PAINWEEK®

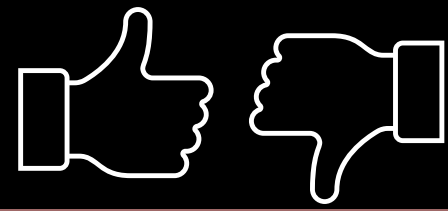
To participate in ‘**Fire in the Lake: War Raging Over Endometriosis**’ lecture activities please link to:

attend.sl/se47

Attendees: 0

PainWeek®

War Raging Over Endometriosis

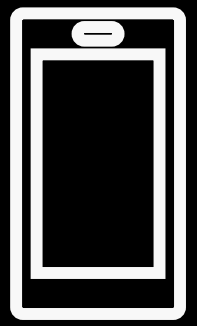


Georgine Lamvu, MD, MPH
Professor of Obstetrics and Gynecology and Pelvic Pain Specialist
University of Central Florida

Disclosures

- Consultant: Abbvie
- Myovant
- SoLá Pelvic Therapy
- Medical Learning Institute (MLI-Peer Review)

Audience Participation



Please silence your phones

To participate in audience poll, ask questions and view slides

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PAINWEEK

What state or country are you from?

Vote at:

What state or country are you from?

Time left: 10

Votes: 0

PAINWEEK

What is your specialty?

Time left: 5

Vote at: **attend.sl/se47**

Votes: 0

What is your specialty?

