

MINISTERIAL CONFERENCE

WOMEN'S HEALTH: A LIFE COURSE APPROACH

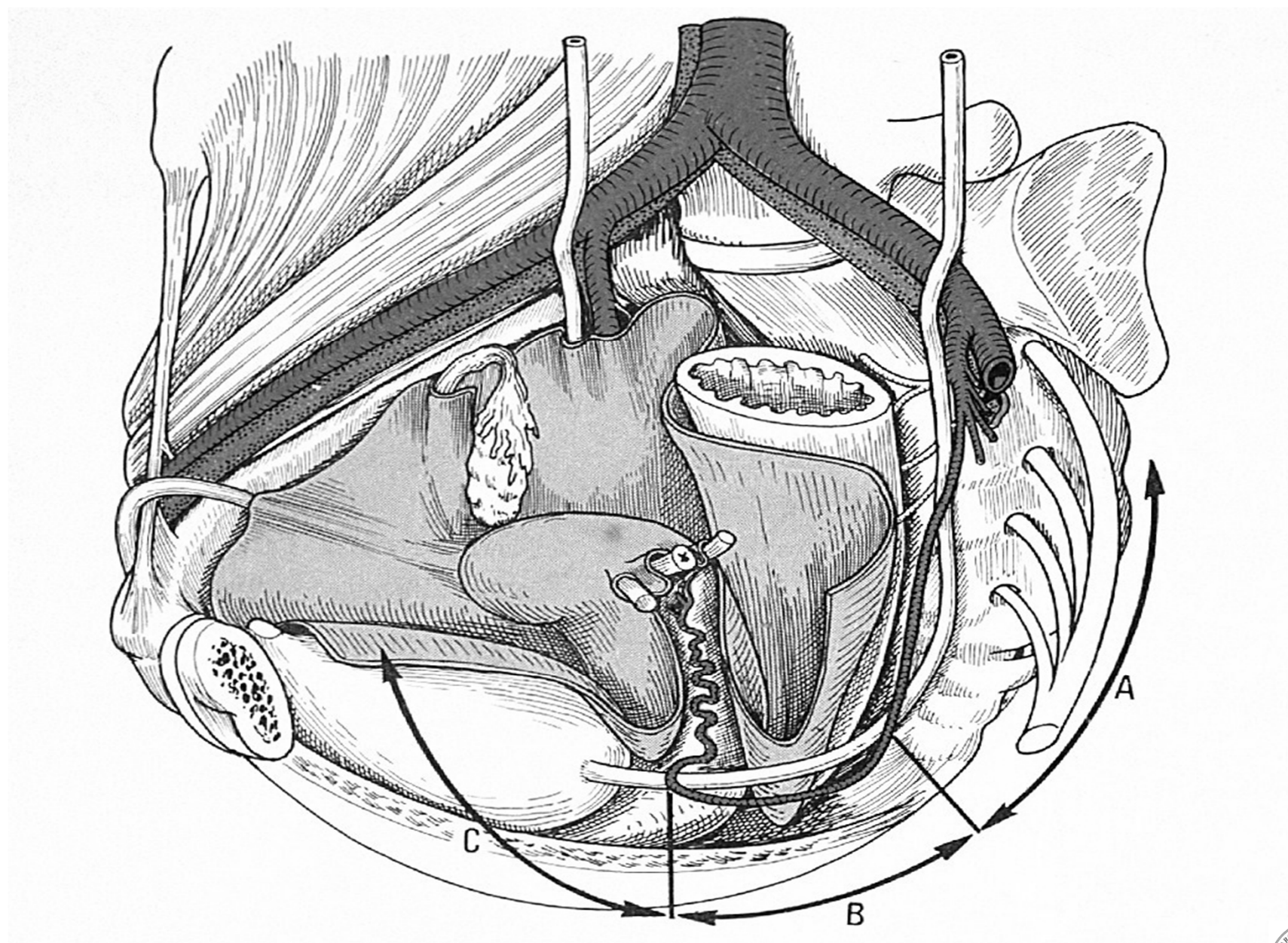
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# ENDOMETRIOSIS AND SEXUAL PAIN

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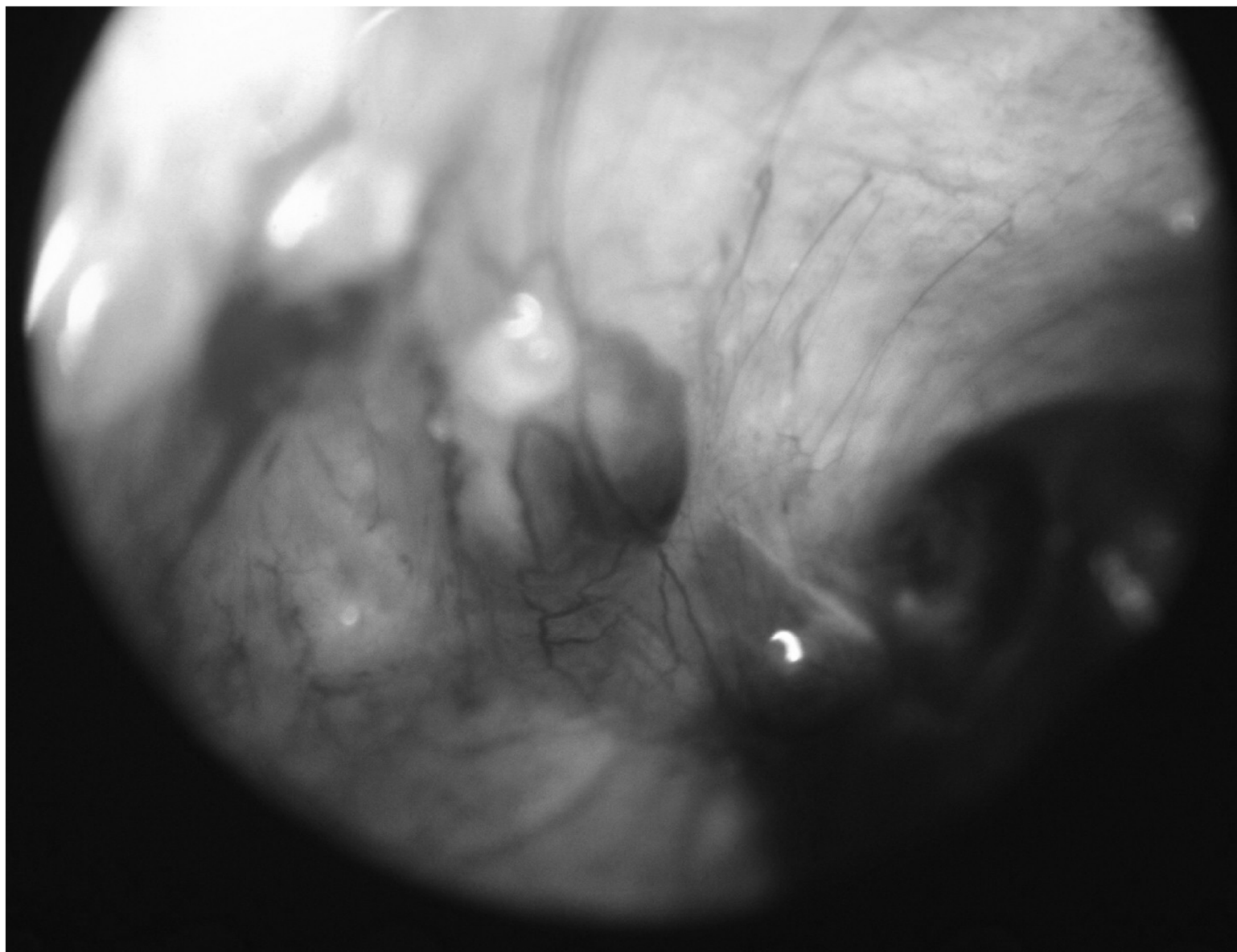


