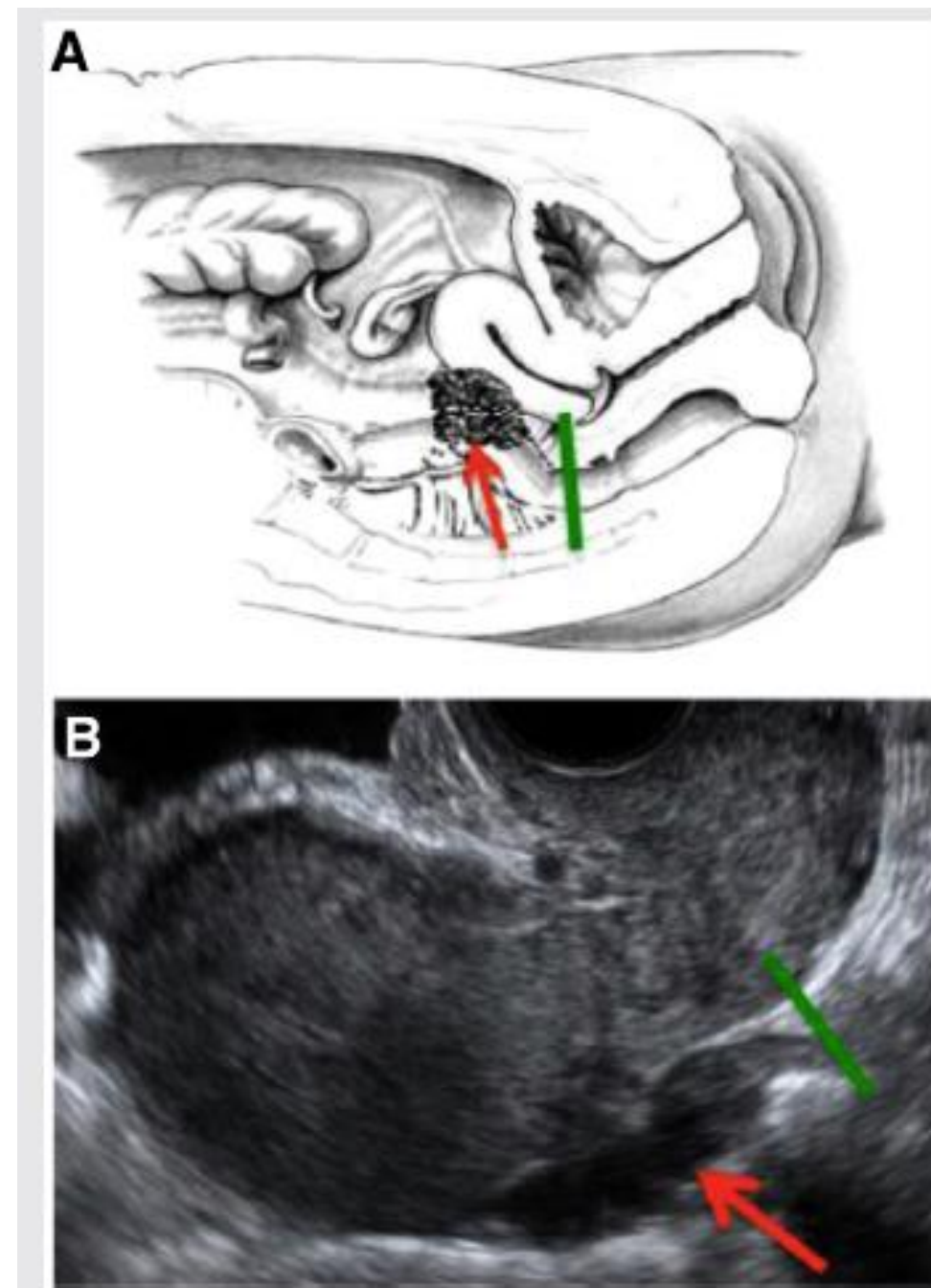
Ultrasound mapping system for the surgical management of deep infiltrating endometriosis

Caterina Exacoustos, M.D.,^a Mario Malzoni, M.D.,^b Alessandra Di Giovanni, M.D.,^b Lucia Lazzeri, M.D.,^c Claudia Tosti, M.D.,^c Felice Petraglia, M.D.,^c and Errico Zupi, M.D.^c

Dx of endometriosis

Endometriosis: Surgery or ART?

LOCATION	LESION		
POSTERO-LATERAL DIE			
NODULE			
No	Yes <1 cm	Yes 1-3 cm	Yes > 3cm
RIGHT USL			
No	Yes		
LEFT USL			
No	Yes		
TORUS			
No	Yes		
RIGHT PARAMETRIUM			
No	Yes		
LEFT PARAMETRIUM			
No	Yes		
RIGHT URETER			
No	Compression	Dilatation	
LEFT URETER			
No	Compression	Dilatation	
RVS			
No	Yes		
VAGINA			
No	Yes	mm	
CRANIAL RECTUM			
No	Yes		
Wall infiltration grade			
Superficial	Full thickness		
CAUDAL RECTUM			
No	Yes		
Wall infiltration grade			
Superficial	Full thickness		
DOUGLAS [D]			
DOUGLAS POUCH OBLITERATION			
No	Yes partial	Yes complete	
ANTERIOR DIE			
BLADDER			
NODULE			
No	Yes	mm	
Distance from right ureter: mm			
Distance from left ureter: mm			
ADHESIONS			
No	Yes		
ADNEXAL ENDOMETRIOSIS			
ADNEXA			
ENDOMETRIOMA (right ovary)			
No	Yes mm		
ADHESIONS (right ovary)			
No	Yes site:		
RIGHT TUBE			
No	Yes mm		
ENDOMETRIOMA (left ovary)			
No	Yes mm		
ADHESIONS (left ovary)			
No	Yes site:		
LEFT TUBE			
No	Yes mm		
OTHER SITES			



Upper rectal endometriotic nodule. (A) Anatomical schematic showing an upper rectum deep infiltrating endometriosis nodule (red arrow) above the hypothetical horizontal plane passing at the level of the insertion of uterosacral ligaments and dividing low (caudal) and upper (cranial) rectum (green line). (B) Transvaginal ultrasound view showing the uterus in longitudinal section with a hypoechoic retrouterine lesion adherent to the rectosigmoid junction (red arrow).
Exacoustos. DIE ultrasound-surgical mapping system. Fertil Steril 2014.

Dx of endometriosis

Endometriosis: Surgery or ART?

Magnetic resonance imaging structured reporting in infertility

Guillermina Montoliu-Fornas, M.D., Ph.D. and Luis Martí-Bonmatí, M.D., Ph.D.

Radiology Department, Hospital Universitario y Politécnico La Fe, Valencia, Spain

Dx of endometriosis



Cochrane
Library

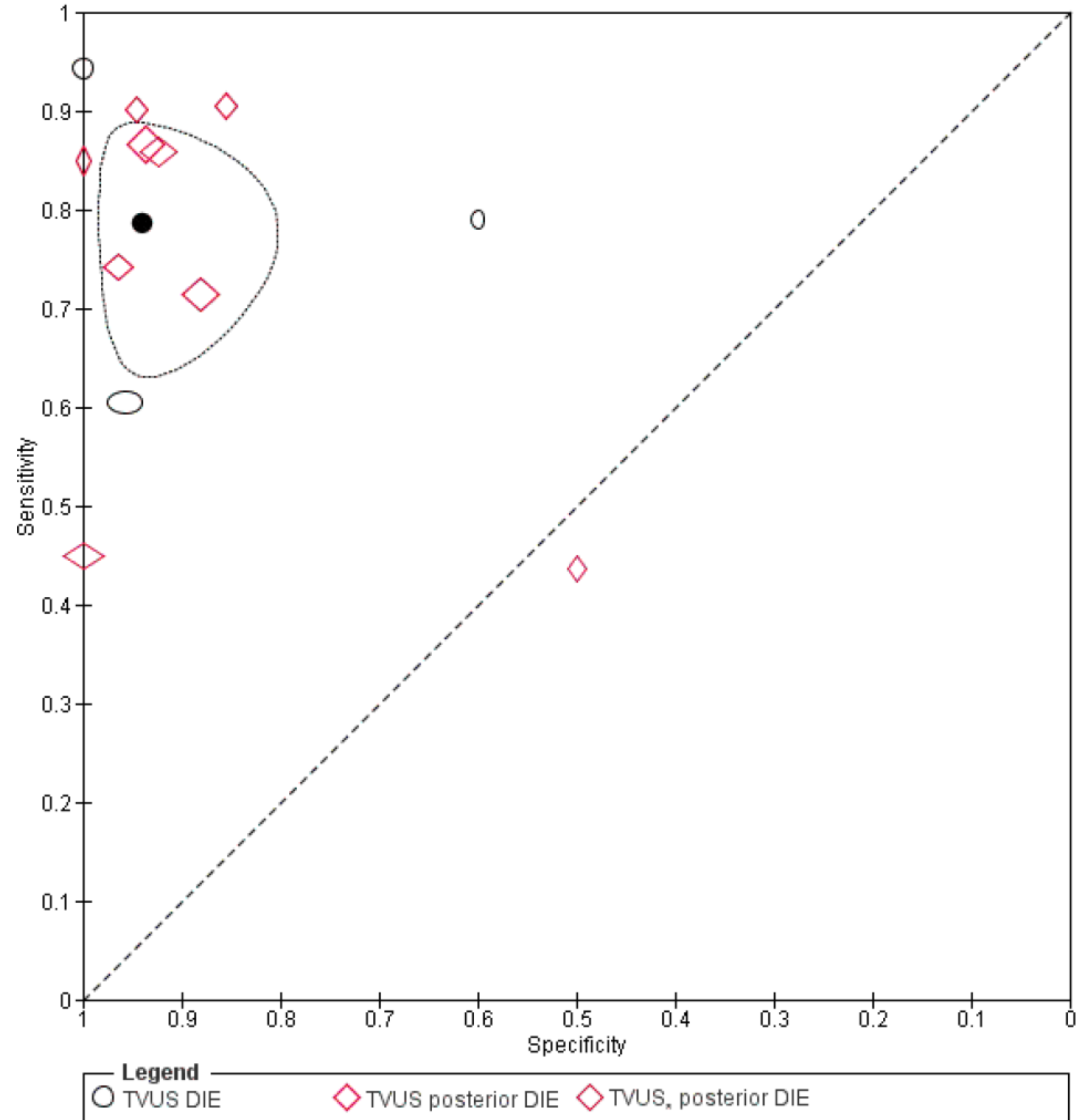
Cochrane Database of Systematic Reviews

Imaging modalities for the non-invasive diagnosis of endometriosis (Review) 2016

Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD009591.

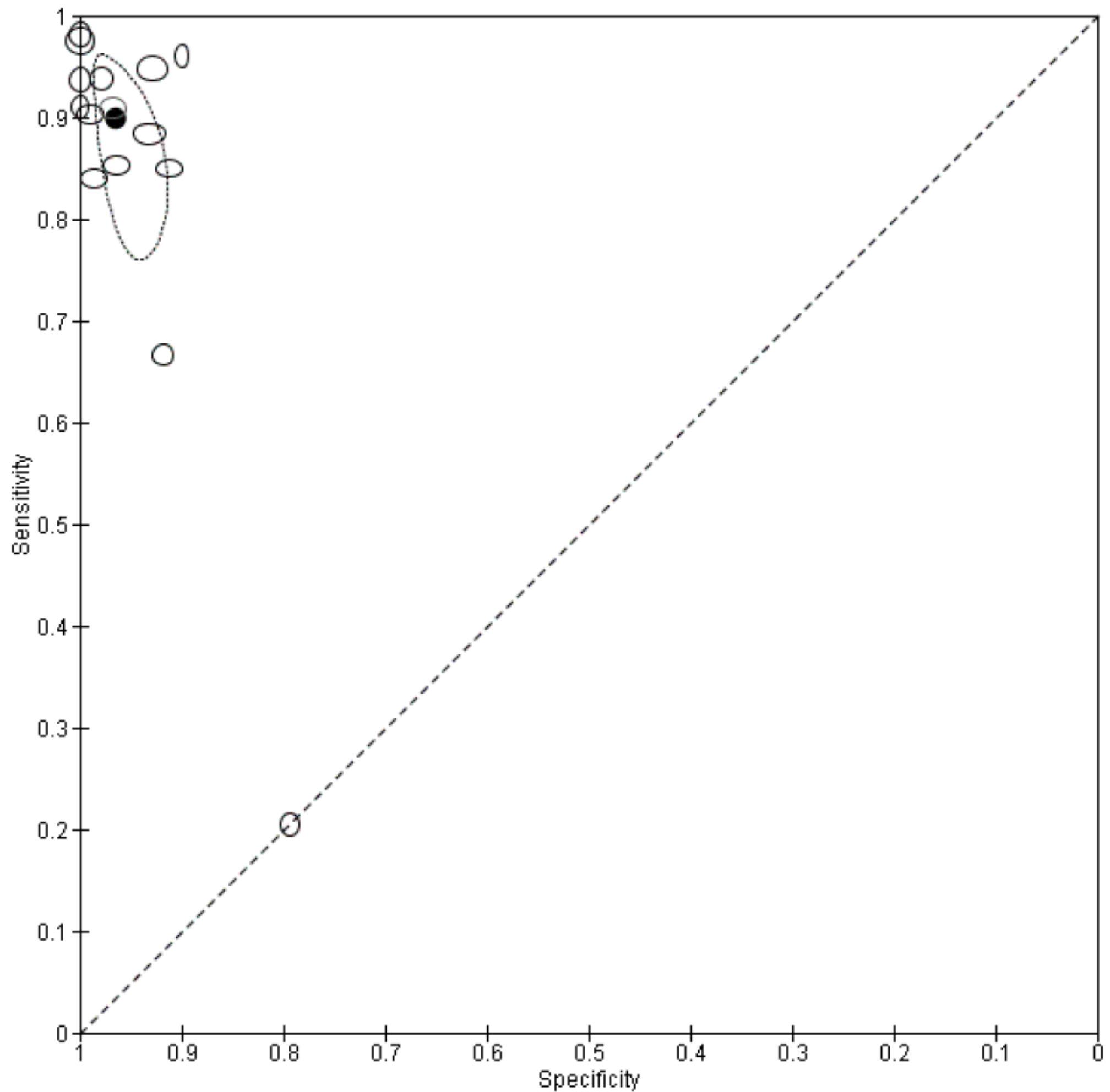
Nisenblat V, Bossuyt PMM, Farquhar C, Johnson N, Hull ML

Figure 19. Summary ROC plot of TVUS for detection of DIE/Posterior DIE. Each point represents the pair of sensitivity and specificity from a study. The size of each point is proportional to the study sample size. Tests on the same population (different TVUS methods) are presented separately as TVUS*. The solid black circle represents the pooled sensitivity and specificity, which is surrounded by a 95% confidence region (dashed line)



TVUS for DIE

Figure 52. Summary ROC plot of TVUS for detection of rectosigmoid involvement. Each point represents one pair of sensitivity and specificity from a study. The size of each point is proportional to the study sample size. Tests on the same population (different TVUS methods) are presented separately as TVUS*. The solid black circle represents the pooled sensitivity and specificity, which is surrounded by a 95% confidence region (dashed line).



TVUS for Recto-sigmoid

Dx of endometriosis

Figure 51 Summary of all imaging tests for diagnosis of rectosigmoid involvement. Plot shows study-specific point estimates of sensitivity and specificity (squares) with 95% CI (black line) and country in which the study was conducted. Studies are ordered according to year of publication for each test. Tests on the same patient (using different TVUS and MRI methods) are presented separately as TVUS* and MRI*. FN: false negative; FP: false positive; TN: true negative; TP: true positive. Modifications to the conventional technique are presented as 'modified method'.