Time left: 5

Votes: 0

Learning Objectives

1

Review pathophysiology of endometriosis

2

Compare treatment interventions

3

Discuss treatment selection controversies

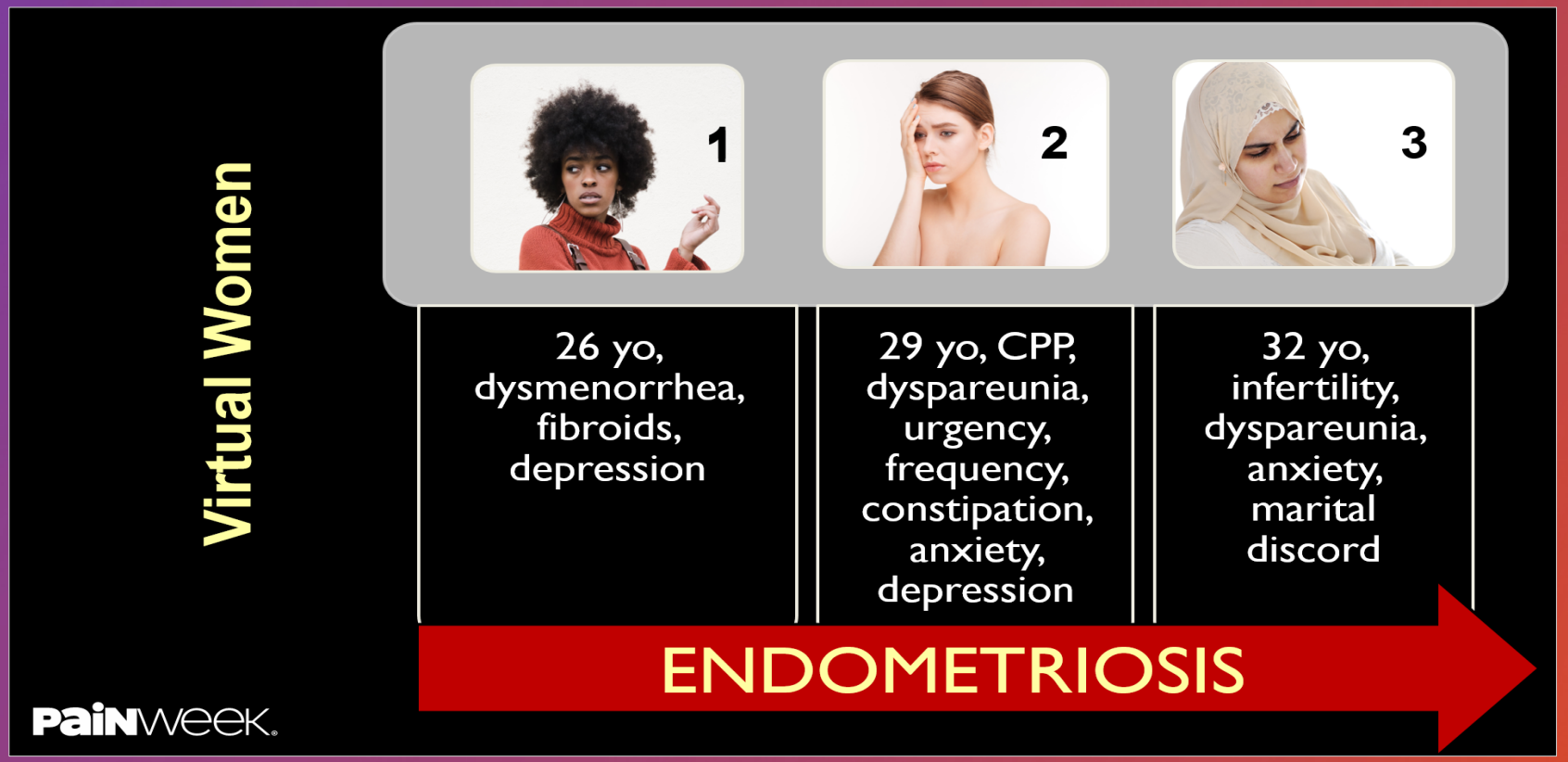
Virtual Women

1	2	3
26 yo, dysmenorrhea, fibroids, depression	29 yo, CPP, dyspareunia, urgency, frequency, constipation, anxiety, depression	32 yo, infertility, dyspareunia, anxiety, marital discord

ENDOMETRIOSIS

PAINWEEK

Do you agree with virtual woman #1 not having a surgical diagnosis of endometriosis?



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Vote at: **attend.sl/se47**

Votes: 0

Do you agree with virtual woman #1 not having a surgical diagnosis of endometriosis?

Time left: 5

SlideLizard

Votes: 0

Virtual Women

26 yo, dysmenorrhea, fibroids, depression

Treatments:

Birth control pills

29 yo, CPP, vulvodynia, urgency, frequency, constipation, anxiety, depression

Treatments:

Birth control pills

Hysterectomy

Antidepressants

32 yo, infertility, dyspareunia, anxiety, marital discord

Treatments:

Laparoscopy x 4

Analgesics

Antidepressants

SYMPTOMS CONTINUE

PainWeek

SlideLizard

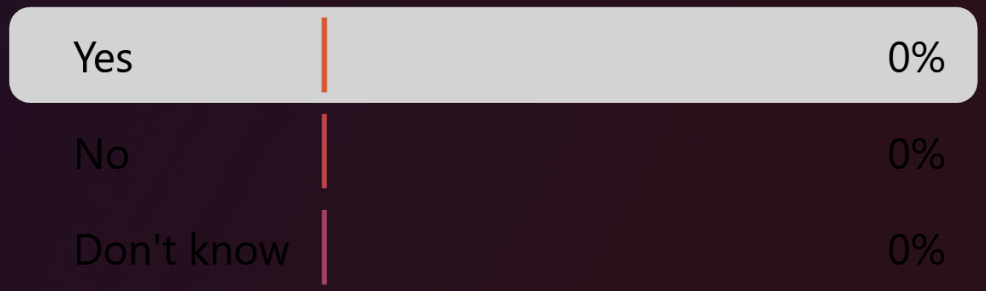
Do you agree with virtual woman #4 having 4 laparoscopies for endometriosis?

Time left: 5

Vote at: **attend.sl/se47**

Votes: 0

Do you agree with virtual woman #4 having 4 laparoscopies for endometriosis?



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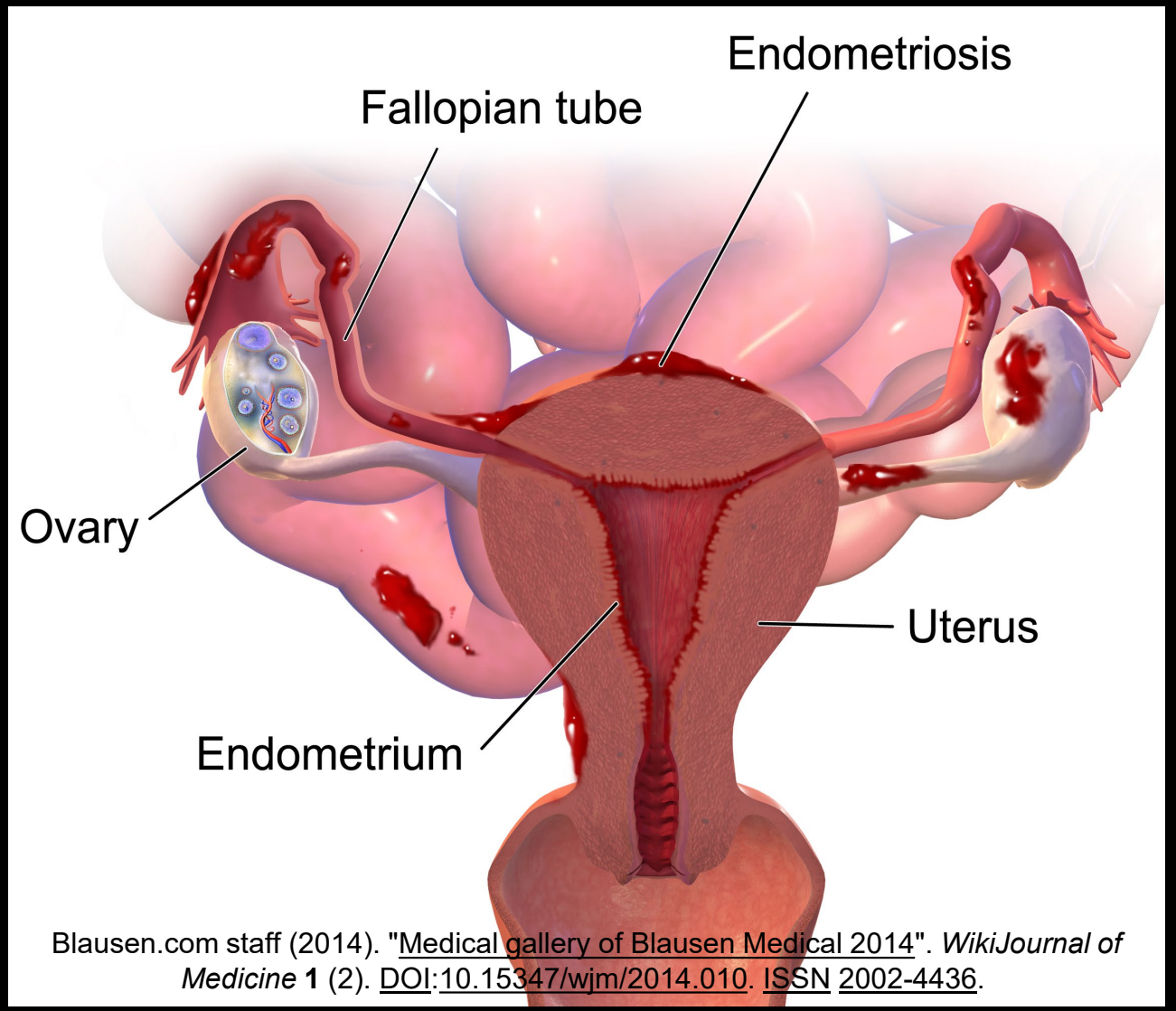
Votes: 0