## VARIATION IN MENSTRUAL AND REPRODUCTIVE FACTORS OVER THE PAST CENTURY

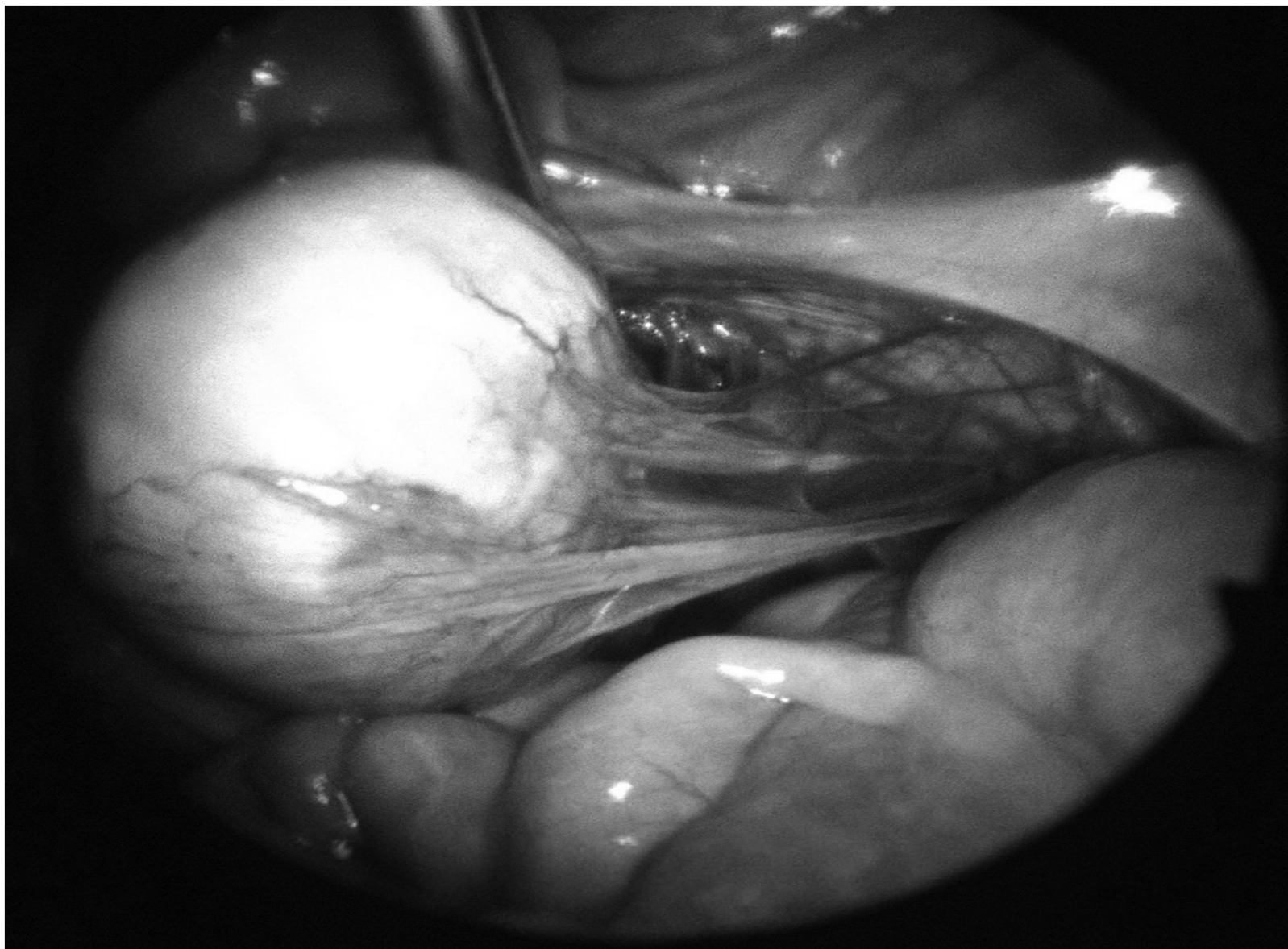
Variable	Foremothers	Modern women
Age at menarche (y)	16	12
Age at first birth (y)	19	24-30
Pregnancies ( <i>n</i> )	6	1-2
Breast feeding	Years	Months
Ovulations and menstruations	30-160	450