TVUS rectosigmoid

Study	TP	FP	FN	TN	Modified Method	Geographical area	Sensitivity (95% CI)	Specificity (95% CI)
Abrao 2007	53	0	0	60	TVUS-BP	South America	0.98 [0.90, 1.00]	1.00 [0.93, 1.00]
Guerrero 2007	21	1	1	45	tg-TVUS	Europe	0.67 [0.50, 0.81]	0.92 [0.80, 0.98]
Bazot 2009	59	0	4	29	No	Europe	0.94 [0.85, 0.98]	1.00 [0.88, 1.00]
Goncalves 2010	79	0	2	113	TVUS-BP	South America	0.98 [0.91, 1.00]	1.00 [0.97, 1.00]
Bergamini 2010	49	1	2	9	RWC-TVUS	Europe	0.96 [0.87, 1.00]	0.90 [0.55, 1.00]
Falco 2011	21	1	4	70	No	Europe	0.84 [0.64, 0.95]	0.99 [0.92, 1.00]
Ferrero 2011	45	1	3	47	RWC-TVUS	Europe	0.94 [0.83, 0.99]	0.98 [0.89, 1.00]
Hudelist 2011a	28	1	3	97	No	Europe	0.90 [0.74, 0.98]	0.99 [0.94, 1.00]
Savelli 2011	51	0	5	13	No	Europe	0.91 [0.80, 0.97]	1.00 [0.75, 1.00]
Mangler 2013	10	6	39	23	No	Europe	0.20 [0.10, 0.34]	0.79 [0.60, 0.92]
Hudelist 2013	29	3	5	60	No	Europe	0.85 [0.69, 0.95]	0.96 [0.90, 0.99]
Reid 2013a	17	7	3	73	No	Australia	0.85 [0.62, 0.97]	0.91 [0.83, 0.96]
Guerrero 2014	73	9	4	116	tg-TVUS	Europe	0.95 [0.87, 0.99]	0.93 [0.87, 0.97]
Reid 2014	38	10	5	136	BVO	Australia	0.88 [0.75, 0.96]	0.93 [0.66, 0.97]

TVUS, rectosigmoid

Study	TP	FP	FN	TN	Modified Method	Geographical area	Sensitivity (95% CI)	Specificity (95% CI)
Guerrero 2014	70	4	7	121	3D-TVUS	Europe	0.91 [0.82, 0.96]	0.97 [0.92, 0.99]

TRUS rectosigmoid

Study	TP	FP	FN	TN	Modified Method	Geographical area	Sensitivity (95% CI)	Specificity (95% CI)
Fedele 1998	9	3	0	128	No	Europe	1.00 [0.88, 1.00]	0.98 [0.93, 1.00]
Ribeiro 2008a	27	1	0	9	No	South America	1.00 [0.87, 1.00]	0.90 [0.55, 1.00]
Bazot 2009	56	2	7	27	No	Europe	0.89 [0.79, 0.95]	0.93 [0.77, 0.99]
Bergamini 2010	45	2	6	8	No	Europe	0.88 [0.76, 0.96]	0.80 [0.44, 0.97]

MRI rectosigmoid

Study	TP	FP	FN	TN	Modified Method	Geographical area	Sensitivity (95% CI)	Specificity (95% CI)
Abrao 2007	45	1	0	49	T1/T2-w + fat-suppressed/Gd	South America	0.83 [0.71, 0.92]	0.98 [0.89, 1.00]
Bazot 2009	55	2	0	27	T1/T2-w + fat-suppressed/Od	Europe	0.87 [0.77, 0.94]	0.93 [0.77, 0.99]
Chamie 2009a	43	3	7	39	T1/T2-w + fat-suppressed/Gd	South America	0.86 [0.73, 0.94]	0.93 [0.81, 0.99]
Hottat 2009	13	1	0	27	3.0T	Europe	1.00 [0.75, 1.00]	0.96 [0.82, 1.00]
Bazot 2013	11	0	2	10	2D FSE T2-w	Europe	0.85 [0.55, 0.98]	1.00 [0.69, 1.00]
Biscaldi 2014	174	3	2	81	Jelly method (T1/T2-w + fat-suppressed)	Europe	0.99 [0.96, 1.00]	0.96 [0.90, 0.99]

MRI, rectosigmoid

Study	TP	FP	FN	TN	Modified Method	Geographical area	Sensitivity (95% CI)	Specificity (95% CI)
Bazot 2013	11	1	2	9	3D-MRI	Europe	0.85 [0.55, 0.98]	0.90 [0.55, 1.00]

MDCT-e rectosigmoid

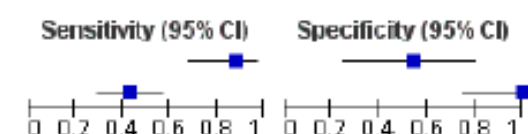
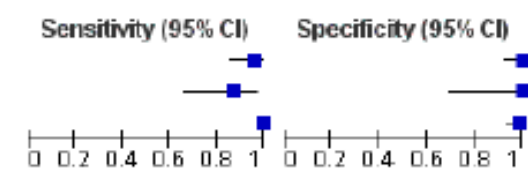
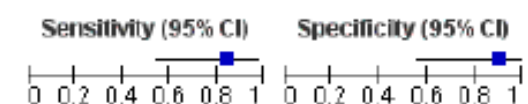
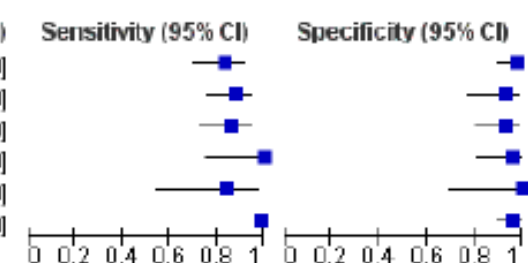
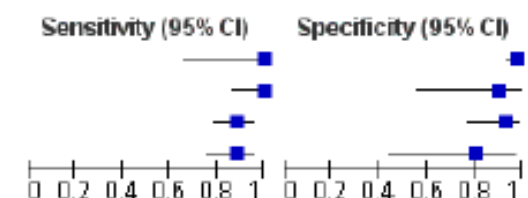
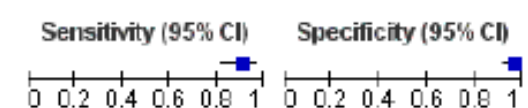
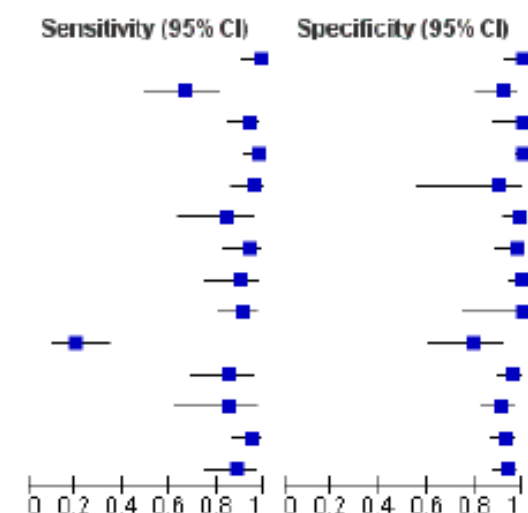
Study	TP	FP	FN	TN	Modified Method	Geographical area	Sensitivity (95% CI)	Specificity (95% CI)
Ferrero 2011	46	0	2	48	No	Europe	0.96 [0.86, 0.99]	1.00 [0.93, 1.00]
Stabile 2013	20	0	3	10	No	Europe	0.87 [0.66, 0.97]	1.00 [0.69, 1.00]
Biscaldi 2014	175	1	1	83	No	Europe	0.99 [0.97, 1.00]	0.99 [0.94, 1.00]

DCBE rectosigmoid

Study	TP	FP	FN	TN	Modified Method	Geographical area	Sensitivity (95% CI)	Specificity (95% CI)
Ribeiro 2008a	21	6	3	7	No	South America	0.68 [0.68, 0.97]	0.64 [0.25, 0.81]
Savelli 2011	24	0	32	13	No	Europe	0.43 [0.30, 0.57]	1.00 [0.75, 1.00]

sensitivity

specificity





Cochrane
Library

Cochrane Database of Systematic Reviews

Blood biomarkers for the non-invasive diagnosis of endometriosis (Review)

Nisenblat V, Bossuyt PMM, Shaikh R, Farquhar C, Jordan V, Scheffers CS, Mol BWJ, Johnson N, Hull ML