Endometriosis

Originally defined as endometrial cells implanting outside the uterus

NEW- re-classified as endometrial-*like* cells (cells similar to endometrial cells) implant outside the uterus, it differs from endometrium in that it can cause inflammation, fibrosis

NEW- emphasis on differentiating superficial from deep infiltrating endometriosis found in the rectovaginal septum, bladder and bowel



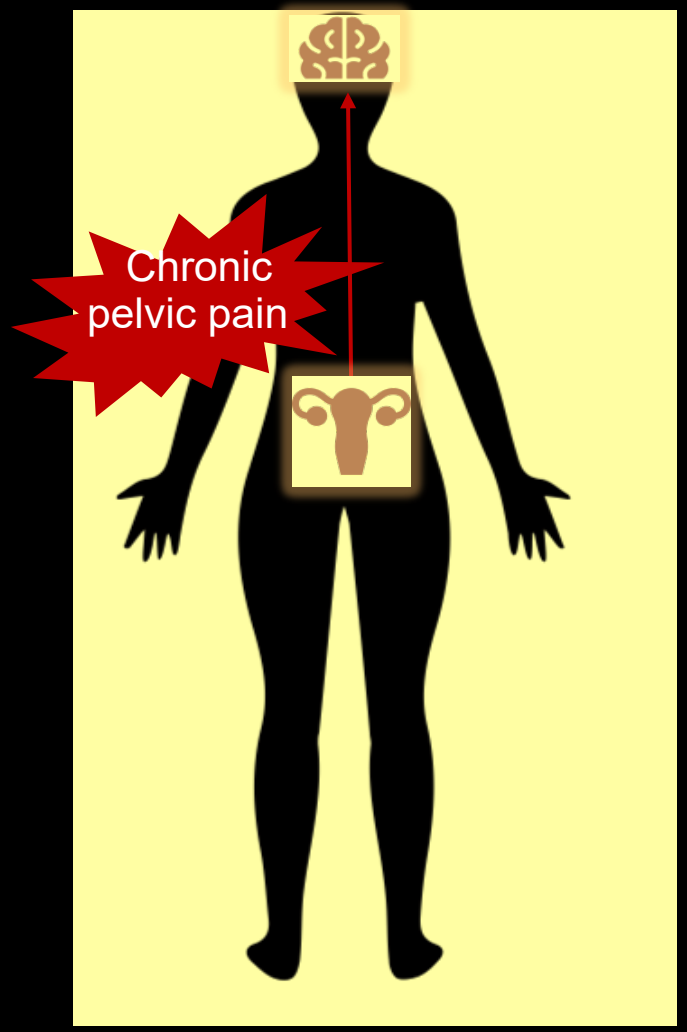
Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014". *WikiJournal of Medicine* **1** (2). DOI:10.15347/wjm/2014.010. ISSN 2002-4436.

https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Endometriosis-guideline.