*From Vercellini et al., RBMO 2010*

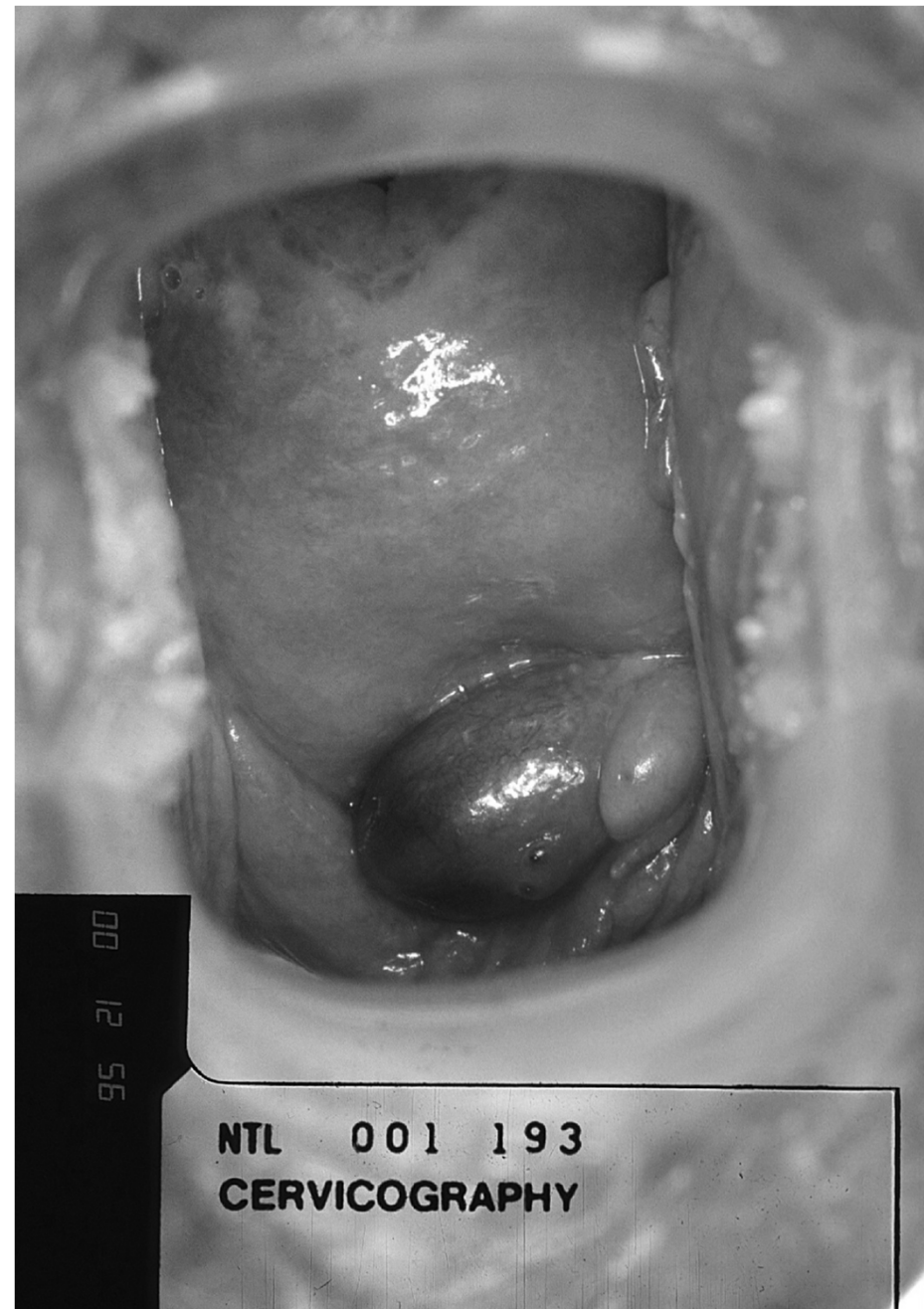




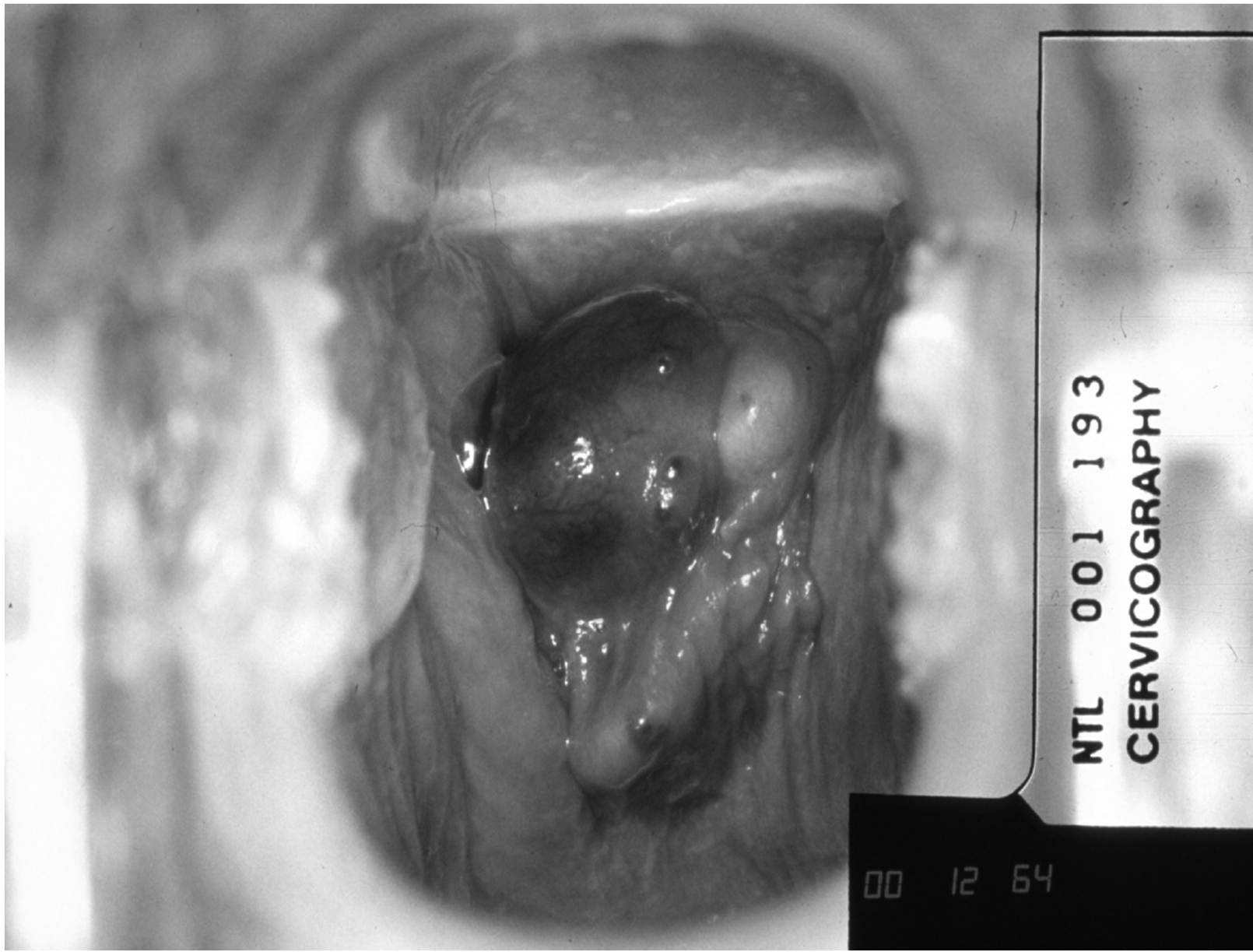




Colposcopic appearance of  
the posterior fornix with  
reddish vegetations and a  
bluish nodule



*Clinica Ostetrica e Ginecologica "Luigi Mangiagalli", University of Milan, Italy*



# ENDOMETRIOSIS AND PELVIC PAIN

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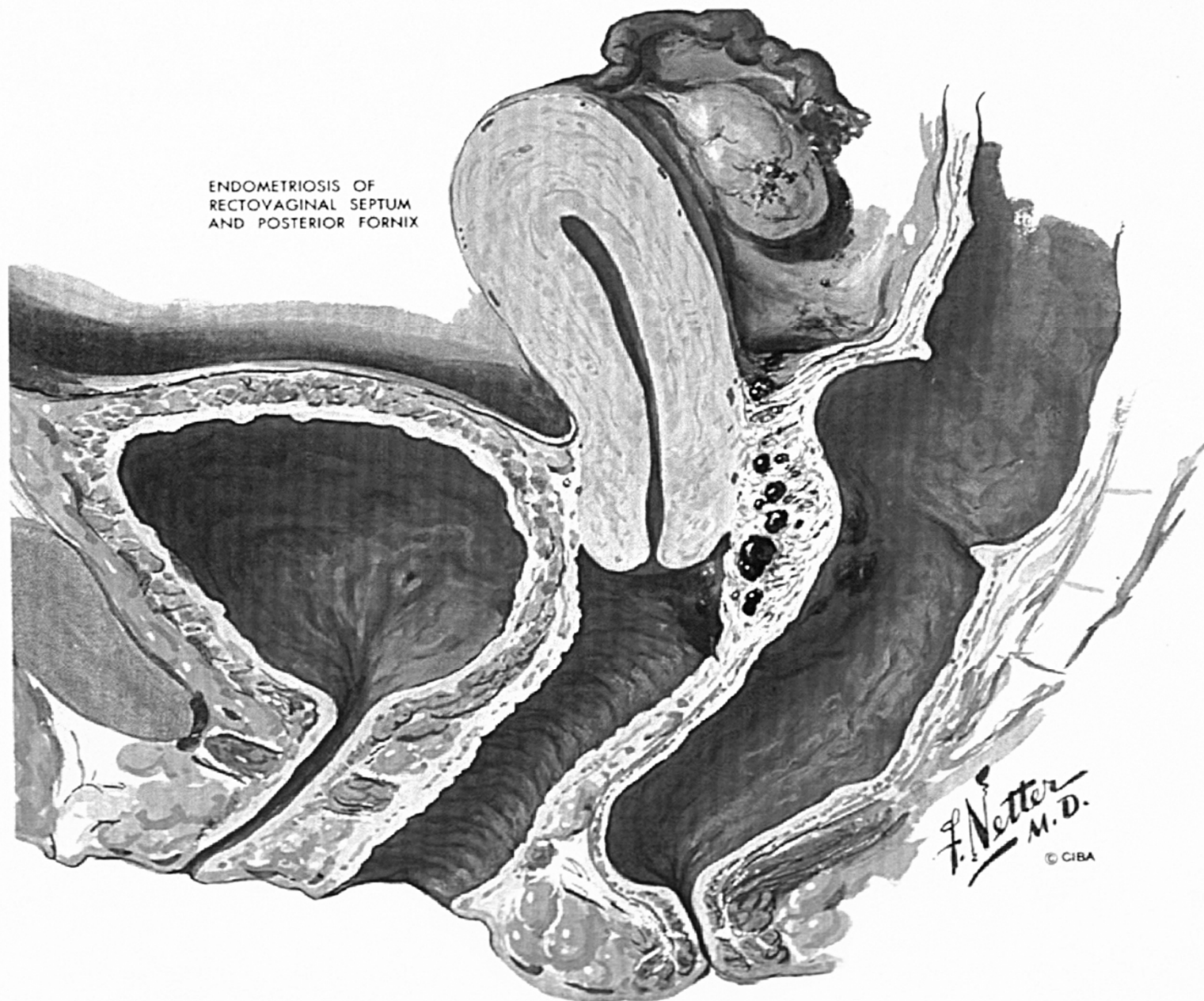
Fresh, metabolically active, intra-peritoneal implants may cause functional pain symptoms such as dysmenorrhea, whereas infiltrating, nodular and fibrotic lesions are responsible for organic-type pain such as deep dyspareunia

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*Vercellini et al., J Reprod Med 1991; Fertil Steril 1996; Semin Reprod Med 1997*



ENDOMETRIOSIS OF  
RECTOVAGINAL SEPTUM  
AND POSTERIOR FORNIX



*F. Netter*  
M.D.  
© GIBA

SYMPTOMS AND DIAGNOSES RECORDED IN THE 3 YEARS BEFORE THE  
INDEX (DIAGNOSIS) DATE AMONG CASES AND CONTROLS, WITH  
UNADJUSTED ODDS RATIOS FOR ENDOMETRIOSIS

	Controls ( <i>n</i> = 21239)	%	Cases ( <i>n</i> = 5540)	%	OR (95% CI)
Dysmenorrhoea	725	3.4	1364	24.6	9.8 (8.8–10.9)
Pelvic pain	312	1.5	862	15.6	13.5 (11.7–15.7)
Dyspareunia	219	1.0	509	9.2	9.4 ( 8.0–11.1)
Infertility/subfertility	377	1.8	533	9.6	6.2 ( 5.4– 7.1)
Depression*	2895	13.6	1197	21.6	1.8 ( 1.6– 1.9)
Symptoms associated with sexual intercourse**	366	1.7	638	11.5	7.4 ( 6.5– 8.5)

\* Not including postnatal depression, diagnoses/treatments prescribed during pregnancy or within 2 years of delivery.