Endometriosis: a New ART Indication

Diagnosis of endometriosis

Pathophysiology of endometriosis: oocyte quality

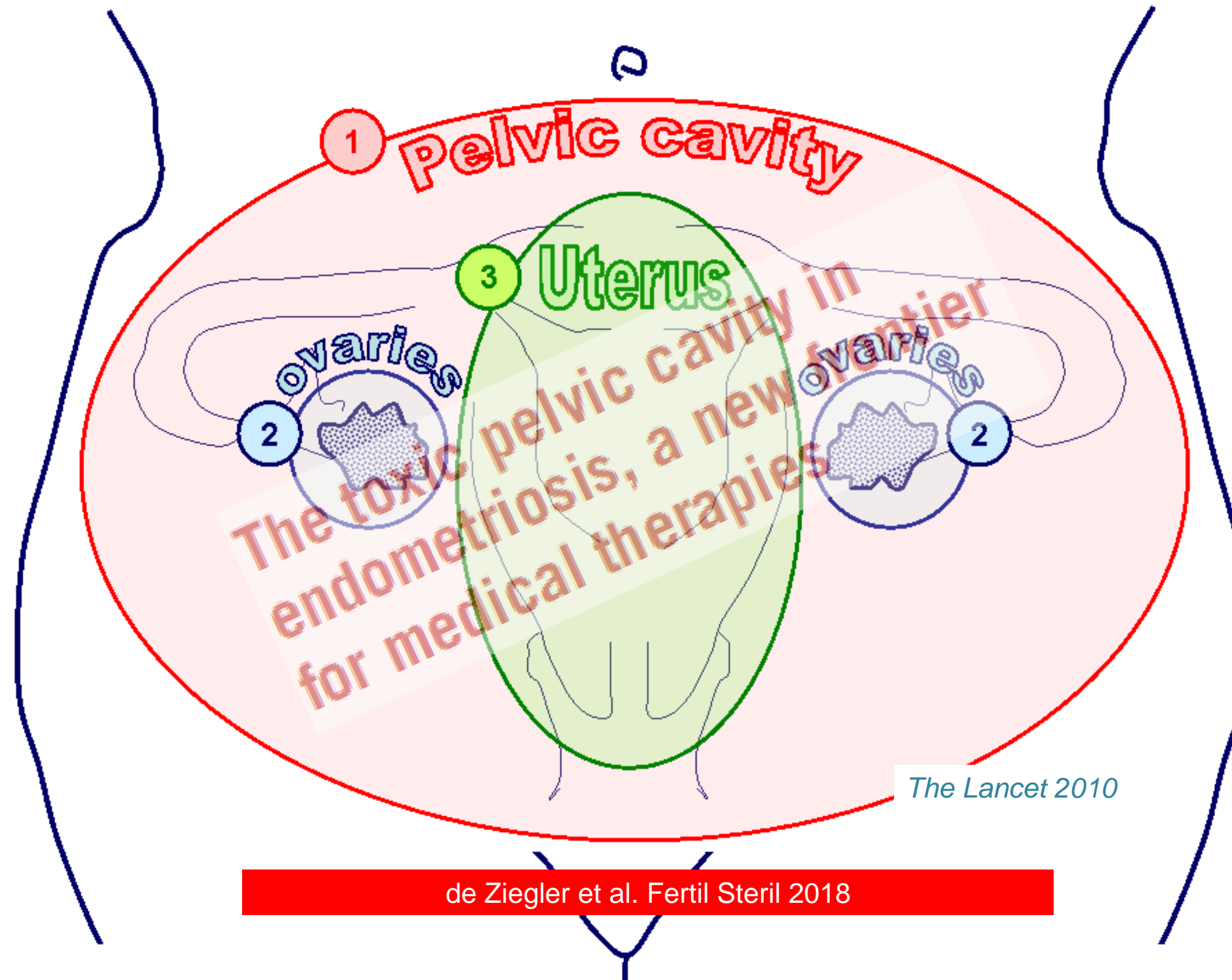
Endometriosis through women's age

Endometrial receptivity

Surgery more harmful on ovarian reserve than endometriosis

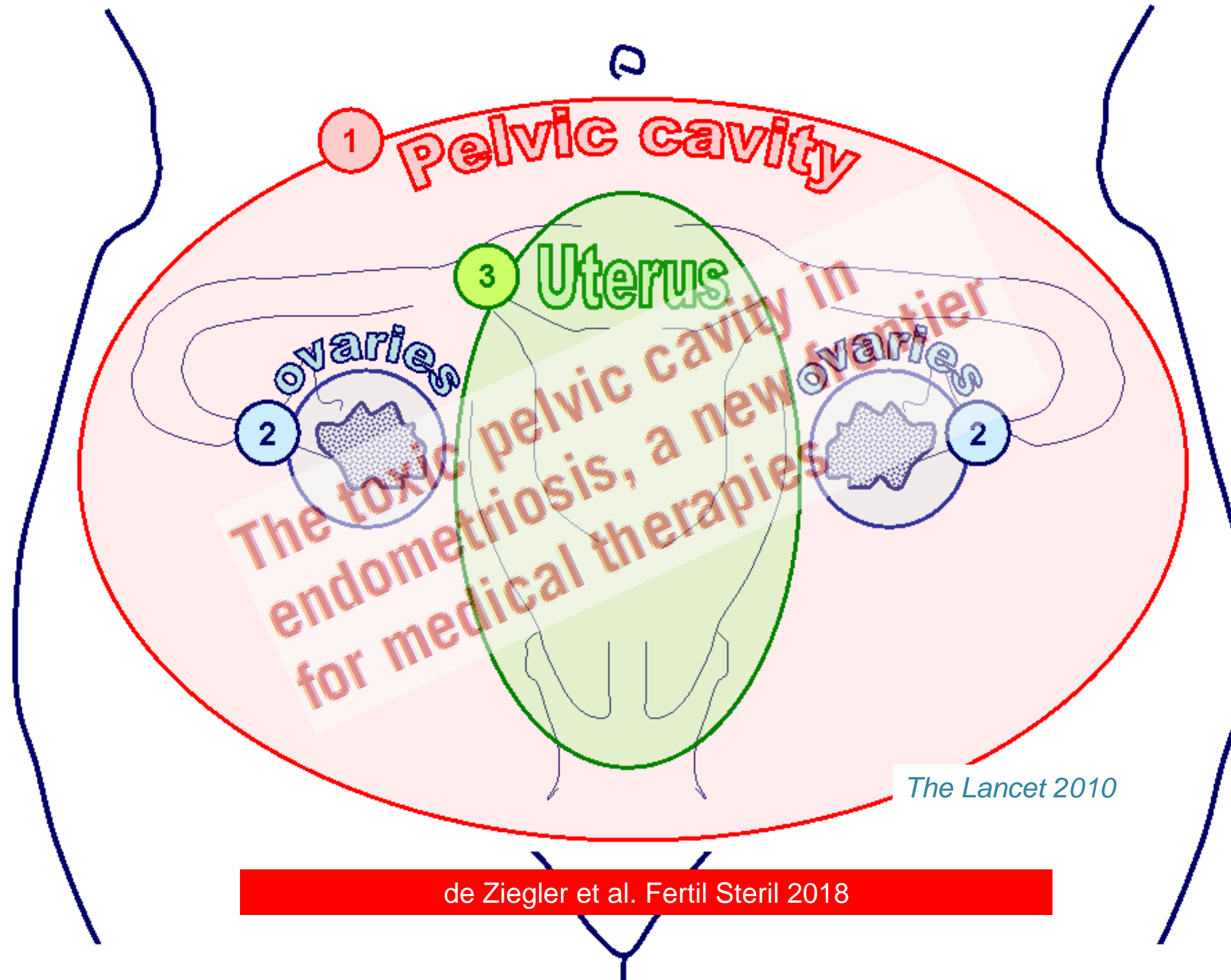
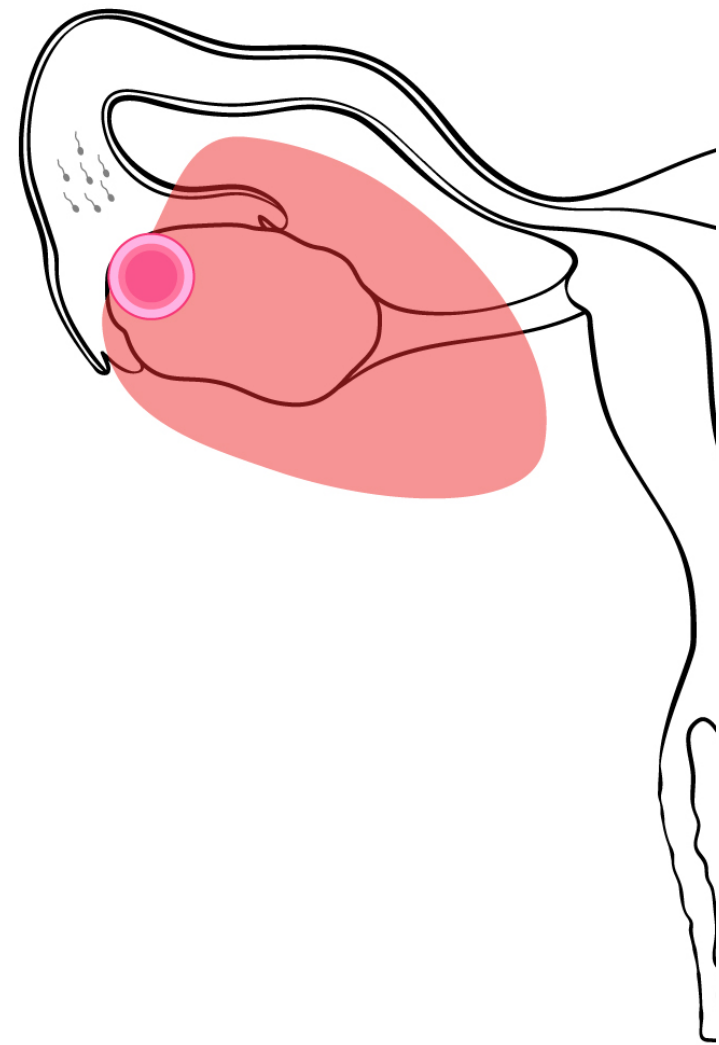
Practical management
itself

Endometriosis: a New ART Indication



Endometriosis: a New ART Indication

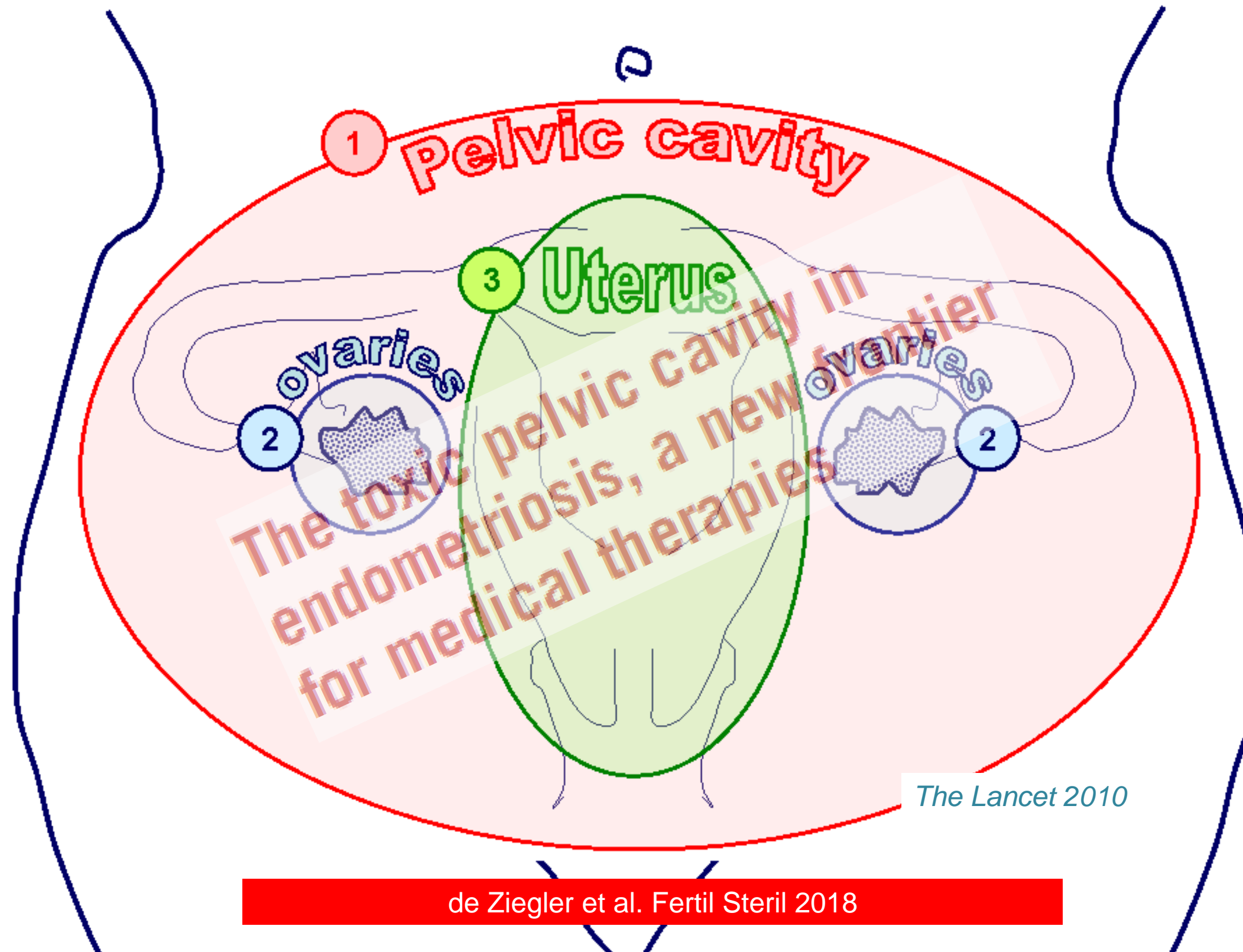
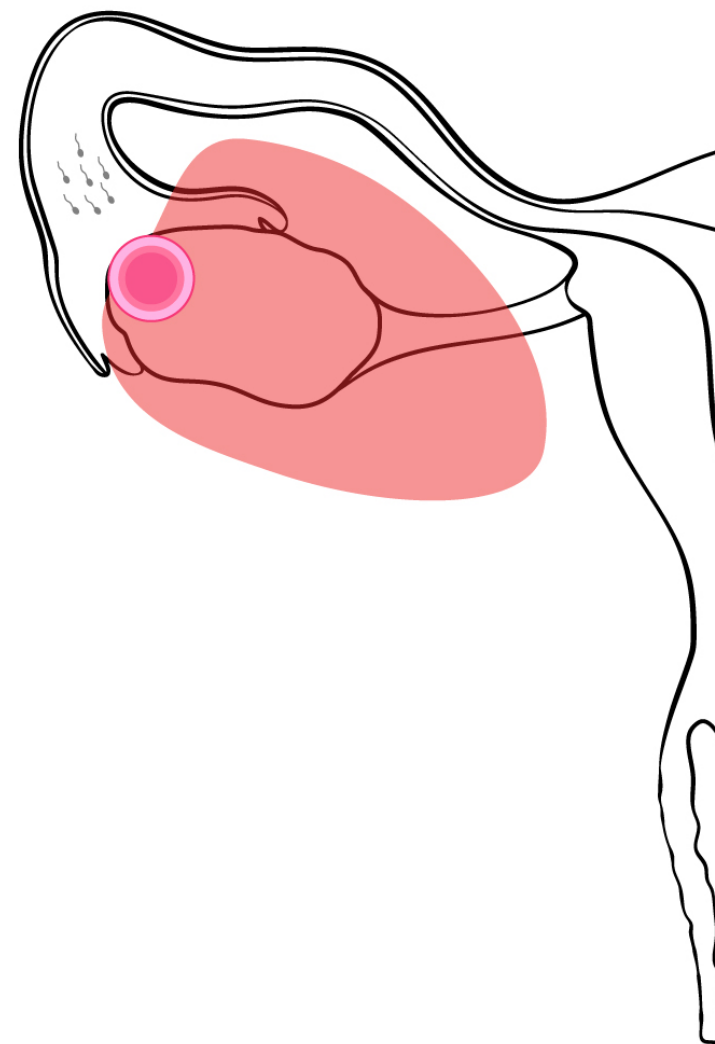
In Vivo



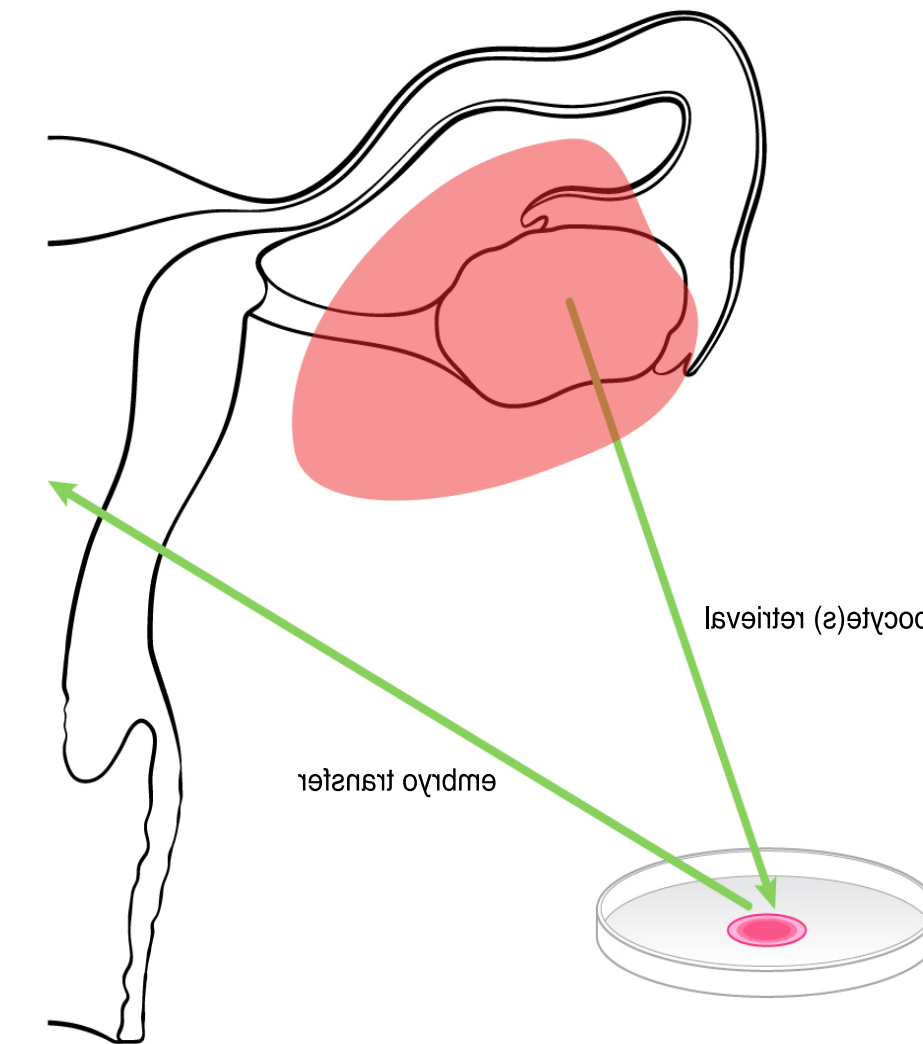
de Ziegler et al. Fertil Steril 2018

Endometriosis: a New ART Indication

In Vivo



In Vitro



de Ziegler et al. Fertil Steril 2018

ART results are unaltered in endometriosis

➤ 2. *Toxic-pelvic* condition on oocytes and embryos

ORIGINAL ARTICLE: ENDOMETRIOSIS

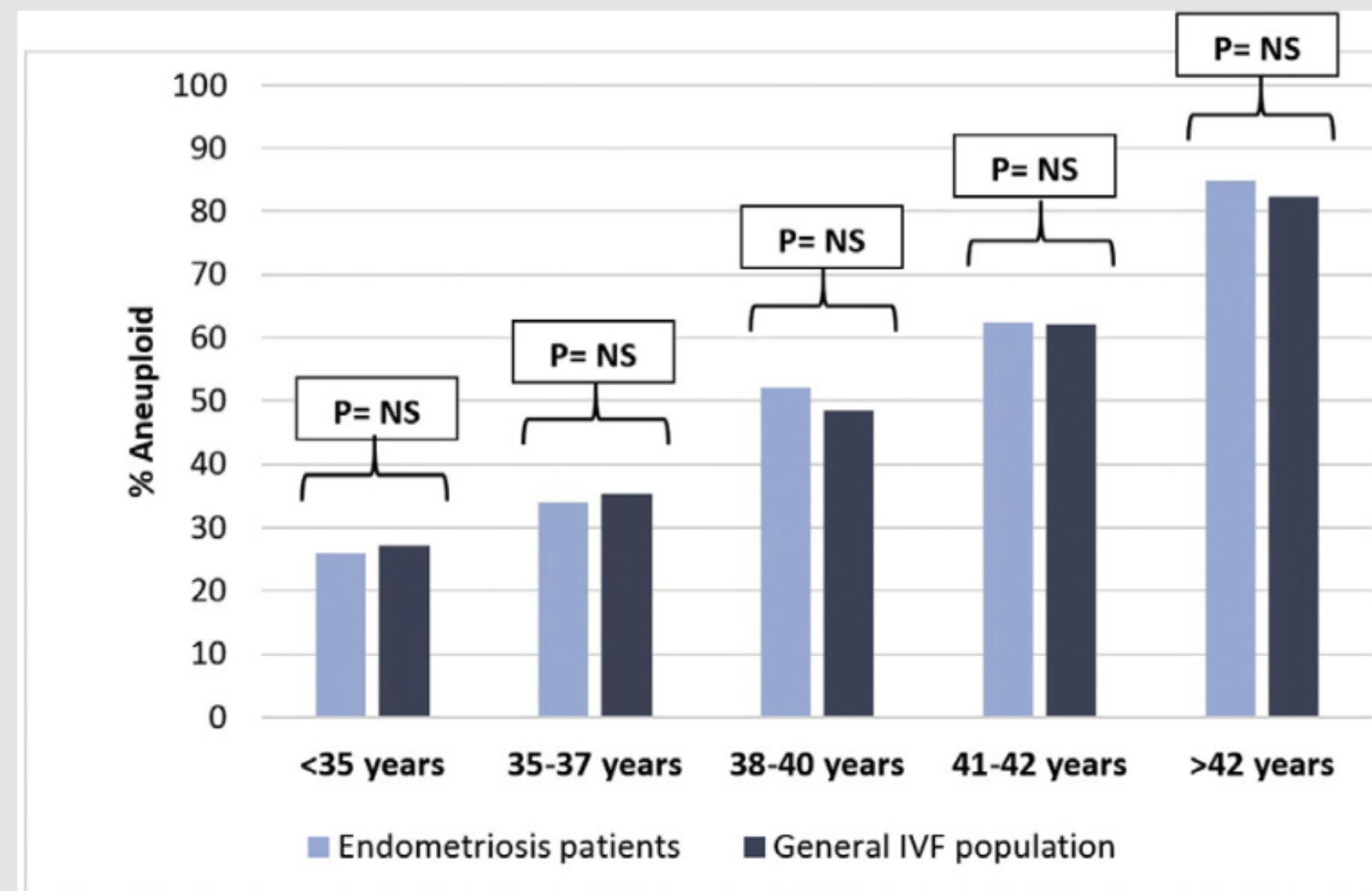
Patients with endometriosis have aneuploidy rates equivalent to their age-matched peers in the in vitro fertilization population

Caroline Juneau, M.D.,^{a,b} Emily Kraus, M.D.,^c Marie Werner, M.D., H.C.L.D.,^a Jason Franasiak, M.D., T.S.,^{a,b} Scott Morin, M.D.,^{a,b} George Patounakis, M.D., Ph.D.,^d Thomas Molinaro, M.D., M.S.C.E.,^a Dominique de Ziegler, M.D.,^e and Richard T. Scott, M.D., H.C.L.D.^{a,b}

^a Reproductive Medicine Associates of New Jersey, Basking Ridge, New Jersey; ^b Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania; ^c Medical University of South Carolina, Charleston, South Carolina; ^d Reproductive Medicine Associates of Florida, Lake Mary, Florida; and ^e Hôpital Cochin, University Paris Descartes, Paris, France

➤ 2. Toxic-pelvic condition on oocytes and embryos

FIGURE 1



In women undergoing in vitro fertilization, the rate of aneuploidy in the embryos of endometriosis patients did not differ from that of women without endometriosis.