Disclaimer

Because this is Painweek, we will focus on Endometriosis associated pain

Mechanisms of Pain in Endometriosis



- Chronic inflammation characterized by systemic and local cytokines and growth factors resulting in pain

- **NEW:** Long-term exposure to these pro-inflammatory substances can lead to peripheral and central sensitization, hyperalgesia, and chronic pain

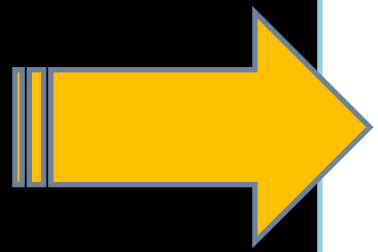
Pathophysiology and Epidemiology

- Estrogen stimulates lesion growth, inflammation, and pain
- 6%-10% of women of reproductive age in the United States have endometriosis
- **NEW:** On average, women experience pain for 6-10 years
- 55% of women see three or more doctors before the diagnosis is made

Burney RO, Giudice LC. Fertil Steril. 2012.
Fuldeore MJ, Soliman A. *Gynecol Obstet Invest*. 2017.
Mowers EL et al. *Obstet Gynecol*. 2016.
Green R et al. *Fertil Steril*. 2009.
Zondervan KT et al. *N Engl J Med*. 2020.

Symptoms of Endometriosis

- Primary symptoms
  - Pain and infertility
- Other common symptoms
  - Painful menstrual cramps
  - Pain during/after sex
  - Painful bowel movements or urination during menstrual periods
  - Heavy menstrual periods
  - Premenstrual spotting or bleeding between periods



Symptoms are more common in younger women (aged 18-29 years)

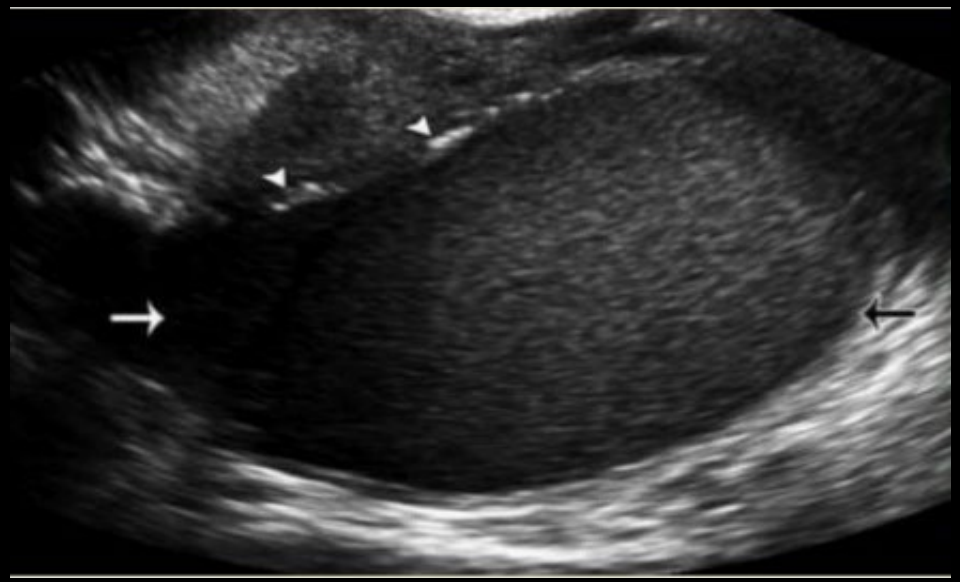
- 73% dysmenorrhea
- 57% noncyclical pelvic pain
- 43% dyspareunia

In women of reproductive age, **the triad of dysmenorrhea, noncyclic pelvic pain, and dyspareunia (± infertility**) should trigger an evaluation for endometriosis to prevent delay in diagnosis

Fuldeore MJ, Soliman A. *Gynecol Obstet Invest*. 2017.
Mowers EL et al. *Obstet Gynecol*. 2016.
https://www.nichd.nih.gov/health/topics/endometri/conditioninfo/symptoms.