\*\* Postcoital bleeding, dyspareunia.

*Modified from Ballard et al.,BJOG 2008*

# ENDOMETRIOSIS AND PELVIC PAIN

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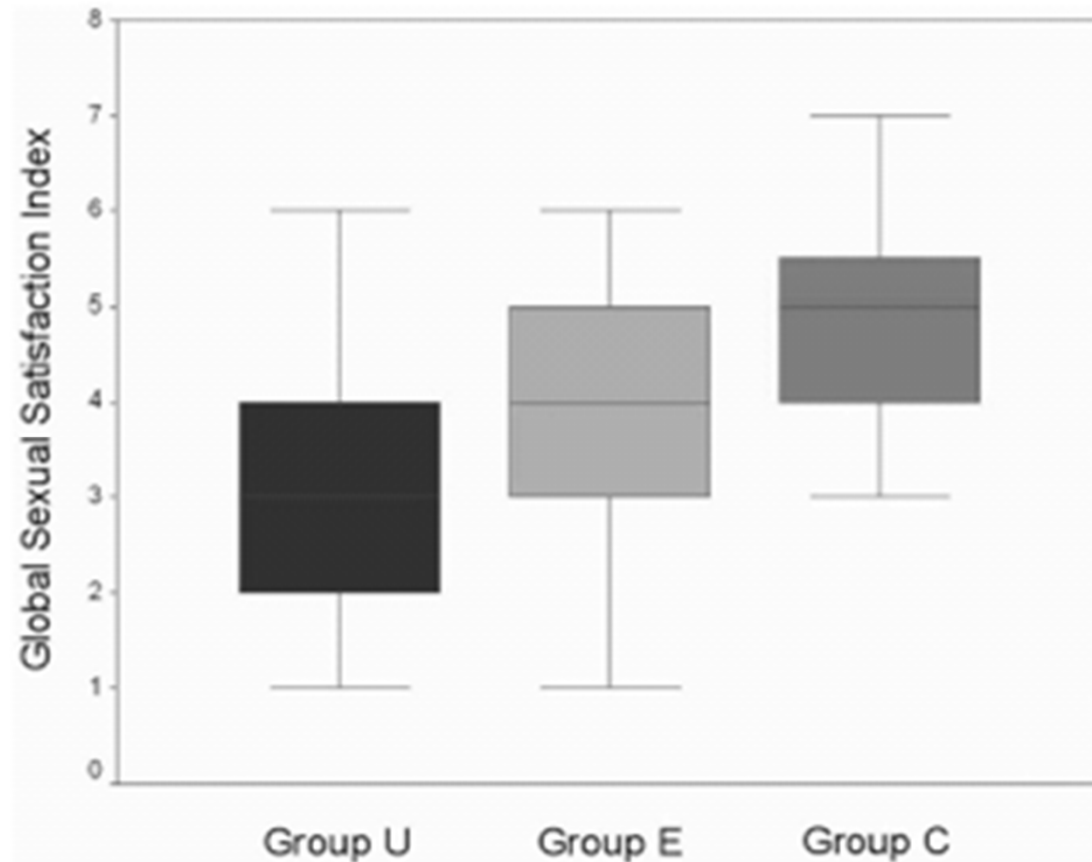
Patients with vaginal endometriosis had a significantly increased risk of deep dyspareunia compared with those whose lesions were at other sites  
(OR, 2.55; 95% C.I., 1.21-5.39)

Stage was not correlated with frequency and severity of pain symptoms

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*Vercellini et al., Fertil Steril 1996*

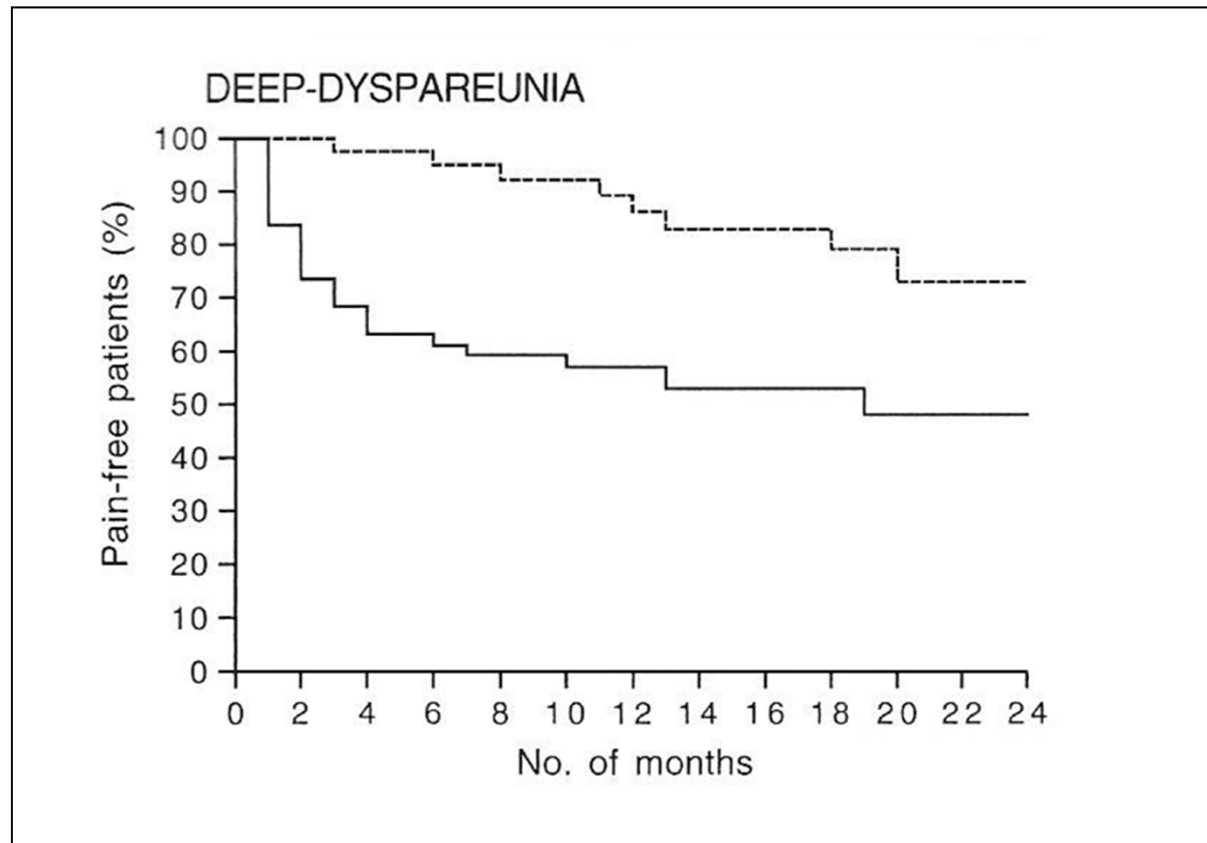
Global Sexual Satisfaction Index (GSSI). GSSI asks subjects to self-rate their overall level of sexual satisfaction on a scale of 0 to 8. The *boxes* delimit scores falling between the 25th and the 75th percentiles, and the *horizontal lines* refer to median scores.