Human Reproduction Update, Vol.21, No.6 pp. 809–825, 2015

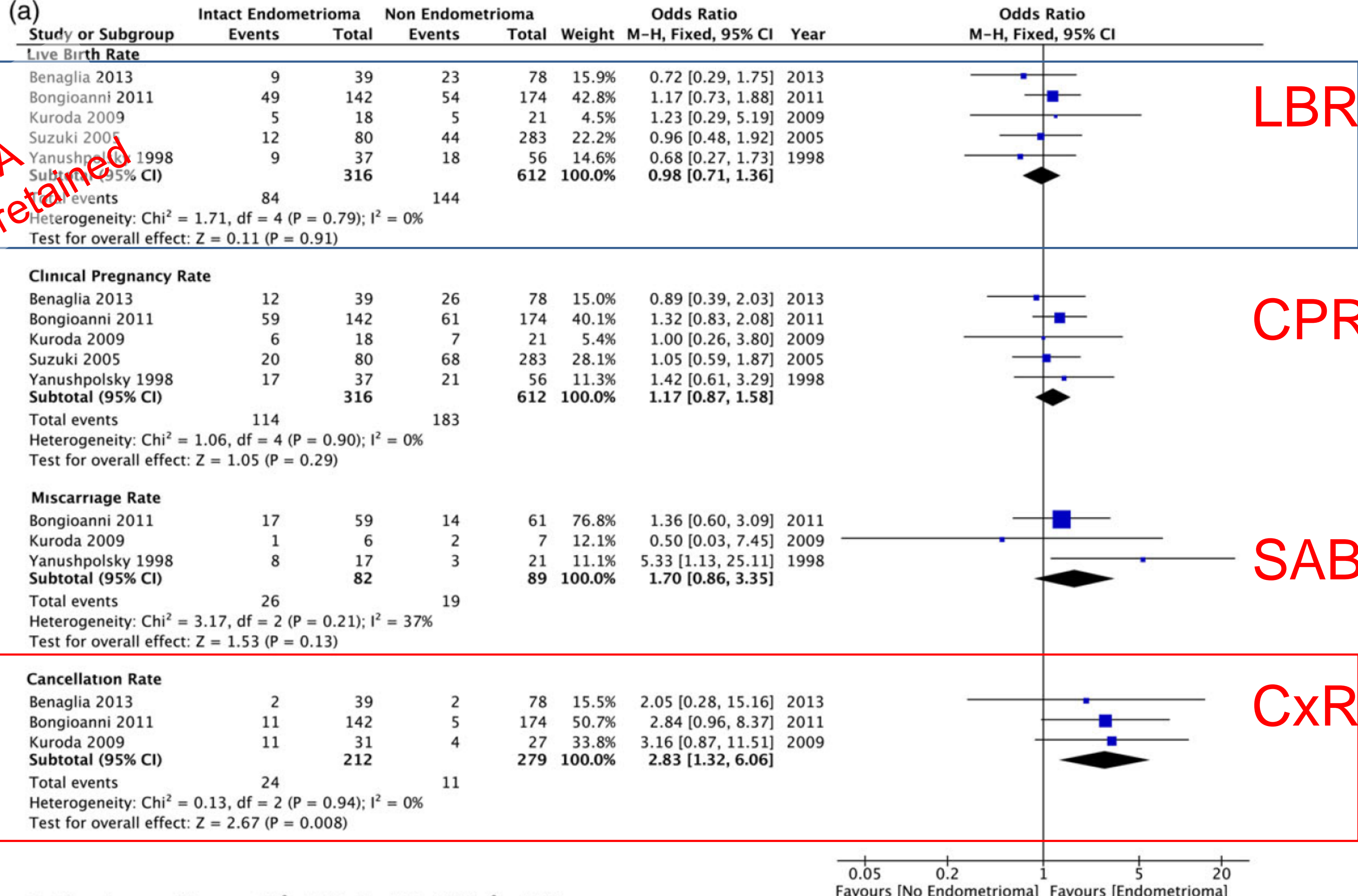
Advanced Access publication on July 12, 2015 doi:10.1093/humupd/dmv035

human
reproduction
update

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

M. Hamdan^{1,2,3}, G. Dunselman⁴, T.C. Li⁵, and Y. Cheong^{1,3,*}

(a)



OMA vs.
No OMA
33 studies retained

Test for subgroup differences: Chi² = 7.33, df = 3 (P = 0.06), I² = 59.1%

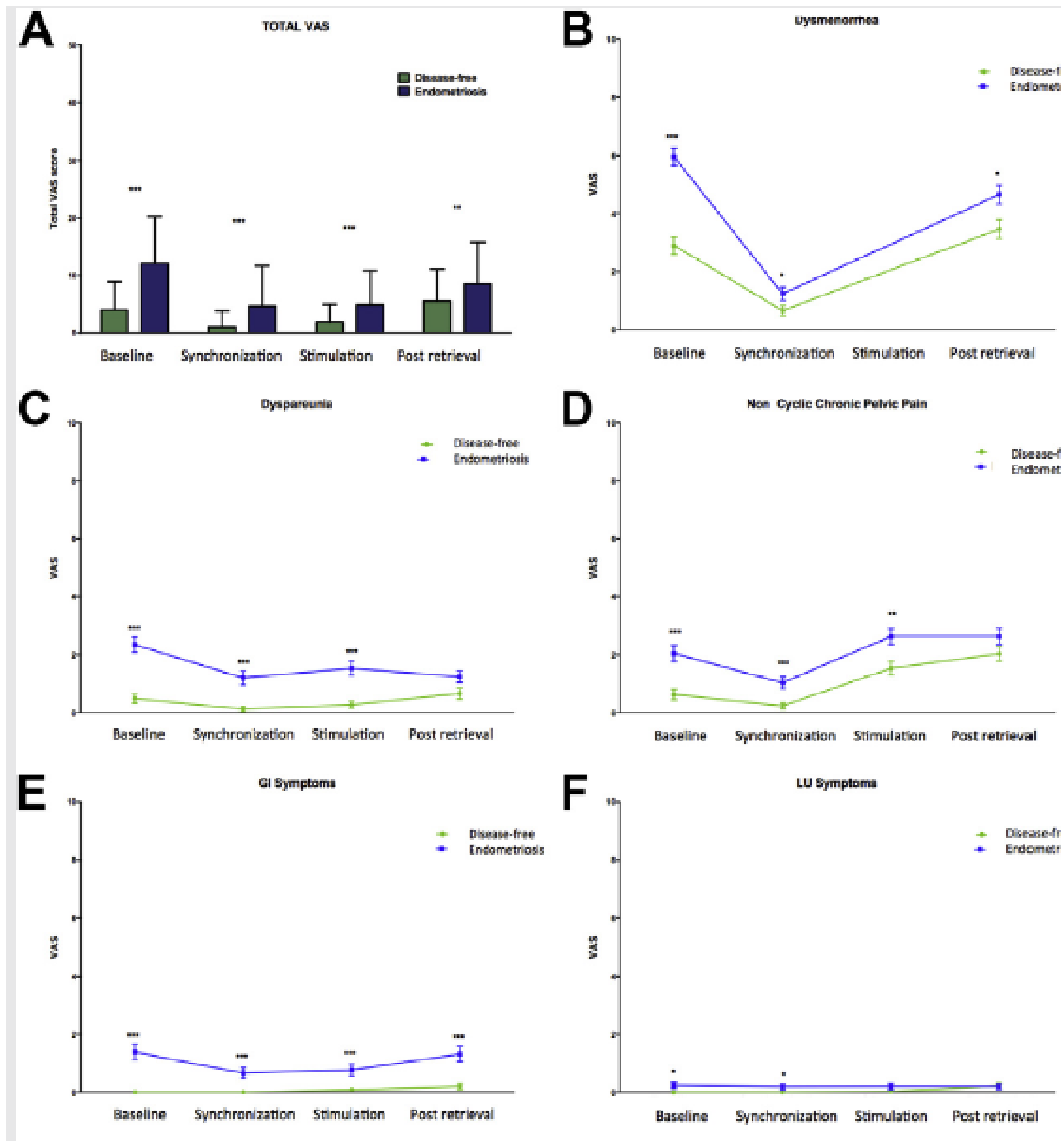
0.05 0.2 1 5 20
Favours [No Endometrioma] Favours [Endometrioma]

Endometriosis: Surgery or ART?

**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}

Effects of ART on endometriosis



Endometriosis: Surgery or ART?

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

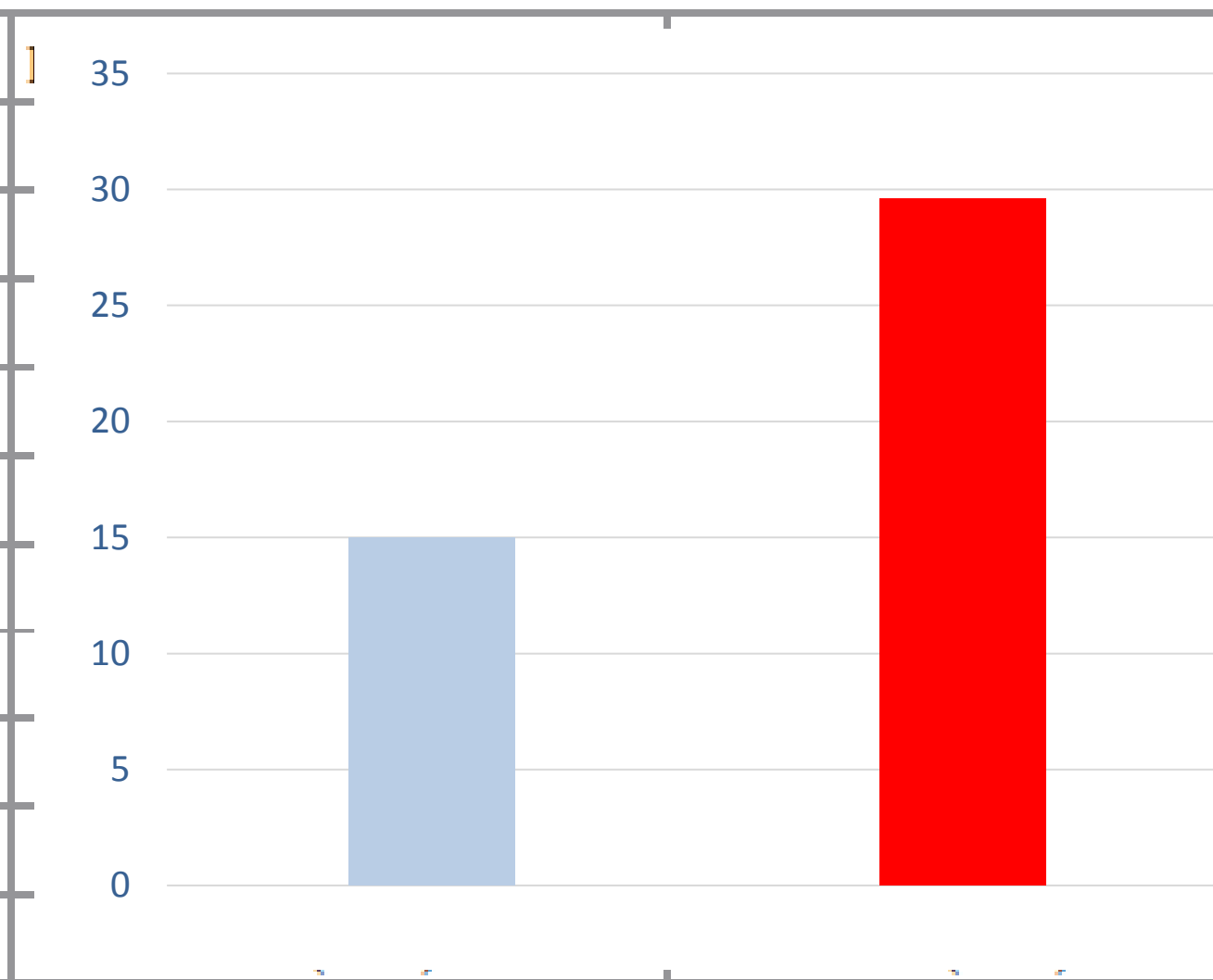
ART is different from COS-IUI
No “ovulation” in ART

Pietro Santulli, M.D., Ph.D.,^a Raphaël Bourdier,^a Valérie Proulx,^a Virena 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}

Fresh ET Def ET

Table 2. IVF/ICSI-characteristics and outcomes in matched fresh and deferred frozen embryo transfer groups.

		p-value
Number of oocytes retrieved (mean ± SD)	35	0.001 ^{pt}
Total number of embryos transferred		NA
Mean No. of embryos transferred (mean ± SD)	25	<0.001 ^{pt}
Total number of embryo transfers	20	NA
Mean No. of transfers (mean ± SD)	15	0.132 ^{pt}
Cumulative clinical pregnancy rate—(n,%)	10	0.047 ^{mn}
Miscarriage—(n,%)	5	0.022 ^k
Multiple pregnancy—(n,%)	0	0.220 ^k
Cumul. LBR	0	0.005 ^{mn}
Cumulative live birth rate ^a —(n,%)	0	0.012 ^{mn}



IVF/ICSI, in vitro fertilization / intra cytoplasmic sperm injection; Fresh-ET, Fresh embryo transfer; Def-ET, Deferred frozen- thawed embryo transfer; NA, non applicable

^{pt}, Paired t-test;

^{mn}, McNemar test;

^k Pearson's chi-square test.