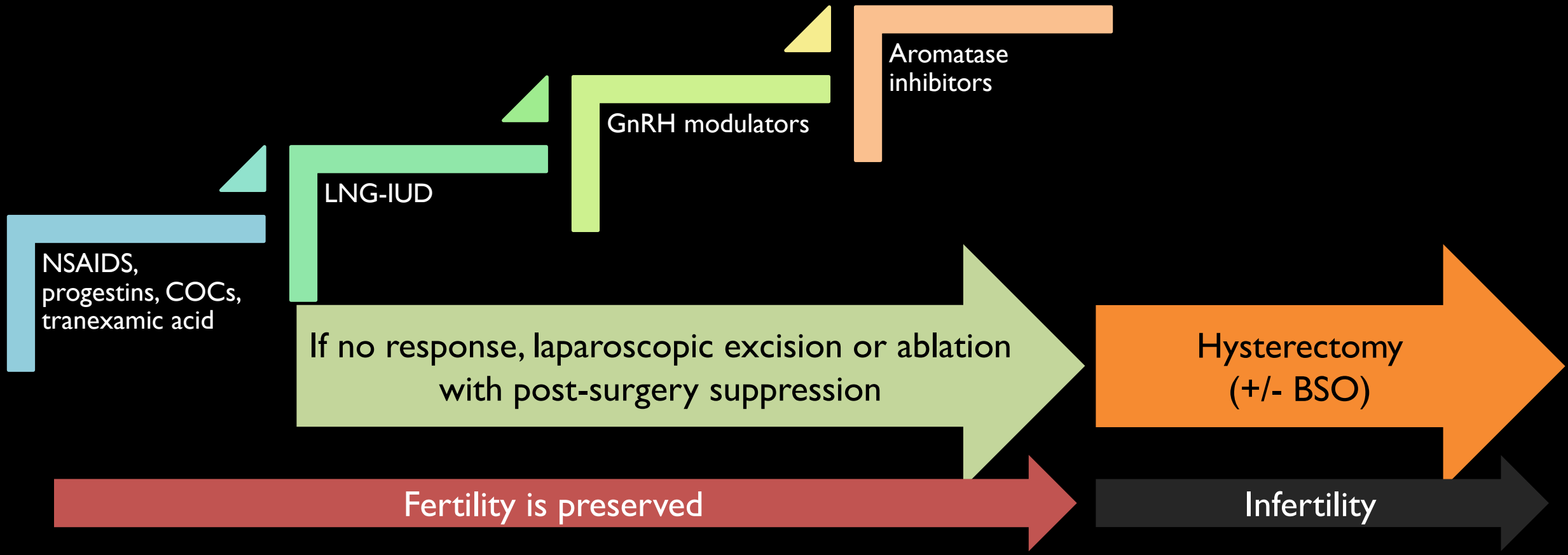
Diagnosis

- History
- Pelvic exam
- Pelvic ultrasound adequate for large lesions, endometriomas, but not smaller implants or adhesions
  - MRI: deeply may be helpful for invasive endometriosis (e.g., bowel, bladder)
  - NO: Serum markers (CA-125, cytokines, MCP1, adhesion molecules) are nonspecific



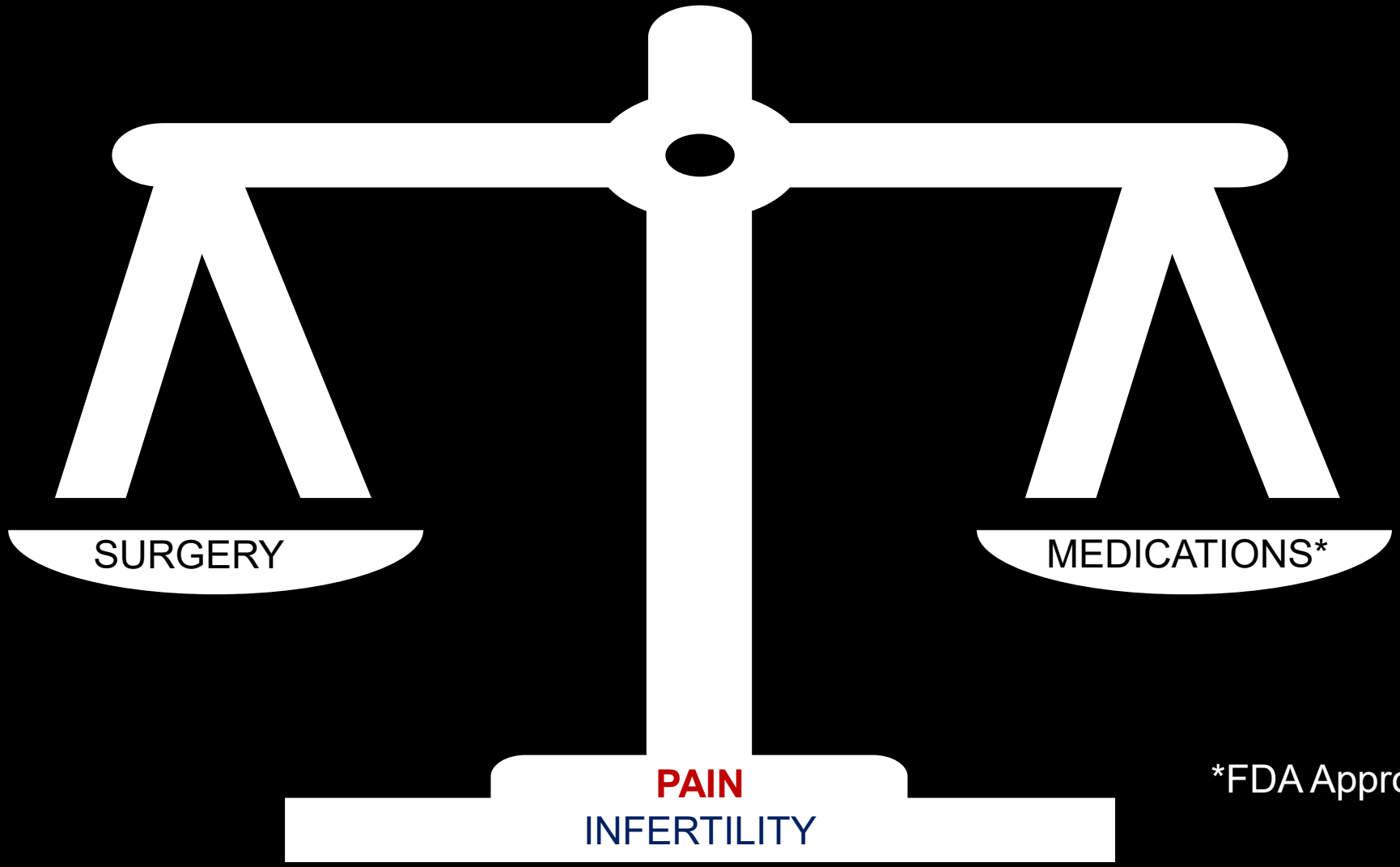
American College of Obstetricians and Gynecologists Practice Bulletin No. 218. *Obstet Gynecol* 2020, Seeber B et al. *Fertil Steril*. 2008, Falcone T, Flyckt R, 2018;.