*From Ferrero et al., Fertil Steril 2005*



TWENTY-FOUR MONTH SYMPTOM-FREE SURVIVAL ANALYSIS IN  
105 WOMEN WITH RECTOVAGINAL ENDOMETRIOSIS  
UNDERGOING CONSERVATIVE SURGERY AT LAPAROTOMY ( $n = 44$ ;  
*dashed line*) OR EXPECTANT MANAGEMENT ( $n = 61$ ; *solid line*)



*From Vercellini et al., Am J Obstet Gynecol 2006*

# MAIN RESULTS OF INDIVIDUAL STUDIES IN SYSTEMATIC REVIEW OF MEDICAL TREATMENTS FOR RECTOVAGINAL ENDOMETRIOSIS. EFFECT ON DEEP DYSPAREUNIA

Author	Year	Treatment	Pain at baseline *	Pain during treatment*
Fedele <i>et al.</i>	2000	GnRHa	2.0 (0.7) <sup>†</sup>	1.2 (0.4)
Fedele <i>et al.</i>	2001	Lng-IUD	1.9 (0.9) <sup>†</sup>	0.5 (0.5)
Vercellini <i>et al.</i>	2005	EE + CPA	46 (22) <sup>‡</sup>	11 (23)
		NETA	51 (25)	14 (23)
Razzi <i>et al.</i>	2007	Vaginal danazol	1.9 (0.8) <sup>†</sup>	0.1 (0.3)
Remorgida <i>et al.</i>	2007	Letrozole + NETA	7.6 (1.5) <sup>‡</sup>	2.2 (2.0)
Vercellini <i>et al.</i>	2009 <sup>§</sup>	Vaginal ring	71 (12) <sup>‡</sup>	30 (19)
		Transdermal patch	71 (22)	42 (26)

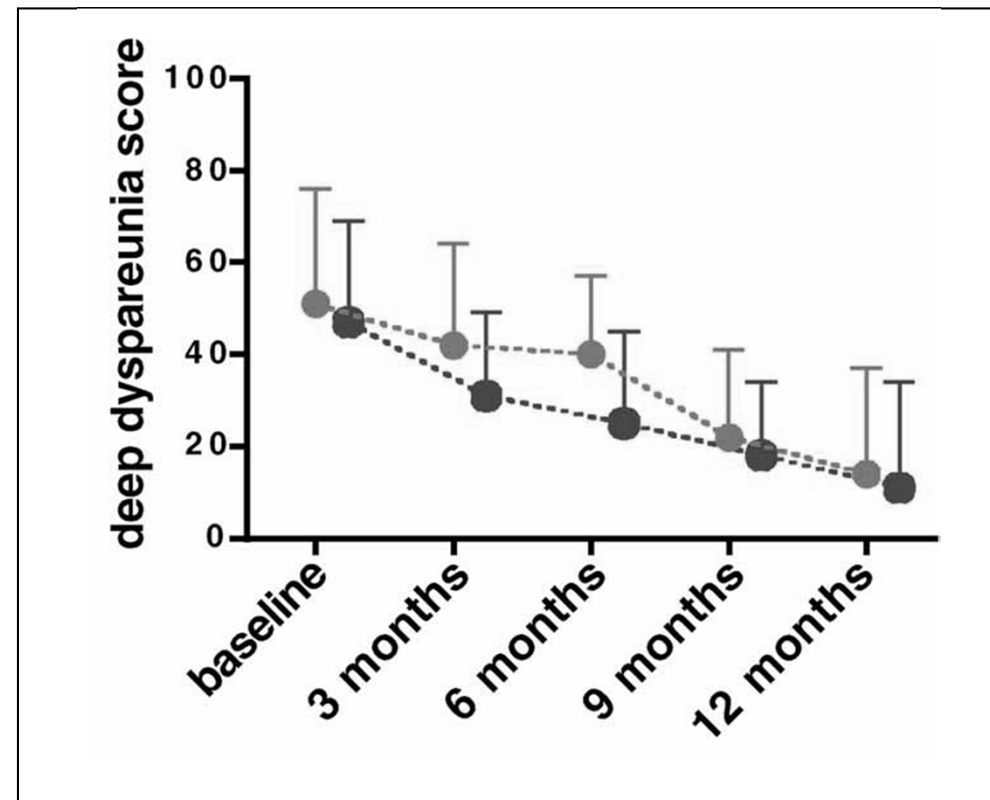
EE + CPA = ethinylestradiol + cyproterone acetate; NETA = norethindrone acetate.

\* Values are mean (SD); <sup>†</sup> verbal rating scale scores; <sup>‡</sup> visual analog scale scores; <sup>§</sup> only subjects with rectovaginal endometriotic lesions are considered.

*Modified from Vercellini et al., Hum Reprod 2009*

# EP vs NETA FOR RECTOVAGINAL ENDOMETRIOSIS

VARIATION OF DEEP DYSPAREUNIA INTENSITY AS ASSESSED ON A VISUAL ANALOG SCALE DURING THE STUDY PERIOD



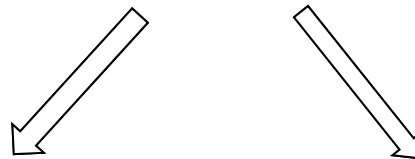
Values are mean  $\pm$  SD shown by vertical bars; *Violet*, ethinyl E<sub>2</sub> plus cyproterone acetate group; *red*, norethindrone acetate group.

*Modified from Vercellini et al., Fertil Steril 2005*

# MEDICAL VS SURGICAL TREATMENT FOR SEVERE DEEP DYSPAREUNIA ASSOCIATED WITH ENDOMETRIOSIS

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- Prospective parallel cohort study; patient-preference trial
- Study population: subjects with a surgical diagnosis of endometriosis and severe deep dyspareunia (VAS  $\geq$  80 mm)



Medical treatment  
(oral nor-ethisterone acetate  
2.5 mg/die)

Second-line surgical  
treatment

- Subgroup analysis: rectovaginal vs non-rectovaginal lesions
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# MEDICAL VS SURGICAL TREATMENT FOR SEVERE DEEP DYSPAREUNIA ASSOCIATED WITH ENDOMETRIOSIS

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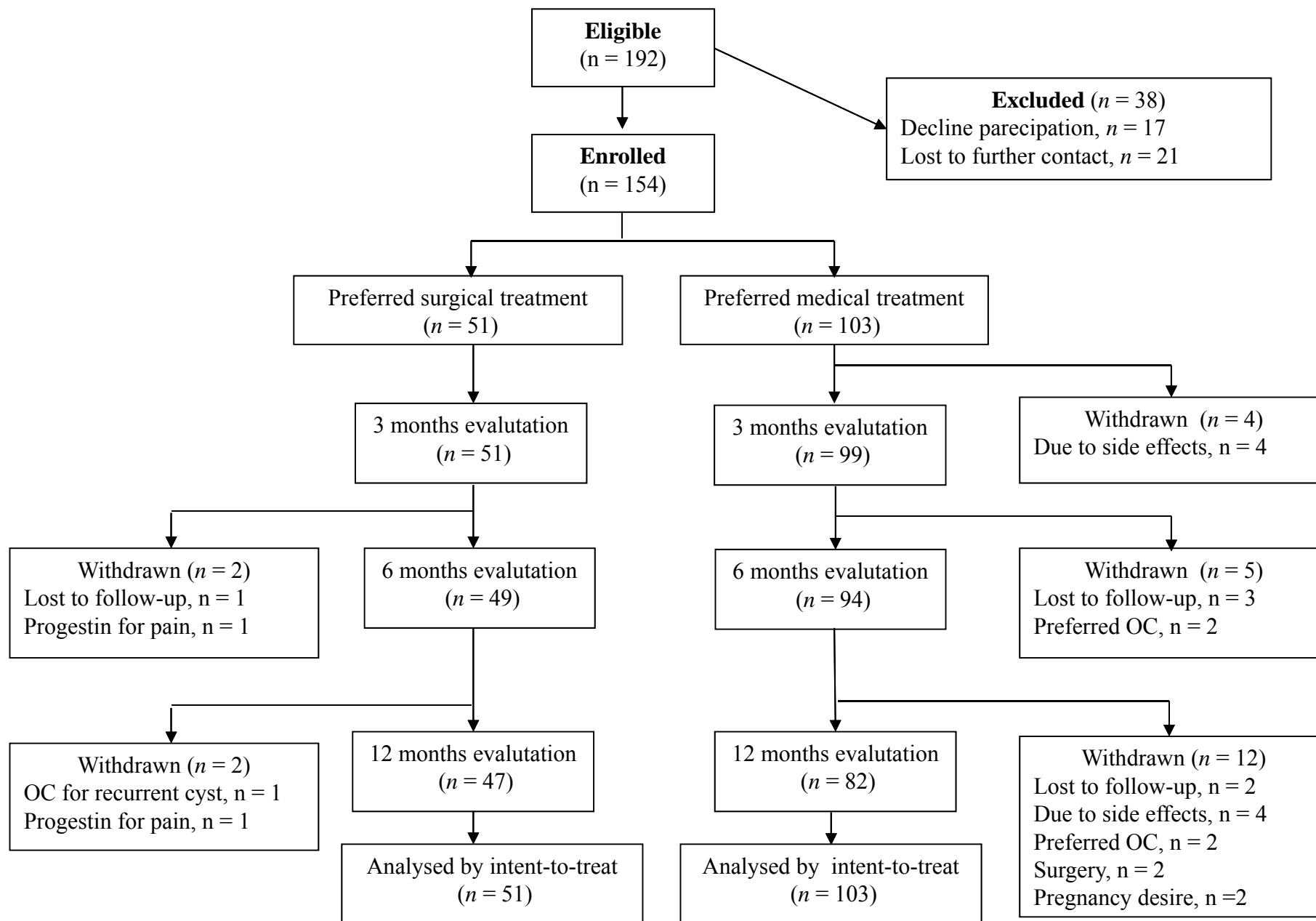
## *Main study objective:*