^a 2 and 5 women were lost to follow up in Fresh and Def-ET group respectively

Endometriosis: a New ART Indication

➤ 3. Effects of endometriosis on the eutopic endometrium

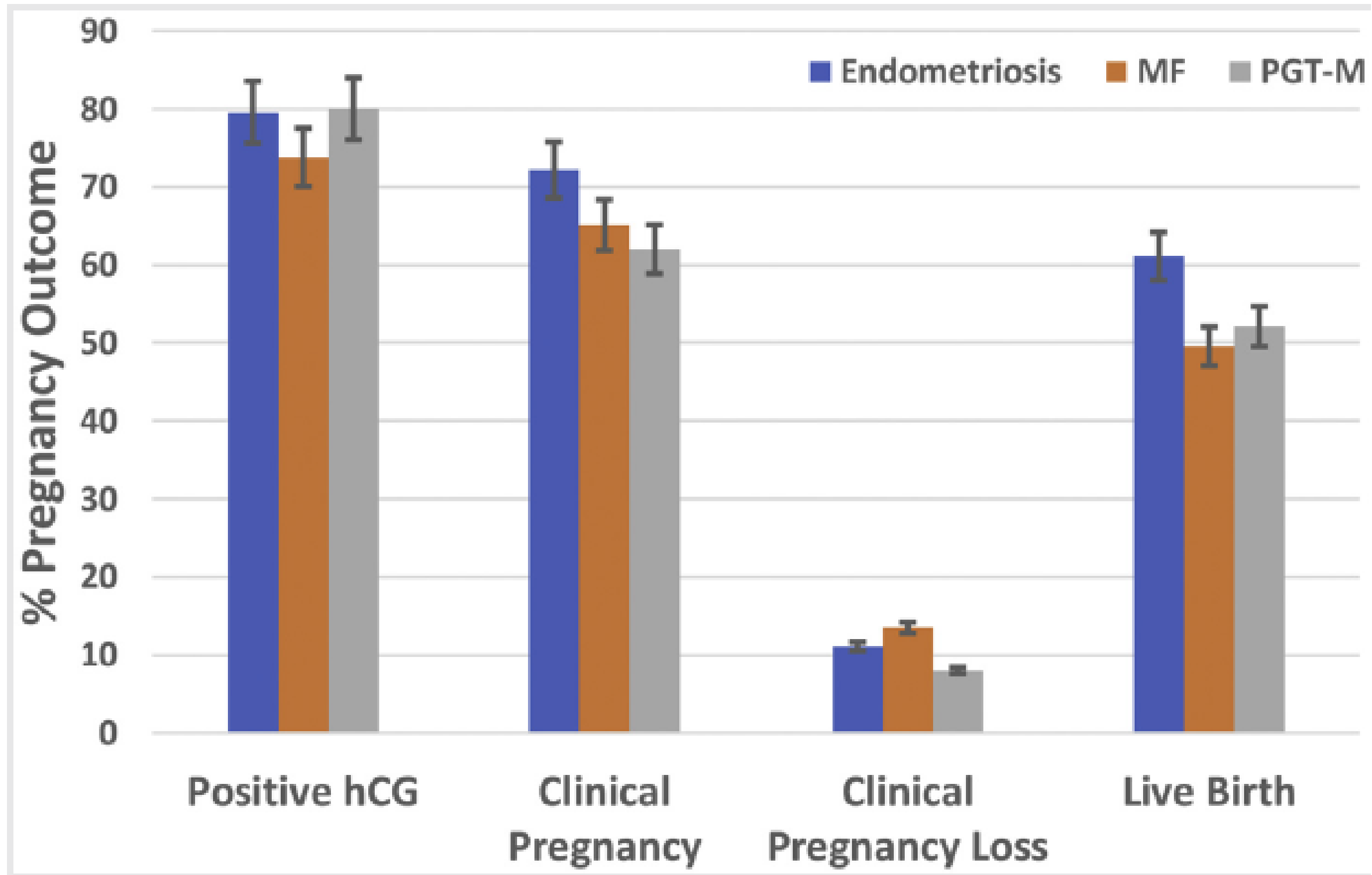
Endometriosis does not impact live-birth rates in frozen embryo transfers of euploid blastocysts

Lauren A. Bishop, M.D.,^a Justin Gunn, B.S.,^b Samad Jahandideh, Ph.D.,^c Kate Devine, M.D.,^d
Alan H. Decherney, M.D.,^a and Micah J. Hill, D.O.^e

^a Reproductive Endocrinology and Infertility, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, Maryland; ^b Uniformed Services University of the Health Sciences, Bethesda, Maryland; ^c Shady Grove Fertility Reproductive Science Center, Rockville, Maryland; ^d Shady Grove Fertility Reproductive Science Center, Washington, DC; and ^e Walter Reed National Military Medical Center, Bethesda, Maryland

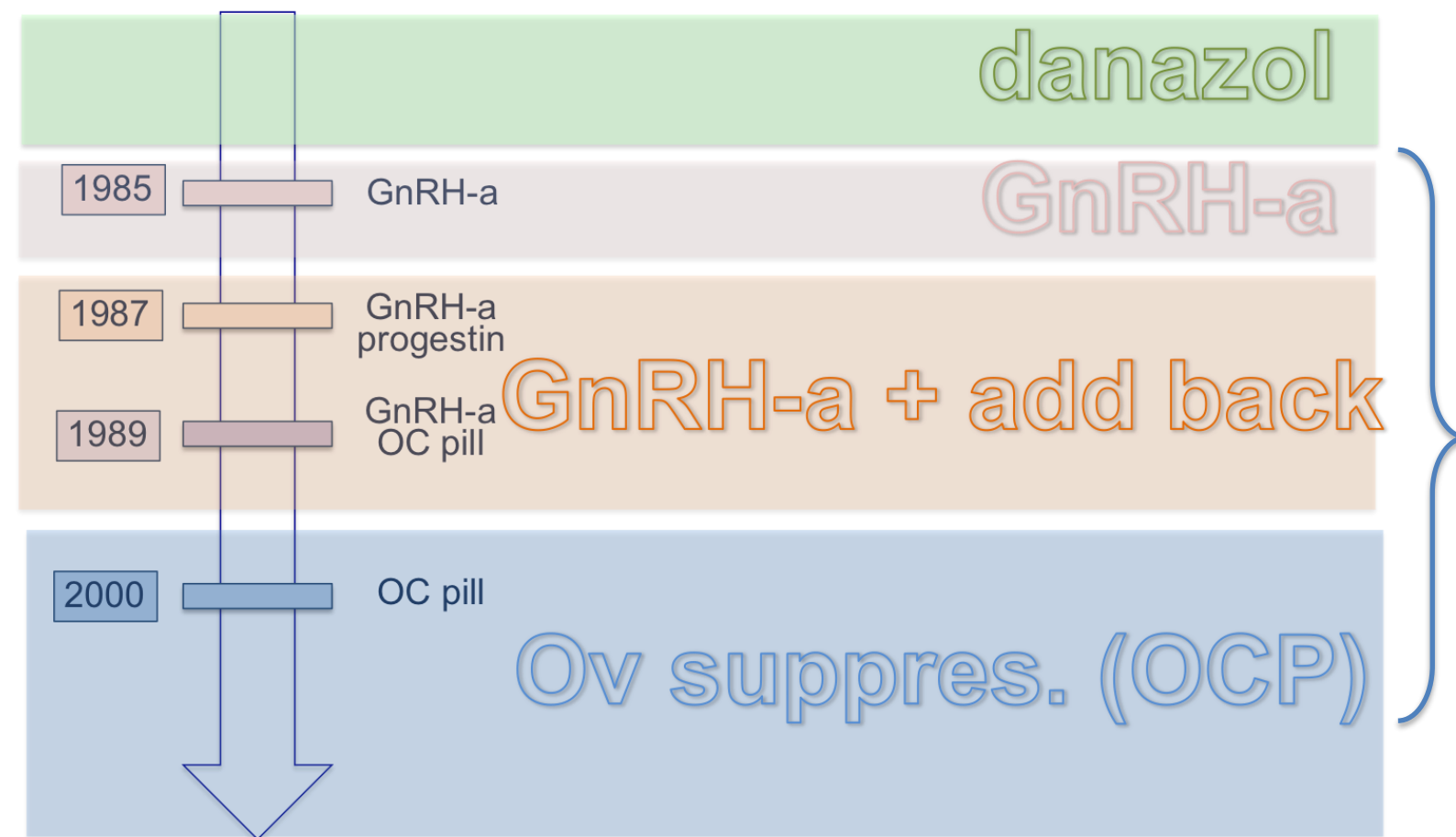
Endometriosis: Surgery or ART?

Bishop et al. Fertil Steril 2020



Endometriosis: Surgery or ART?

Medical treatment of endometriosis



All treatments are
contraceptive

Equally Effective

1. Pelvic pain
2. Recurrence after surgery

Ineffective

1. Fertility after surgery
2. Enhancing fertility

Endometriosis: Surgery or ART?

Sx w/ & w/o post-op medical treatment

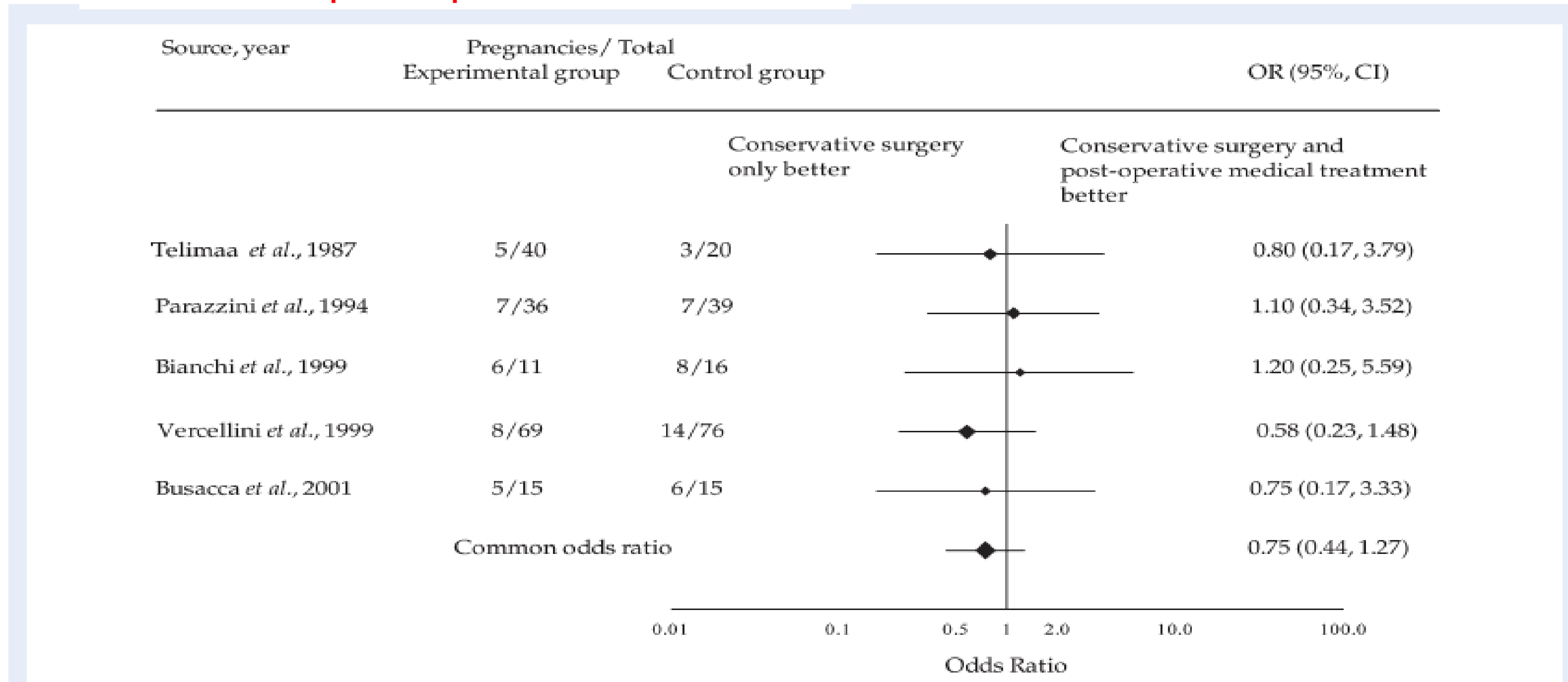
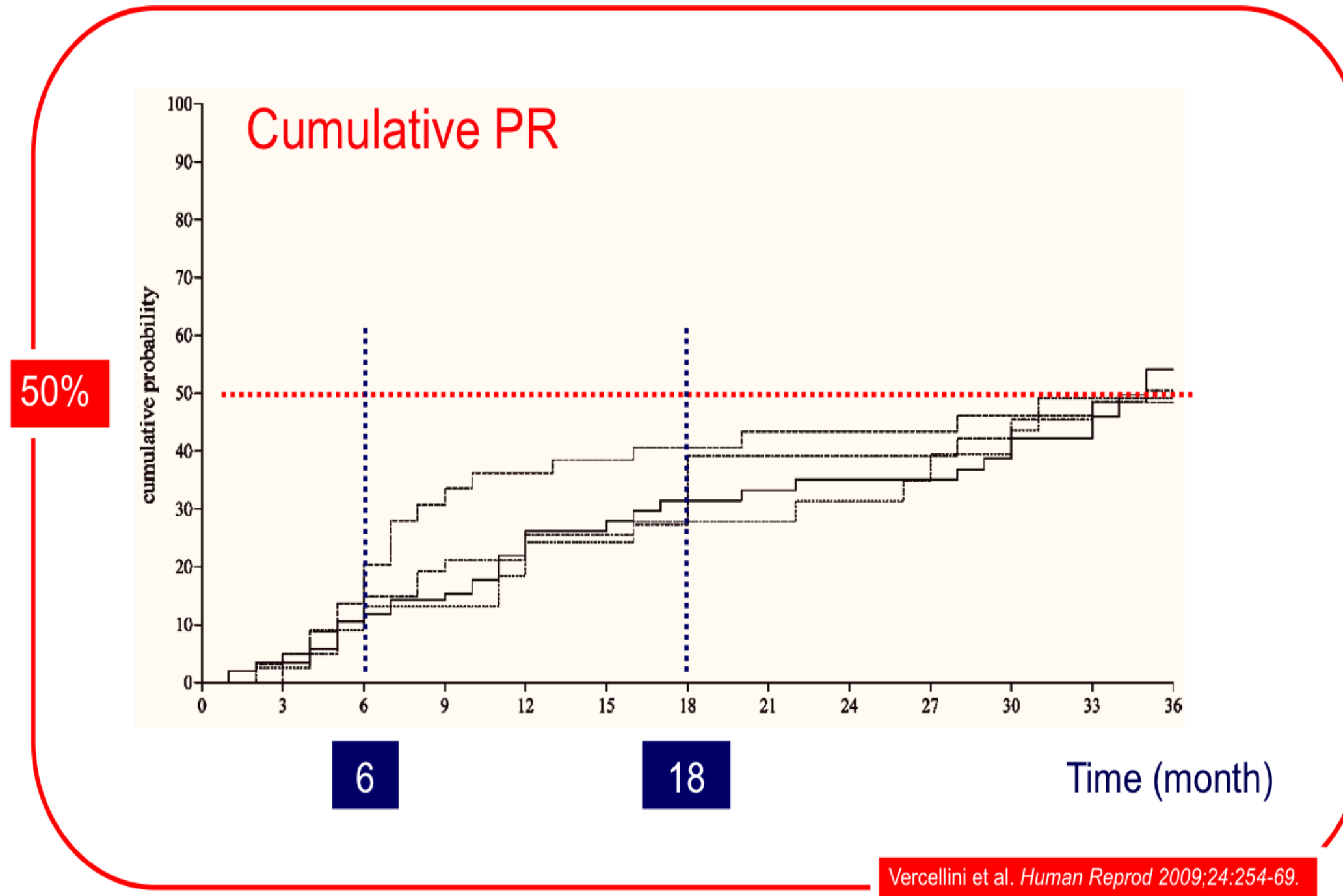


Figure 6 Overview of RCTs comparing conservative surgery for endometriosis with or without post-operative medical treatment. Diamonds represent odds ratio of conception, and horizontal lines are 95% CIs. Breslow-Day test for heterogeneity: $\chi^2_4 = 0.95$, $P = 0.91$. Modified from Vercellini *et al.* (2003b), with permission.