Therapy Options for Endometriosis Symptoms



Kuznetsof L et al. *BMJ*. 2017, ACOG Practice Bulletin No. 114. *Obstet Gynecol*. 2010, https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Endometriosis-guideline, Hirsch M et al. *BJOG*. 2018, Fuldeore MJ, Soliman A. *Gynecol Obstet Invest*. 2017, Zondervan KT et al. *Nat Rev Dis Primers*. 2018, Zondervan KT et al. *N Engl J Med*. 2020.

Traditional Treatment Regimens



*FDA Approved

FDA-Approved Pharmacotherapy for Endometriosis

Treatment	Type	Year Approved
Norethindrone	Synthetic progestin	2005
Medroxyprogesterone acetate	Progestin	2005
Leuprolide acetate	GnRH agonist	1999
Nafarelin acetate	GnRH agonist	1990
Goserelin acetate	GnRH agonist	1989
Danazol	Synthetic androgen	1971
Elagolix	GnRH antagonist	2018

LNG-IUD for Endometriosis is Comparable to GnRH Agonist

Human Reproduction Vol.20, No.7 pp. 1993–1998, 2005
Advance Access publication March 24, 2005
doi:10.1093/humrep/deh869

Randomized clinical trial of a levonorgestrel-releasing intrauterine system and a depot GnRH analogue for the treatment of chronic pelvic pain in women with endometriosis

Carlos A.Petta[1,4], Rui A.Ferriani[2], Mauricio S.Abrao[3], Daniela Hassan[1], Julio C.Rosa e Silva[2], Sergio Podgaec[3] and Luis Bahamondes[1]

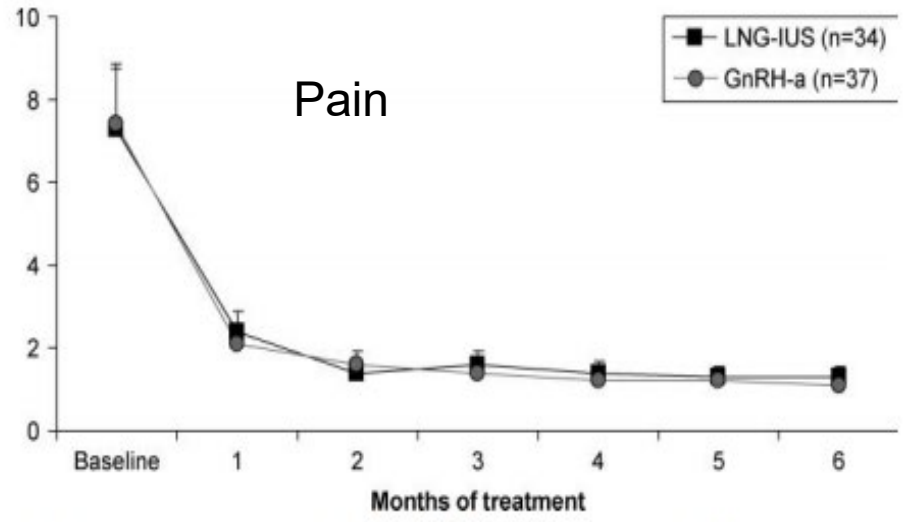


Figure 2. Changes in the visual analogue score pain scores between the two treatment groups. Values are mean ± SEM. *P*-value: not cant between both groups.