- Degree of patient satisfaction at 12-month follow-up

## *Secondary study objectives:*

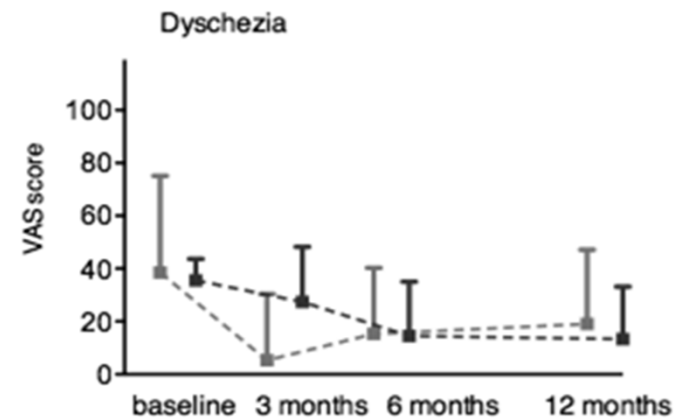
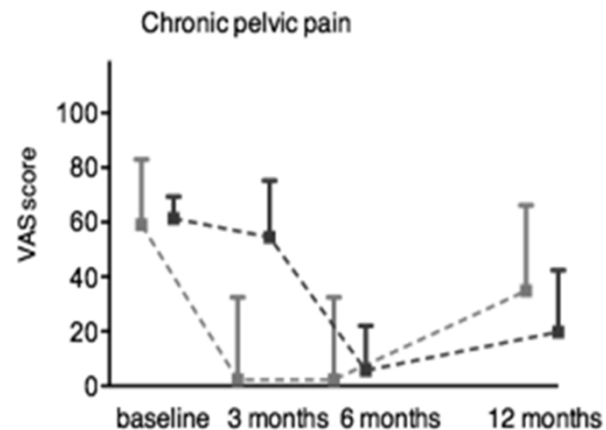
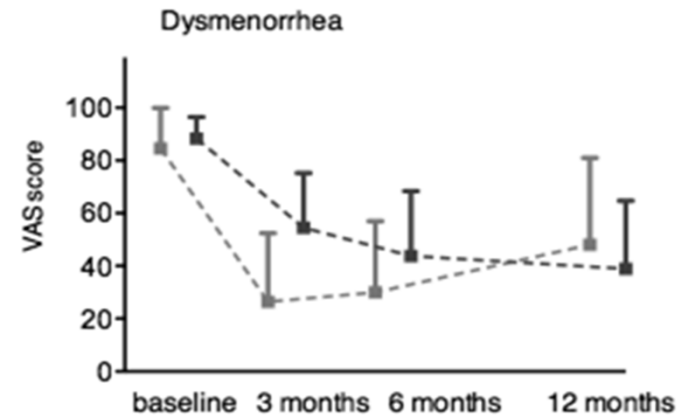
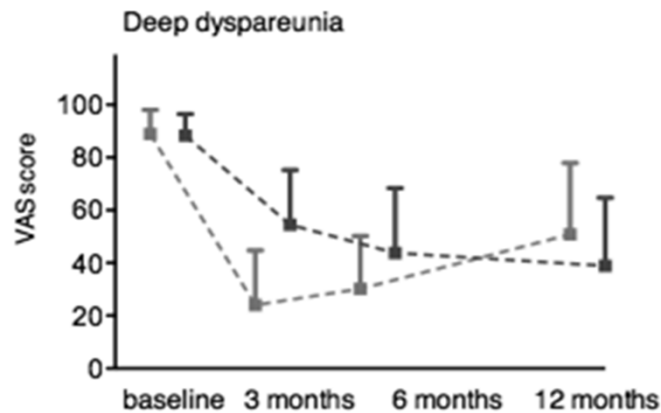
- Pain symptoms variation (VAS)
  - Sexual function  
(FSFI and number of monthly intercoursess)
  - Psychological aspects (HADS)
-

# STUDY FLOW CHART



## PAIN SYMPTOMS VAS SCORES VARIATION DURING THE STUDY PERIOD ACCORDING TO TREATMENT ALLOCATION

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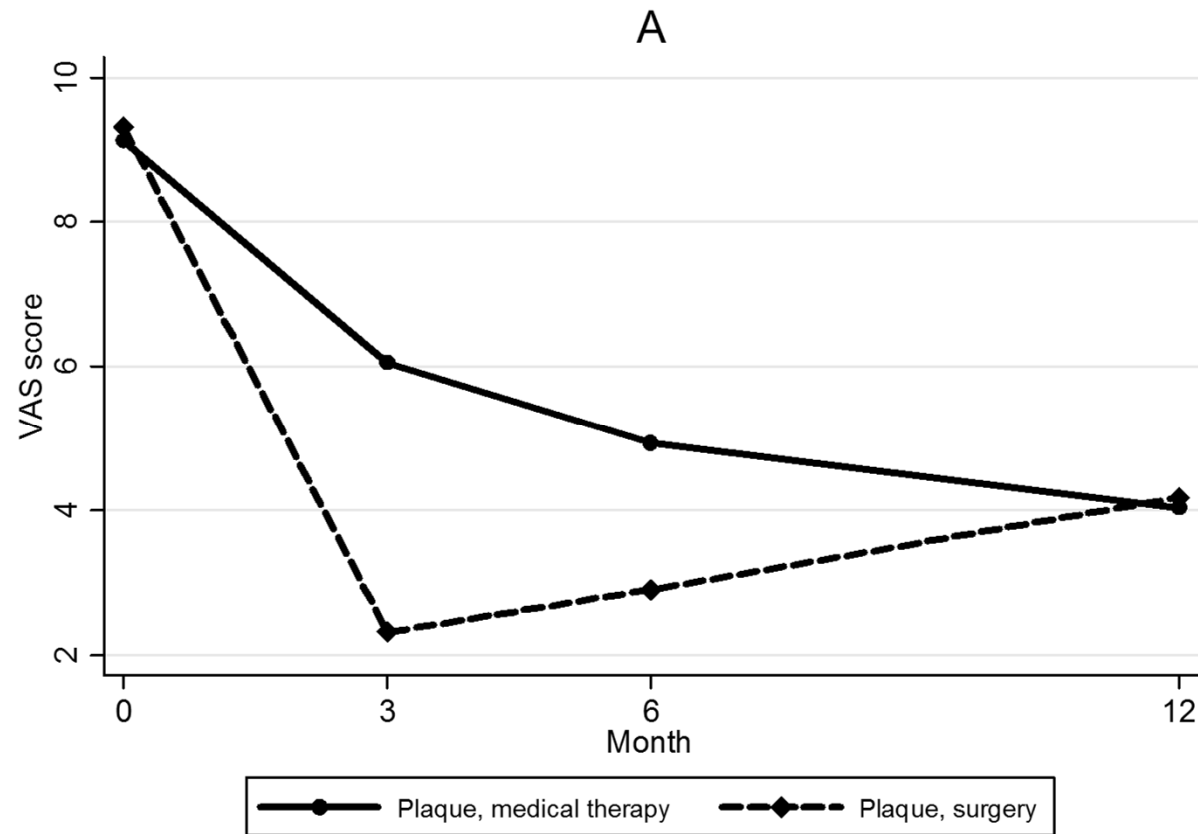


□ Surgery

□ NETA 2,5 mg/die

# DEEP DYSPAREUNIA VAS SCORE VARIATION DURING THE STUDY PERIOD ACCORDING TO TREATMENT ALLOCATION AND PRESENCE OF RECTOVAGINAL ENDOMETRIOSIS