Endometriosis: Surgery or ART?



At all stages of OSIS, Sx provides 50% chances on conceiving naturally in 12-18 months.

Endometriosis: Surgery or ART?

Resection of endometriomas

Source, year	Pregnancies/Total
--------------	-------------------

Daniell <i>et al.</i> , 1991	12/32
Marrs <i>et al.</i> , 1991	7/23
Bateman <i>et al.</i> , 1994	9/21
Crosignani <i>et al.</i> , 1996	6/22
Montanino <i>et al.</i> , 1996	5/11
Donnez <i>et al.</i> , 1996	415/814
Sutton <i>et al.</i> , 1997	30/66
Beretta <i>et al.</i> , 1998	6/9
Busacca <i>et al.</i> , 1999	39/67
Milingos <i>et al.</i> , 1999	17/32
Jones & Sutton, 2002	15/39
Alborzi <i>et al.</i> , 2004	19/32
Fedele <i>et al.</i> , 2006	29/90
Vercellini <i>et al.</i> , 2006a	128/237
Overall weighted mean	

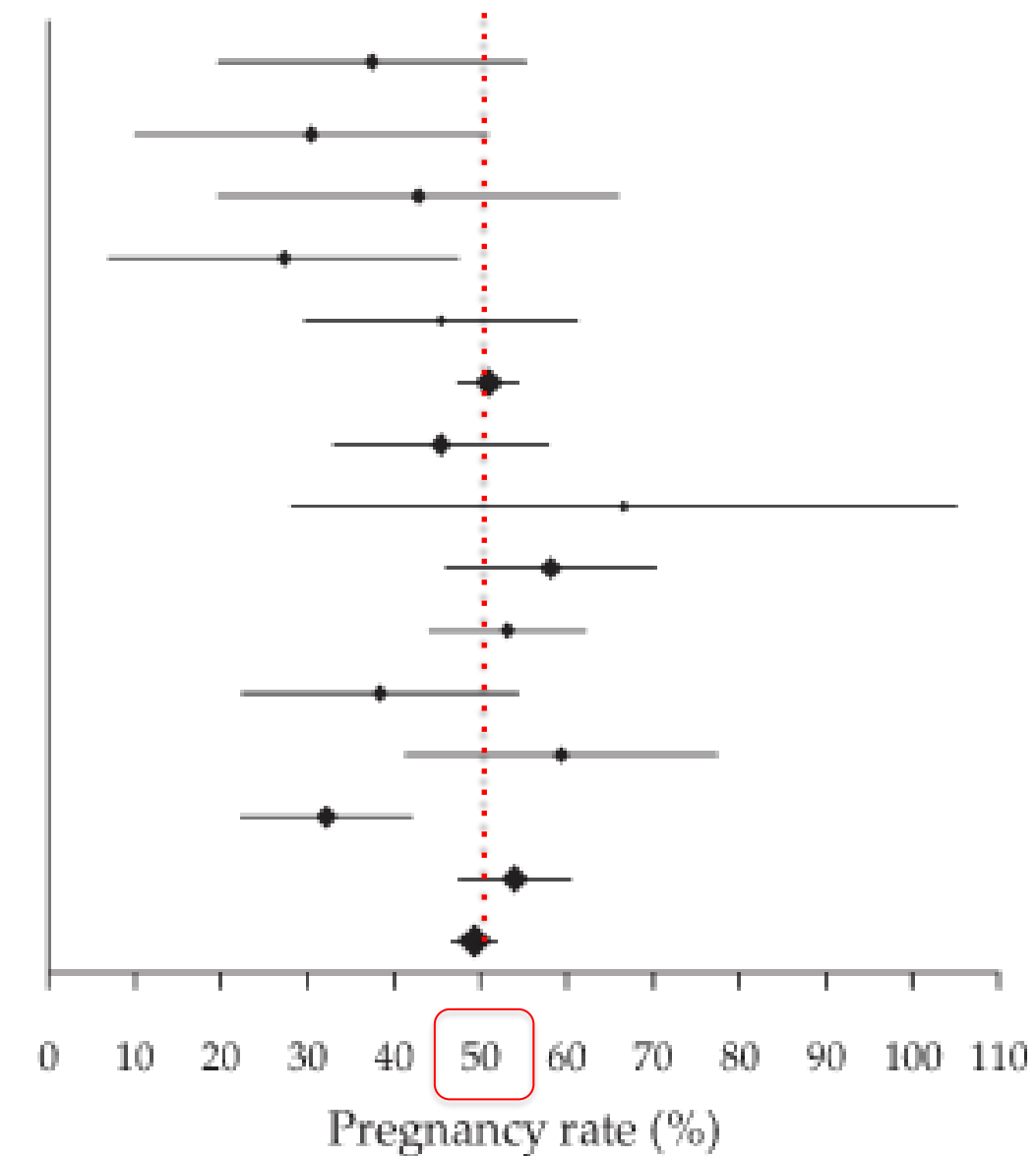


Figure 3 Pregnancy rates observed after laparoscopic excision of endometriomas. Diamonds represent percentage point estimates and horizontal lines represent 95% CIs. Modified from Jones and Sutton (2002), with permission.

Endometriosis: Surgery or ART?

Human Reproduction, Vol.30, No.3 pp. 558–568, 2015

Advanced Access publication on January 7, 2015 doi:10.1093/humrep/deu354

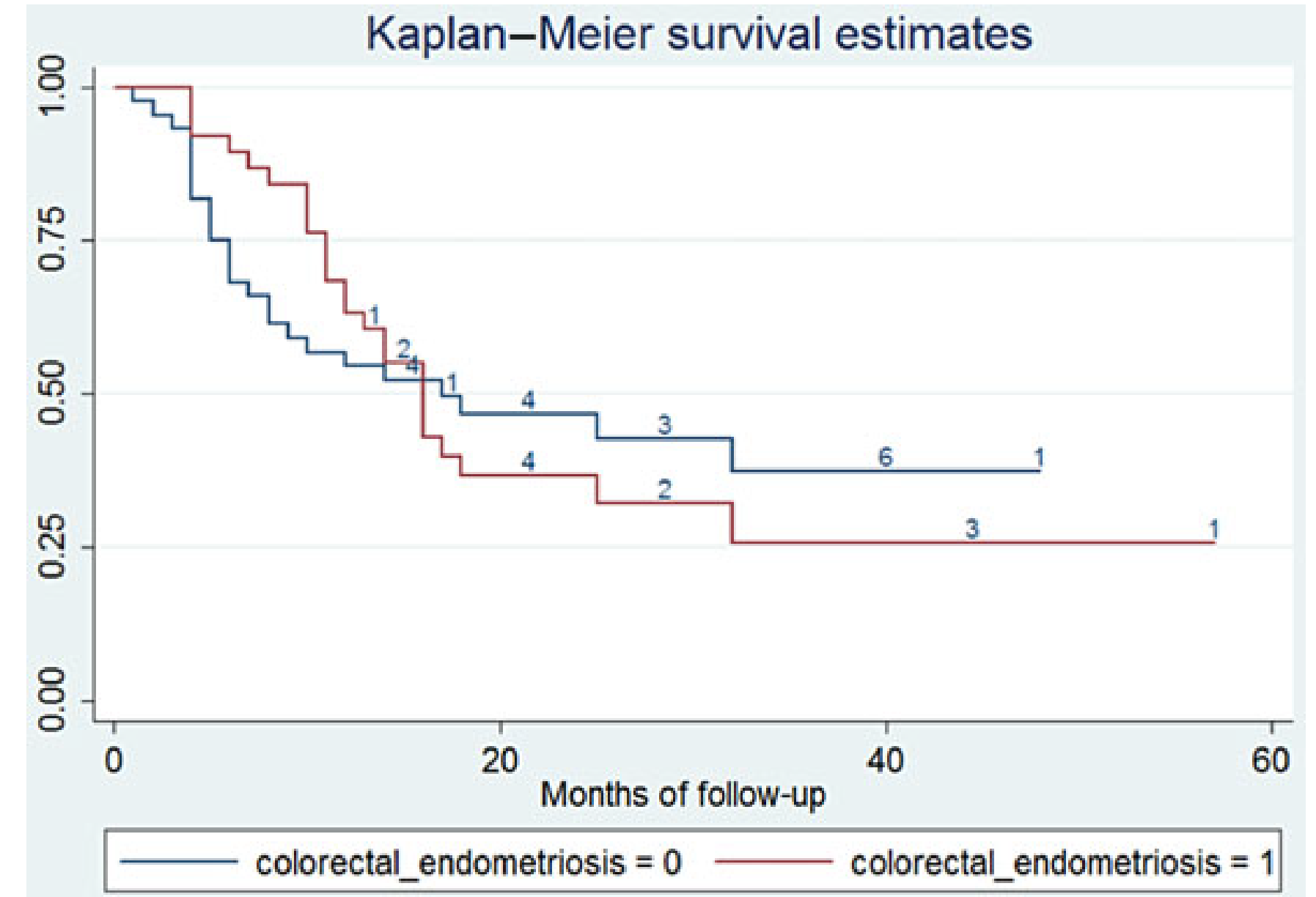
human
reproduction

ORIGINAL ARTICLE *Gynaecology*

Recurrences and fertility after endometrioma ablation in women with and without colorectal endometriosis: a prospective cohort study[†]

Horace Roman^{1,2*}, Solène Quibel¹, Mathieu Auber¹, Hélène Muszynski¹, Emmanuel Huet³, Loïc Marpeau¹, and Jean Jacques Tuech³

Colorectal surgery does not hamper the benefit of endometriosis surgery



Endometriosis: Surgery or ART?

No surgery before ART rule

Not everyone agrees

Colorectal endometriosis-associated infertility: should surgery precede ART?

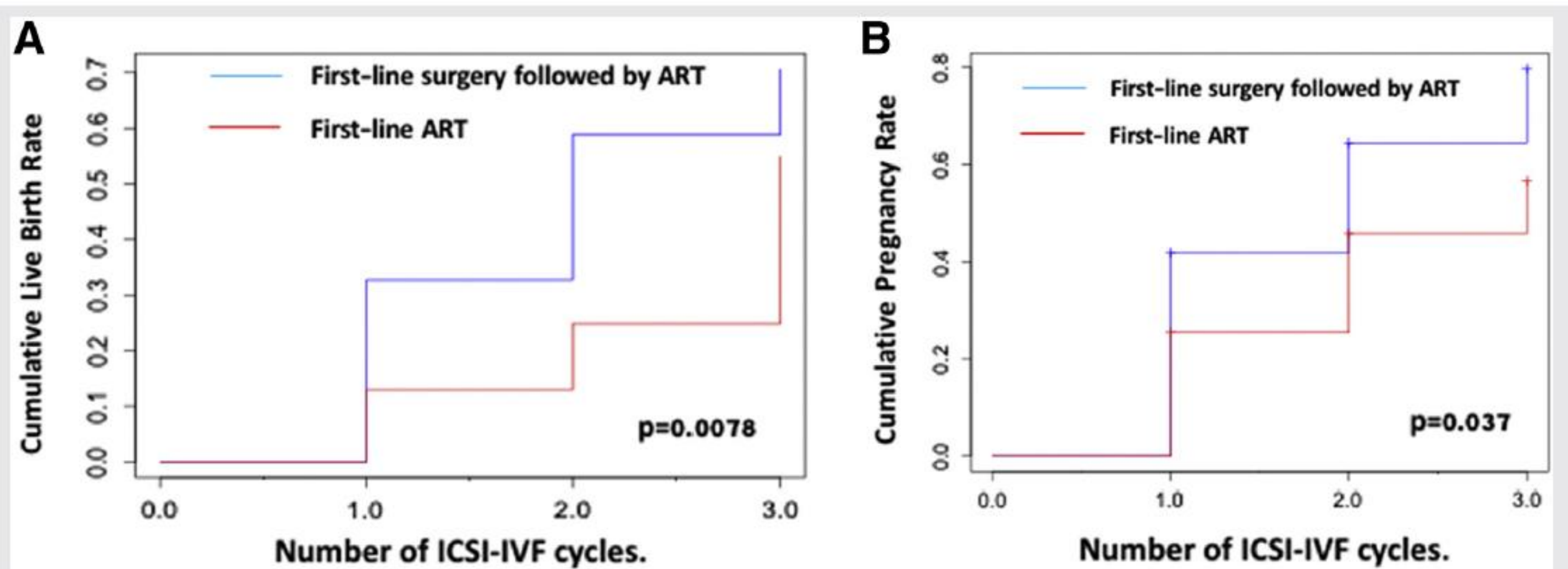
Sofiane Bendifallah, M.D., Ph.D.,^{a,b} Horace Roman, M.D., Ph.D.,^c Emmanuelle Mathieu d'Argent, M.D.,^a Salma Touleimat, M.D.,^c Jonathan Cohen, M.D., Ph.D.,^a Emile Darai, M.D., Ph.D.,^{a,d,e} and Marcos Ballester, M.D., Ph.D.^{a,d,e}

^a Department of Gynaecology and Obstetrics, Tenon University Hospital, Assistance Publique des Hôpitaux de Paris, University Pierre and Marie Curie, Institut Universitaire de Cancérologie, Paris; ^b INSERM UMRS 707, Epidemiology, Information Systems, Modeling, University Pierre and Marie Curie, Paris; ^c Expert Center in the Diagnosis and Multidisciplinary Management of Endometriosis, Department of Gynecology and Obstetrics, Rouen University Hospital, Rouen; ^d UMRS 938 Université Pierre et Marie Curie, Paris; and ^e Groupe de Recherche Clinique GRC6-UPMC, Centre Expert En Endométrie, Paris, France

Endometriosis: Surgery or ART?