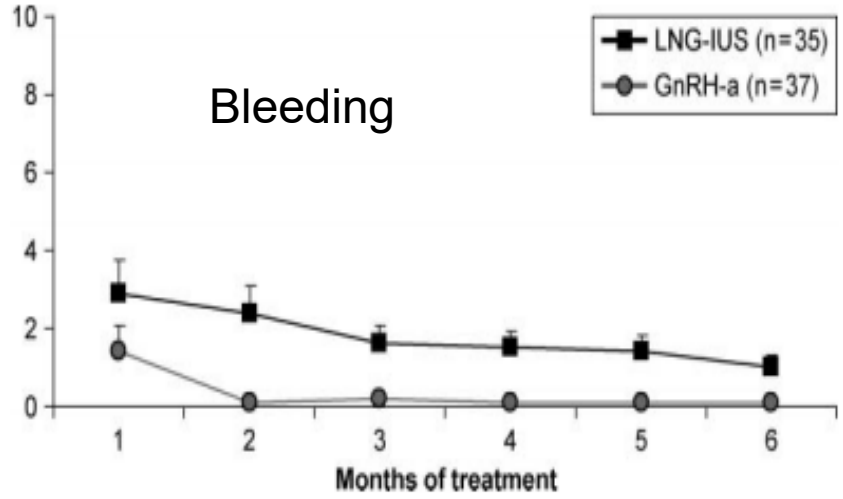
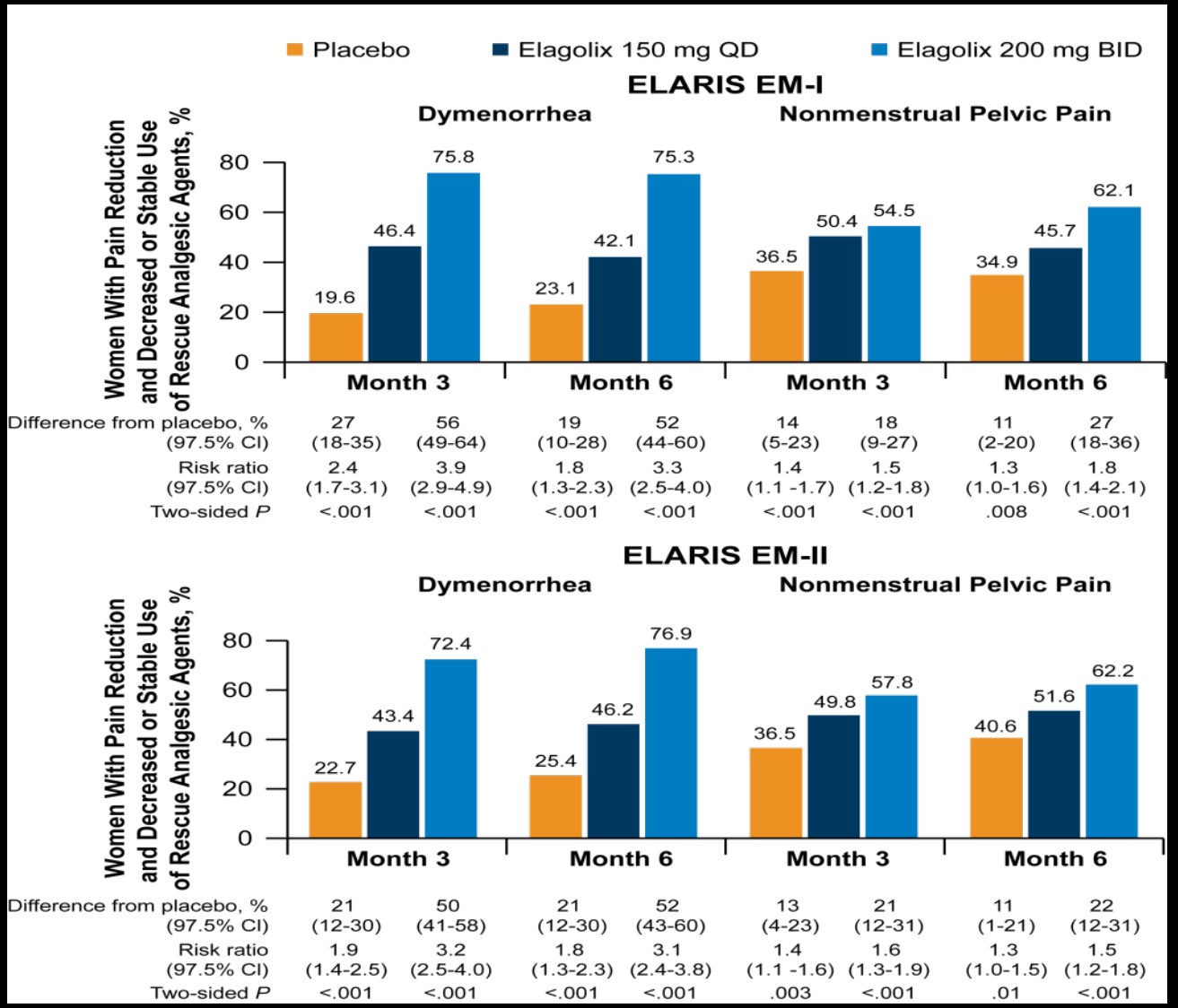


Figure 3. Changes in the bleeding scores between the two treatment groups. Values are mean ± SEM.