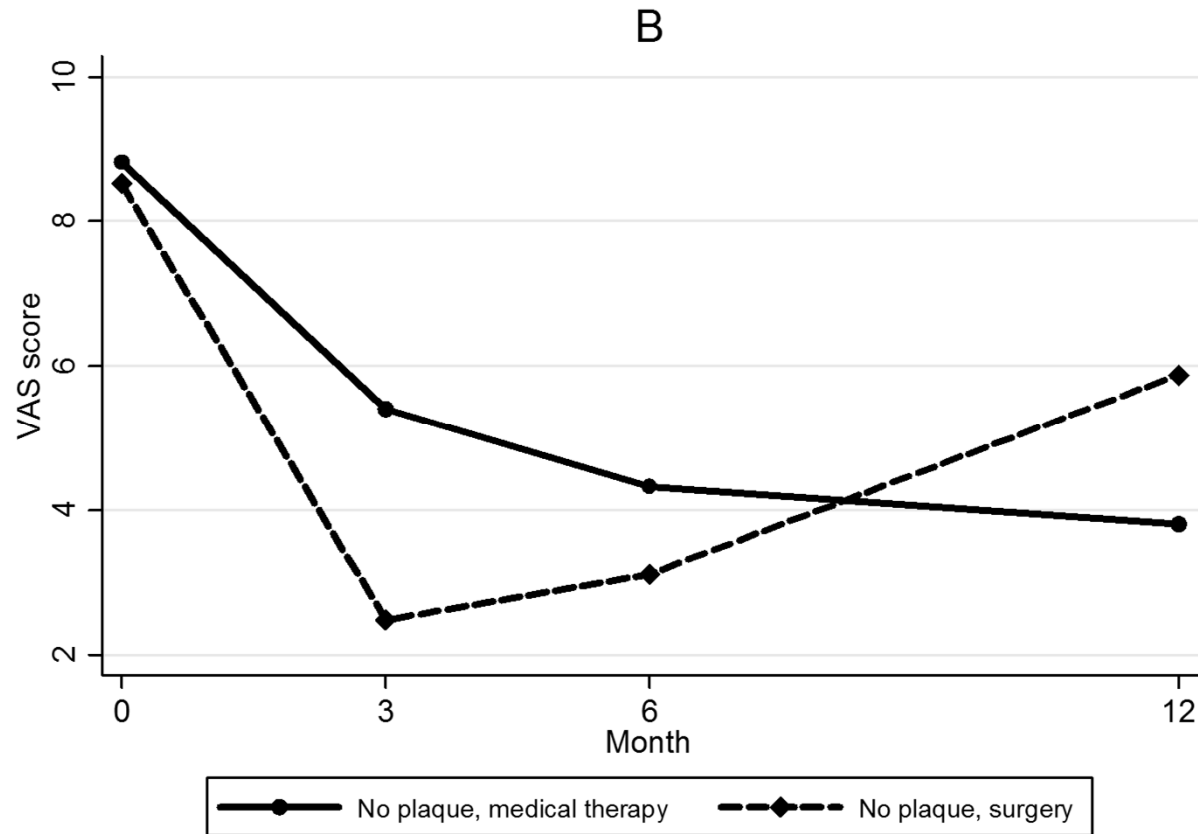
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# DEEP DYSPAREUNIA VAS SCORE VARIATION DURING THE STUDY PERIOD ACCORDING TO TREATMENT ALLOCATION AND ABSENCE OF RECTOVAGINAL ENDOMETRIOSIS

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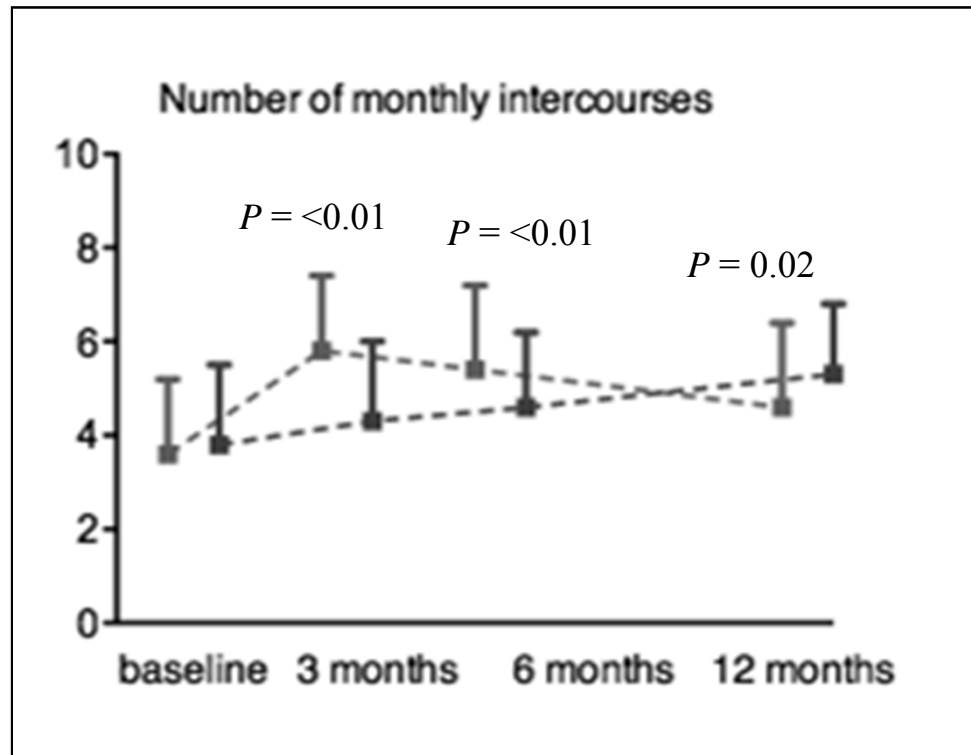


# FEMALE SEXUAL FUNCTION INDEX SCORE VARIATION DURING THE STUDY PERIOD ACCORDING TO TREATMENT ALLOCATION AND ENDOMETRIOTIC LESION TYPE

	Rectovaginal endometriosis			Non-rectovaginal endometriosis		
	Surgery group (n = 22)	Progestin group (n = 29)	<i>P</i>	Surgery group (n = 25)	Progestin group (n = 53)	<i>P</i>
Baseline	19 ± 4	20 ± 5	0.4	19 ± 5	18 ± 4	0.1
3 months	26 ± 5	21 ± 5	<0.01	26 ± 5	22 ± 5	<0.01
6 months	26 ± 4	21 ± 5	<0.01	25 ± 5	23 ± 6	0.21
12 months	24 ± 4	21 ± 5	0.1	23 ± 4	23 ± 6	0.8

## VARIATION IN THE NUMBER OF MONTHLY INTERCOURSES DURING THE STUDY PERIOD ACCORDING TO TREATMENT ALLOCATION

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□ Surgery

□ NETA 2,5 mg/die

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# HOSPITAL ANXIETY AND DEPRESSION SCALE SCORE VARIATION DURING THE STUDY PERIOD ACCORDING TO TREATMENT ALLOCATION

	Surgery Group ( <i>n</i> = 47)	Progestin Group ( <i>n</i> = 82)
<b>Baseline</b>		
Anxiety	11.4 ± 4.3	10.7 ± 4.5
Depression	11.5 ± 5.6	9.7 ± 4.4
Total	22.9 ± 9.6	20.3 ± 8.3
<b>12 months</b>		
Anxiety	6.4 ± 5.0	6.3 ± 4.6
Depression	6.0 ± 5.5	5.7 ± 4.6
Total	12.4 ± 10.1	12.0 ± 8.8



## SIDE EFFECTS REPORTED BY WOMEN USING NOR-ETHISTERONE ACETATE

Side effect	<i>n</i>	(%)
Weight gain	35	35
Breakthrough bleeding	21	20
Decreased libido	20	20
Vaginal dryness	12	12
Spotting	11	11
Breast tenderness	6	6
Bloating/swelling	5	5
Headache	4	4
Depression	4	4
Nausea	2	2

# EVALUATION OF SATISFACTION WITH TREATMENT AT THE END OF THE STUDY PERIOD

	Surgery group		Progestin group		<i>P</i>
	<i>n</i>	(%)	<i>n</i>	(%)	
Satisfied or very satisfied	22/51	(43)	61/103	(59)	0.08



# DEGREE OF SATISFACTION WITH TREATMENT AT THE END OF THE STUDY PERIOD IN PATIENT WITH AND WITHOUT RECTOVAGINAL ENDOMETRIOSIS