No surgery before ART rule

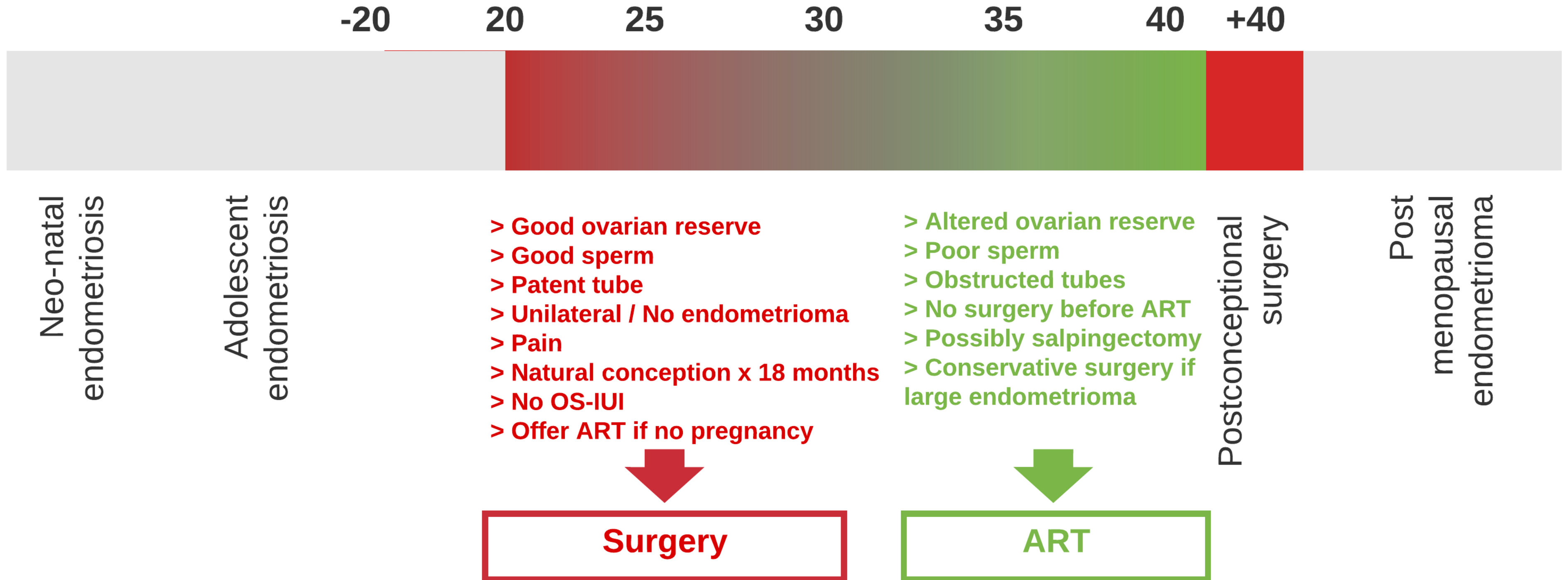
Not everyone agrees



(A) CLBR according to treatment strategy. (B) CPR according to treatment strategy.

Bendifallah. Colorectal endometriosis and infertility. Fertil Steril 2017.

Endometriosis: Surgery or ART?



Endometriosis: a New ART Indication

Diagnosis of endometriosis

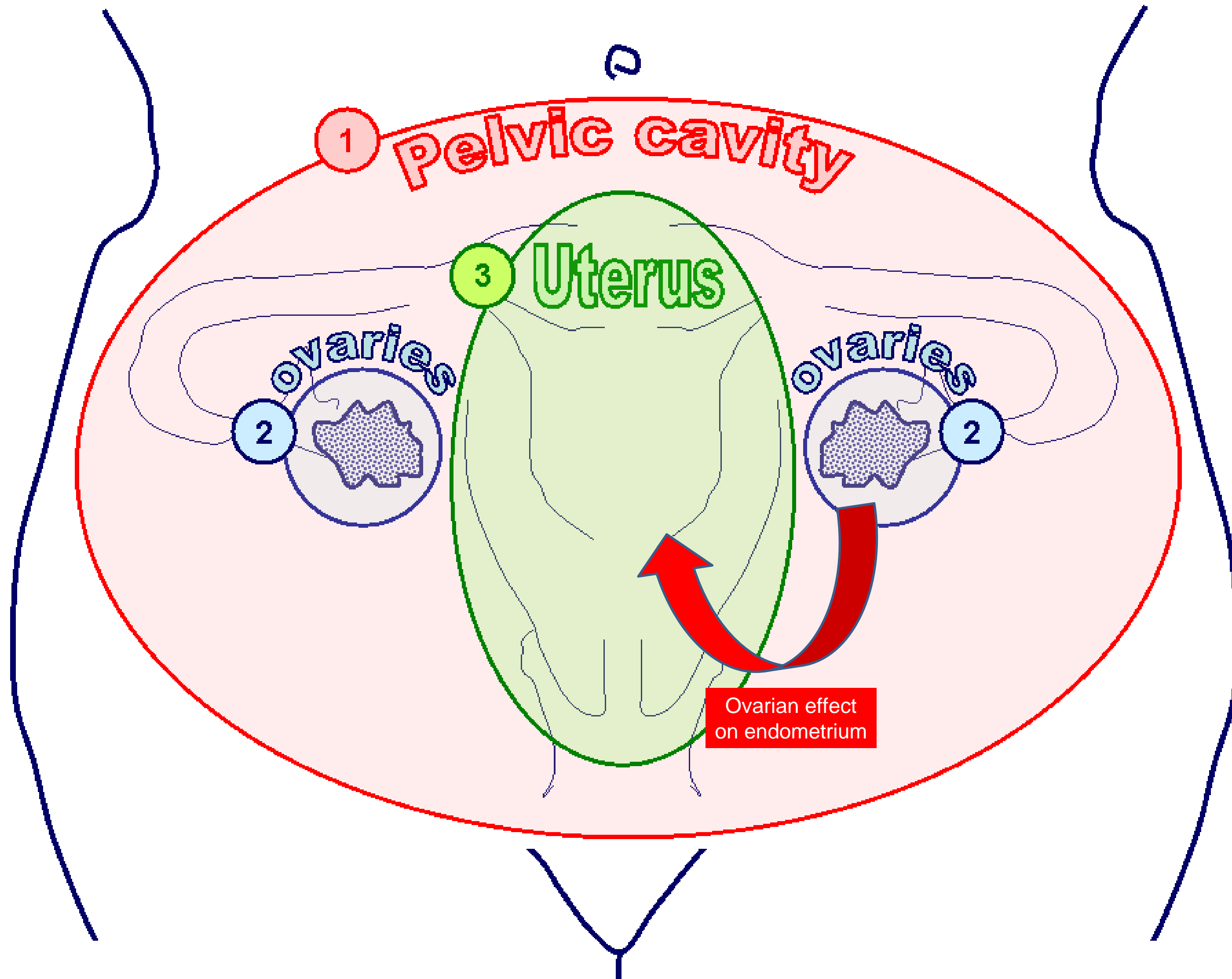
Pathophysiology of endometriosis: oocyte quality

Endometriosis through women's age

Endometrial receptivity

Surgery more harmful on ovarian reserve than endometriosis itself

Practical management

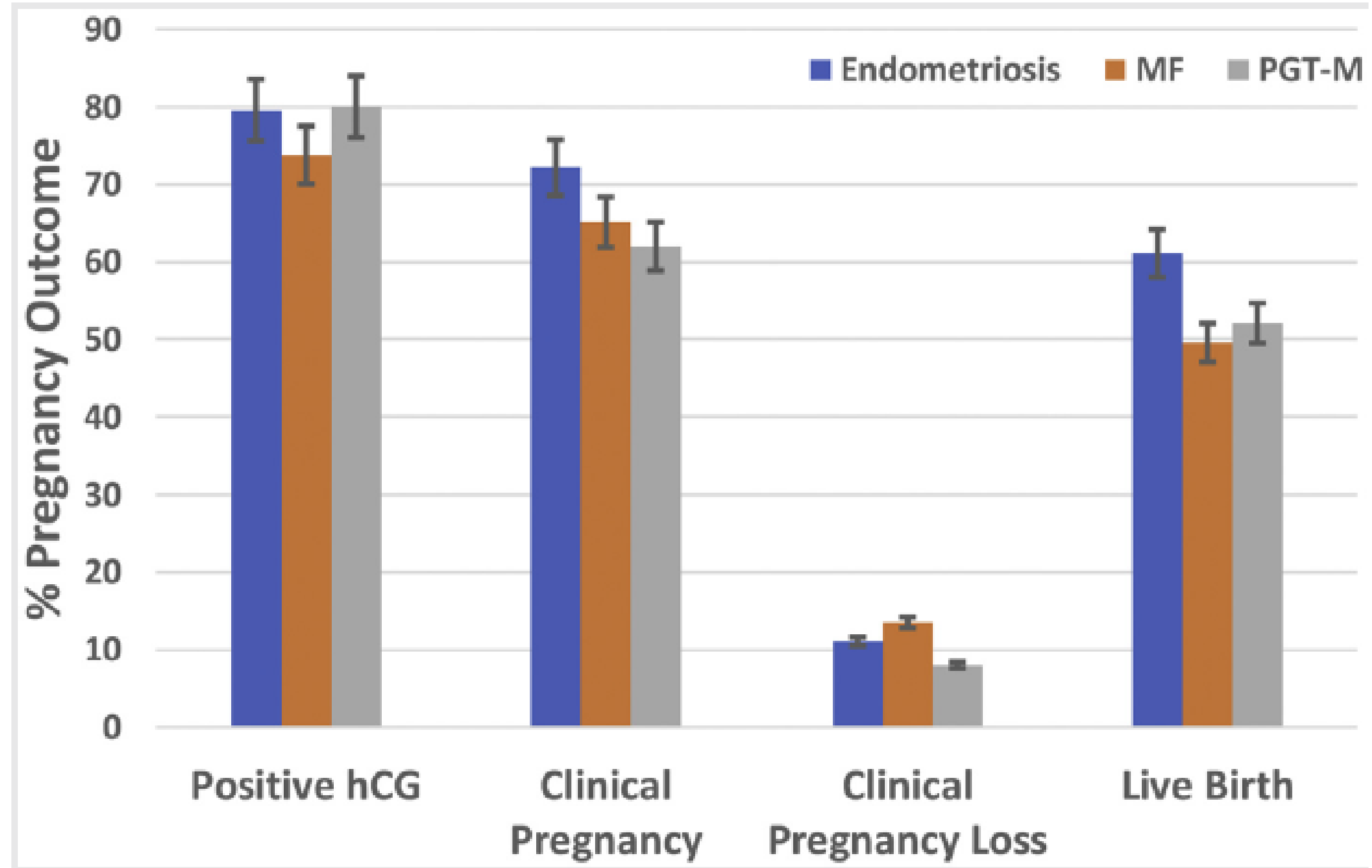


Endometriosis: a New ART Indication

Bishop et al. Fertil Steril 2020

Endometrium
normalized by :

- GnRH-a
- OC-Pill
- E2-P4 for FET



Endometriosis: a New ART Indication

In case of:

- Endometriosis
- Adenomyosis

Offer:

- ART
- Freeze all
- Deferred embryo transfer

Endometriosis: a New ART Indication

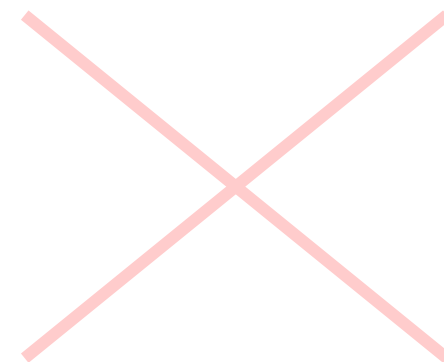
E2 and progesterone normalizes the endometrium in endometriosis.

Parenteral



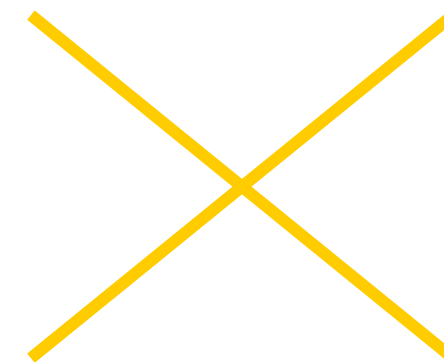
First described

Oral




Poor bioavailability

Transdermic



Poor permeability

Vaginal

An anatomical diagram of the female reproductive system, showing the uterus, fallopian tubes, and vagina. The diagram is set against a dark blue background and is enclosed in a red border.

Pregnancy outcomes of infertile women with ultrasound-diagnosed adenomyosis for in vitro fertilization and frozen-thawed embryo transfer

Zhang XP

Arch Gynecol Obstet 2021 Oct;304(4):1089-96.

A total of 5,087 patients met the inclusion and exclusion criteria, and they were divided into two groups: adenomyosis with tubal factor infertility (study group, n = 193) and only tubal factor infertility (control group, n = 4894). After a 1:1 propensity score match (caliper value = 0.005), 360 cases were matched in the end.

There was no statistical difference in the embryo implantation rate, clinical pregnancy rate, or multiple pregnancy rate between the two groups (28.4% vs. 31.7%, 42.2% vs. 42.8%, and 11.7% vs. 12.8%, respectively; $P > 0.05$).

Endometriosis: a New ART Indication

Diagnosis of endometriosis

Pathophysiology of endometriosis: oocyte quality

Endometriosis through women's age

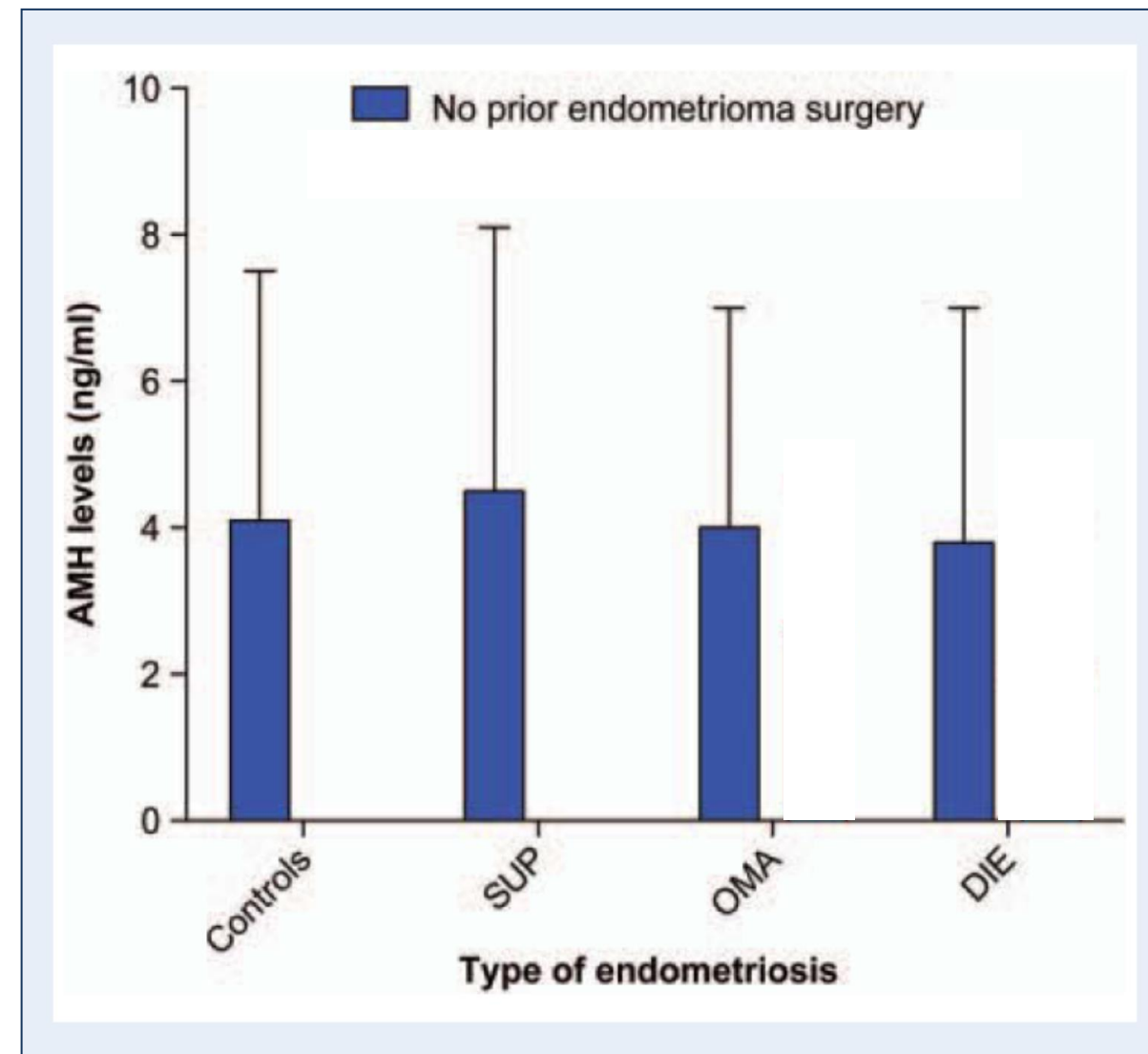
Endometrial receptivity

Surgery more harmful on ovarian reserve than endometriosis itself

Practical management

Sx and AMH

We were first to report that surgery for endometriosis is more harmful for ovarian reserve than endometriosis itself



AMH, OSIS & Sx for OSIS

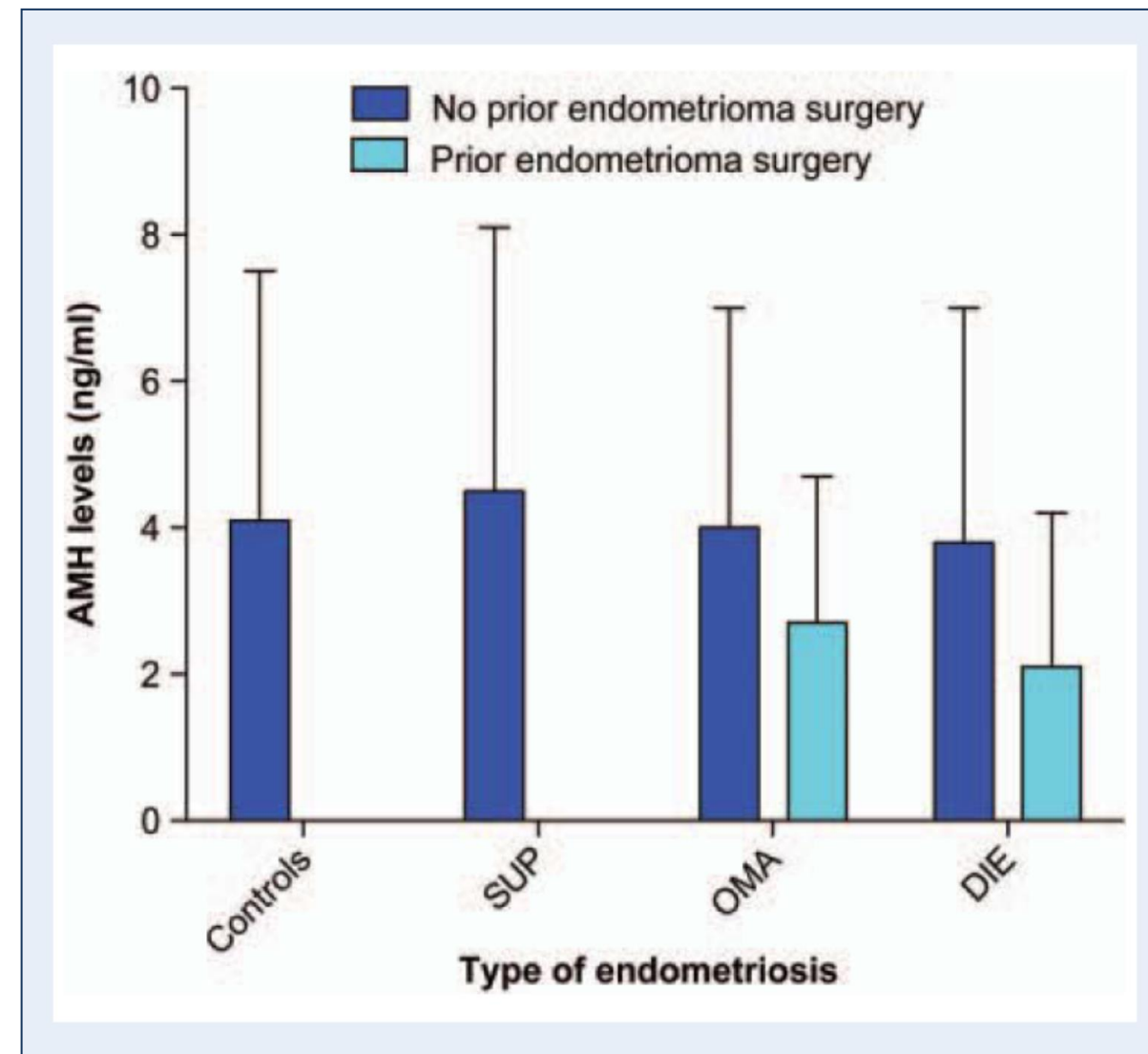
n = 514(E) + 413(C)

Streuli I et al.
Hum Reprod.
2012;27:3294-303

Retrospective measurement of AMH in 927 women with and without OSIS. No difference seen.

Sx and AMH

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AMH, OSIS & Sx for OSIS

n = 514(E) + 413(C)

Streuli I et al.
Hum Reprod.
2012;27:3294-303

Retrospective measurement of AMH in 927 women with and without OSIS. No difference seen.

During the past decade, the role of surgery for managing infertility associated with endometriosis has changed ⁷⁶.

- (i) Surgery has no proven benefit on ART outcome including if endometriomas are present ^{77 78 76}, even if this is still challenged by a few ^{79 80};
- (ii) Contrary to ovarian stimulation and insemination, ART does not worsen endometriosis-related pain symptoms, increase the risk of endometriosis recurrence and has little or no impact on ovarian endometriomas or deep infiltrating endometriosis ⁸¹;
- (iii) Surgery is likely to harm ovarian function, altering ovarian reserve ⁸² and further responses to ovarian stimulation ⁸³

77. Brink Laursen J, et al. Surgery versus conservative management of endometriomas in subfertile women. A systematic review. *Acta Obstet Gynecol Scand* 2017; **96**(6): 727-35.
78. Wu CQ, et al. Live Birth Rate after Surgical and Expectant Management of Endometriomas after In Vitro Fertilization: A Systematic Review, Meta-Analysis, and Critical Appraisal of Current Guidelines and Previous Meta-Analyses. *J Minim Invasive Gynecol* 2019; **26**(2): 299-311 e3.
79. Casals G, et al. Impact of Surgery for Deep Infiltrative Endometriosis before In Vitro Fertilization: A Systematic Review and Meta-analysis. *J Minim Invasive Gynecol* 2021; **28**(7): 1303-12 e5.
80. Bendifallah S, et al. Colorectal endometriosis-associated infertility: should surgery precede ART? *Fertil Steril* 2017; **108**(3): 525-31 e4.
81. Somigliana E, et al. Ovarian stimulation and endometriosis progression or recurrence: a systematic review. *Reprod Biomed Online* 2019; **38**(2): 185-94.
82. Benaglia L, et al. Is endometrioma-associated damage to ovarian reserve progressive? Insights from IVF cycles. *Eur J Obstet Gynecol Reprod Biol* 2017; **217**: 101-5.
83. Bourdon M, et al. Endometriosis and ART: A prior history of surgery for OMA is associated with a poor ovarian response to hyperstimulation. *PLoS One* 2018; **13**(8): e0202399.

Endometriosis: a New ART Indication

Diagnosis of endometriosis

Pathophysiology of endometriosis: oocyte quality

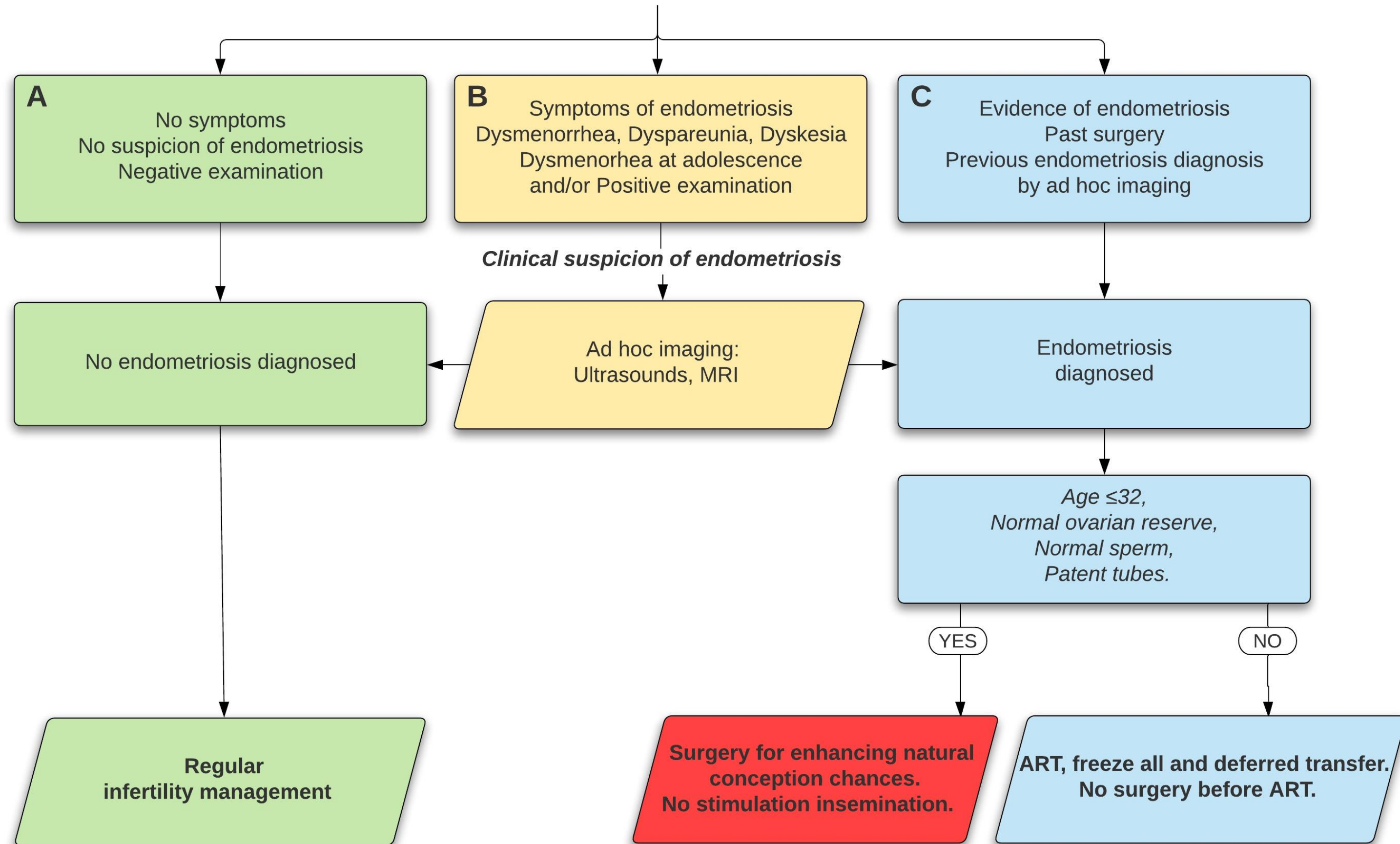
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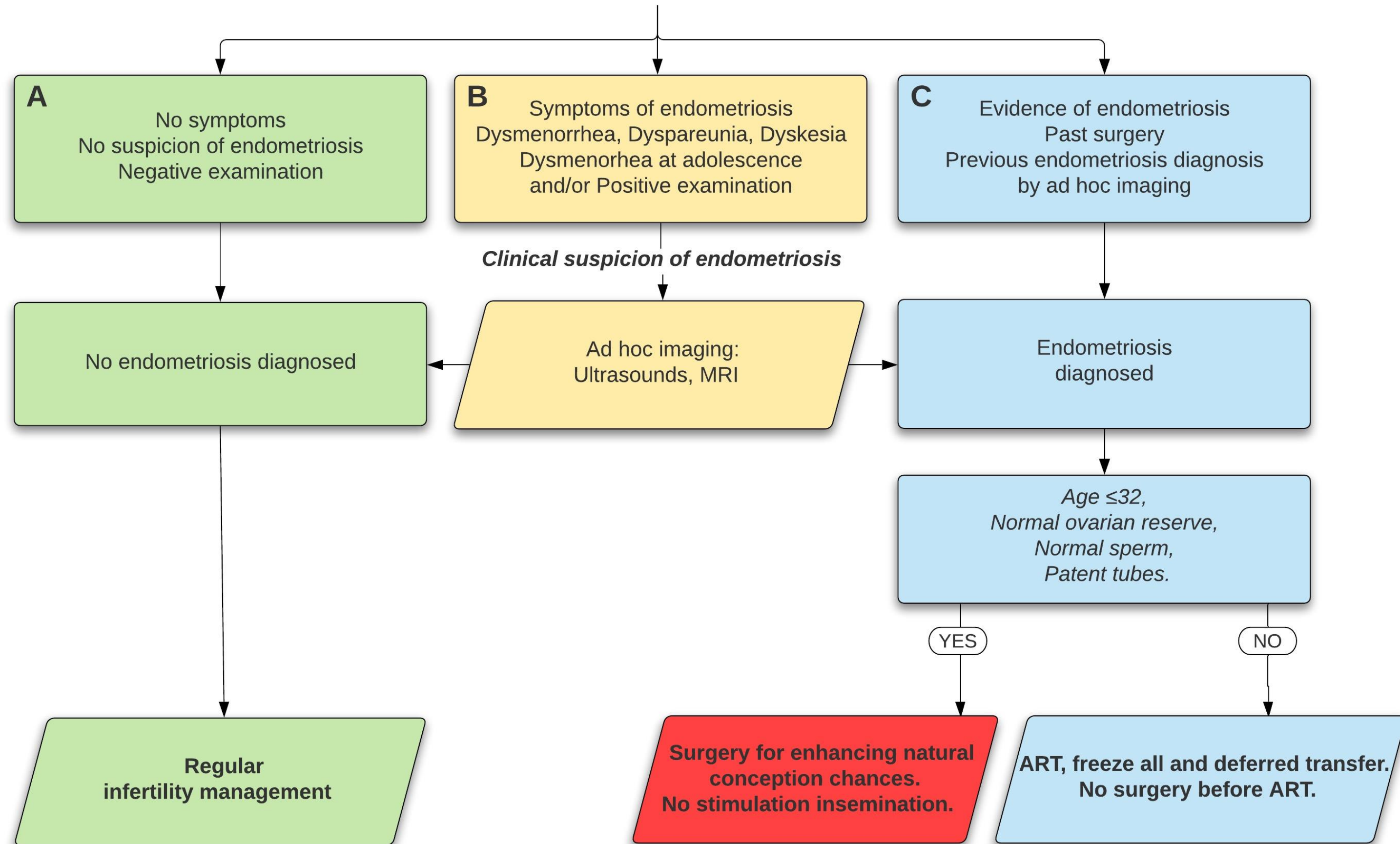
Surgery more harmful on ovarian reserve than endometriosis itself

Practical management

Initial consultation



Initial consultation



Excetions to “**No Sx before ART**” rule:

Very large endometrioma
Hydrosalinx, pelvic pain

Endometriosis: a New ART Indication

Tubal Infertility

Endometriosis

*Premature ovarian failure
donor egg ART*

Male factor (ICSI)

Take-home messages

- ✓ **Endometriosis is diagnosed by image-based approaches**
- ✓ **ART bypasses the toxic pelvic effects of endometriosis**
- ✓ **Endometriosis causes pro-inflammatory changes in the endometrium, implantation is not affected**
- ✓ **Surgery is more harmful on ovarian reserve than the disease itself**
- ✓ **Sx is effective on pain and increases chances of natural conception**

THANK YOU

Pr Jean Marc Ayoubi
Pr René Frydman
Pr Philippe Bouchard
Dr Paul Pirtea
Dr Marine Poulain



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