	Rectovaginal endometriosis		Non-rectovaginal endometriosis	
	Surgery <i>n</i> (%)	NETA <i>n</i> (%)	Surgery <i>n</i> (%)	NETA <i>n</i> (%)
Satisfied or very satisfied	14/24 (54)	18/35 (51)	9/27 (33)	43/68 (63)
	<i>P</i> = 0.84		<i>P</i> = 0.02	



## ENDOMETRIOSIS AND DEEP DYSPAREUNIA

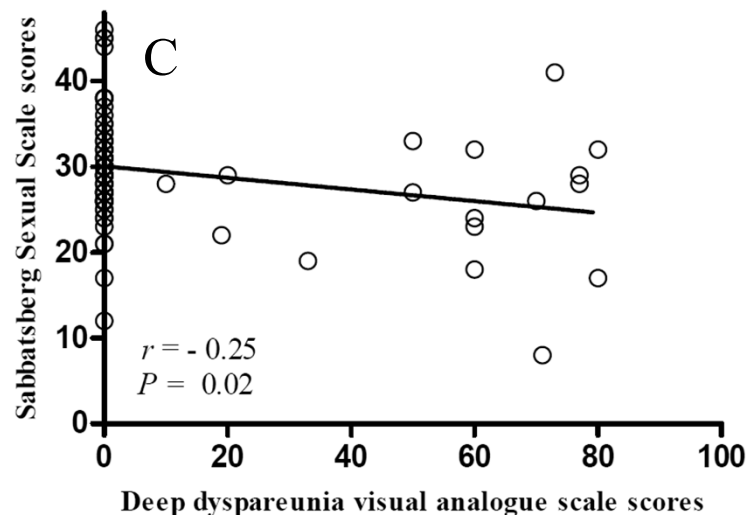
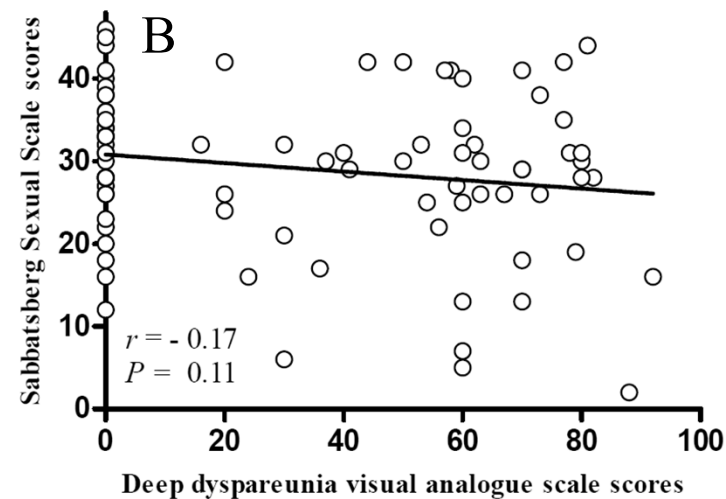
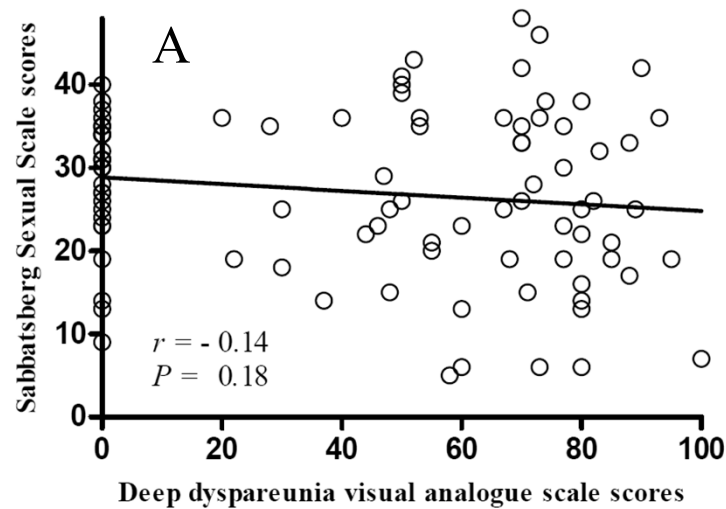
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- In general, both progestin treatment and surgery were effective in reducing endometriosis-associated deep dyspareunia, although with a different time trend
  - Medical treatment revealed as the best choice in patients without recto-vaginal lesions
  - Surgery is a valid therapeutic option for women who desire a spontaneous conception
  - No association was observed between deep dyspareunia intensity and degree of overall sexual satisfaction
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RELATIONSHIP BETWEEN DEEP DYSPAREUNIA VAS SCORES AND SABBATSBERG SEXUAL SELF-RATING SCALE SCORES IN WOMEN WITH RECTOVAGINAL ENDOMETRIOSIS (A), IN THOSE WITH PERITONEAL AND/OR OVARIAN ENDOMETRIOSIS (B), AND IN WOMEN WITHOUT ENDOMETRIOSIS (C)

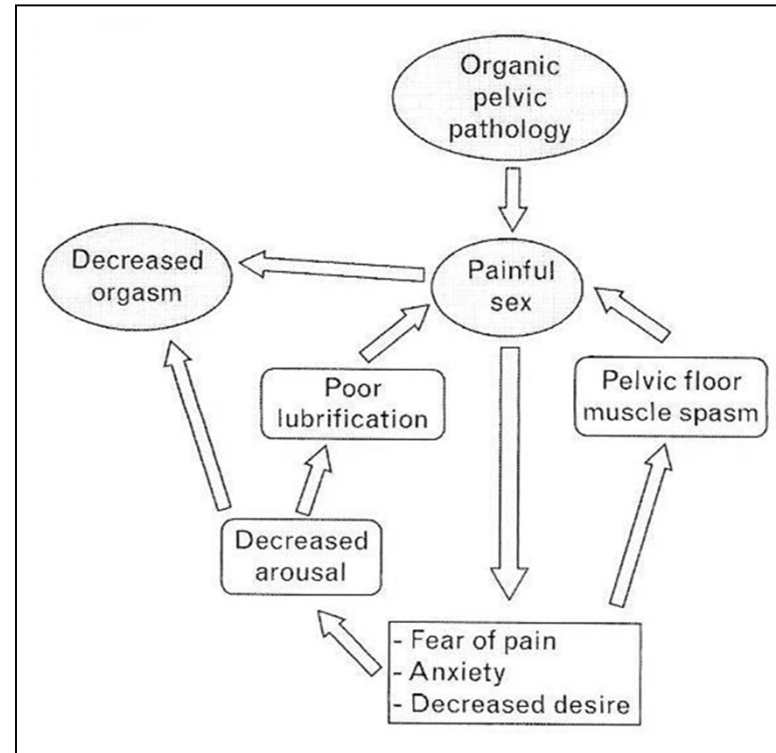
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*From Vercellini et al., Fertil Steril 2012*

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# CAUSES OF DEEP DYSPAREUNIA IN WOMEN WITH PELVIC PATHOLOGIES



This schematic representation shows the factors involved in the pathogenesis of deep dyspareunia in women with organic pelvic pathologies. The resistance to penetration resulting from fear of pain may provoke pelvic floor hyper-tonus and decreased arousal, which contribute to painful intercourse.

*From Ferrero et al., Curr Opin in Obstet Gynecol 2008*

# ENDOMETRIOSIS AND SEXUAL PAIN

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Endometriosis-associated dyspareunia is a visceral pain with several superimposed components, including hyperalgesia, abnormal cortical perception, and psychological factors; it has personal and intimate implications, including unfavorable emotional impact in partners.

A comprehensive assessment of the global impact of the symptom on women's sexual function, psychological wellbeing, body-image, self-esteem, and relational adjustment is needed.

# THE WHO AND SEXUAL HEALTH

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A 2002 WHO report states that sexual rights embrace human rights, including the right of all persons to [...] pursue a satisfying, safe, and pleasurable sexual life

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World Health Organization. Gender and human rights. Sexual health. Available at:

[http: //www.who.int/reproductivehealth/topics/gender rights/sexual health/en/index.html](http://www.who.int/reproductivehealth/topics/gender_rights/sexual_health/en/index.html)

# ENDOMETRIOSIS AND SEXUAL PAIN: CONCLUSION

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Time has come to address this distressing affliction without embarrassment and with a decidedly multidisciplinary perspective.

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