GnRH Antagonist: Elagolix

Reduction of Dysmenorrhea and Non-menstrual Pelvic Pain

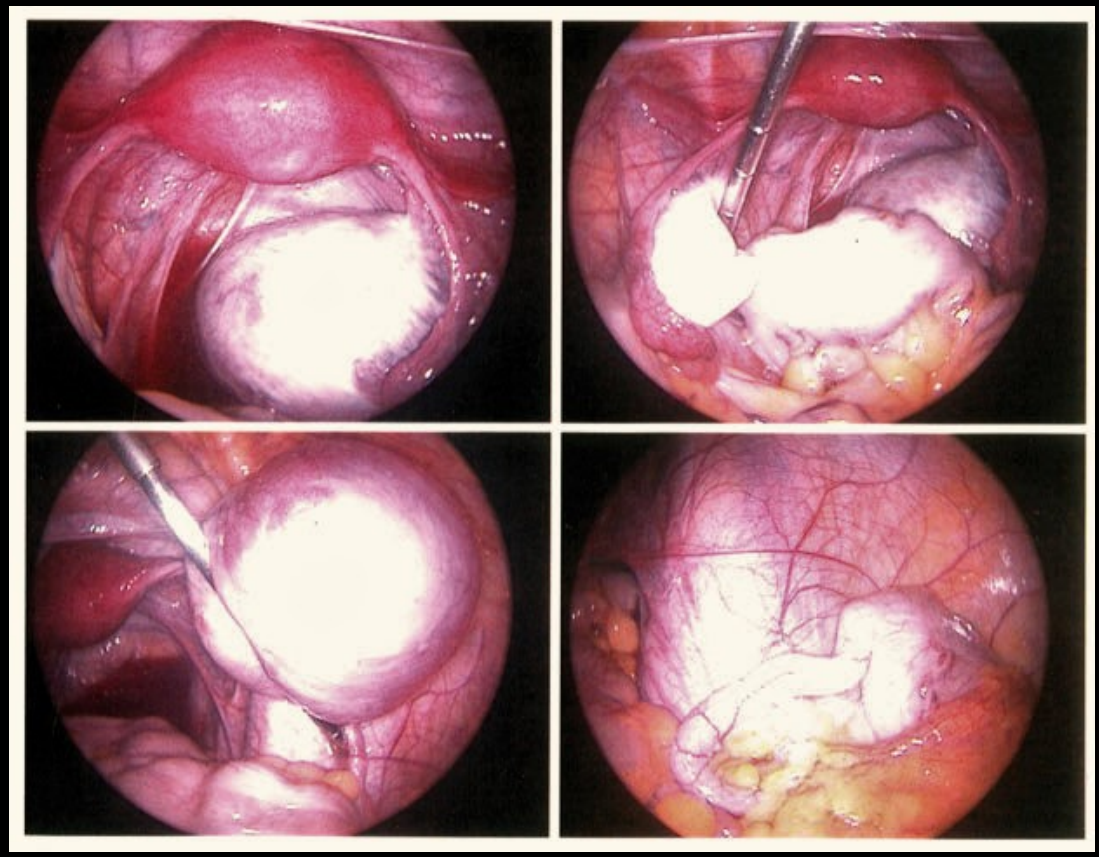
- Double-blind, RCT
- Primary endpoint: clinically meaningful reduction in pain
- 872 patients randomized and followed
  over 6 months, trial extended for additional 12 months
- FDA approved for 24 months of use
- AEs: hot flushes and mild bone density loss



Taylor HS et al. *N Engl J Med*. 2017;377:28-40. 2. https://www.accessdata.fda.gov/scripts/cder/daf/.

Surgery for Endometriosis

- Ablation
  - –Superficial
- Excision
  - –Superficial
  - –Deep
- Hysterectomy
  - –± Salpingoophrectomy



SlideLizard

What proportion of women report improvement in pain after laparoscopic treatment (excision or ablation) of endometriosis?

Time left: 5

Vote at: **attend.sl/se47**

Votes: 0

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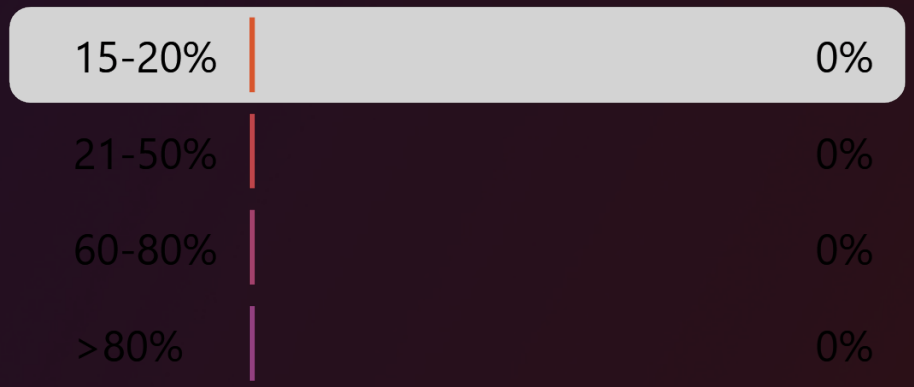

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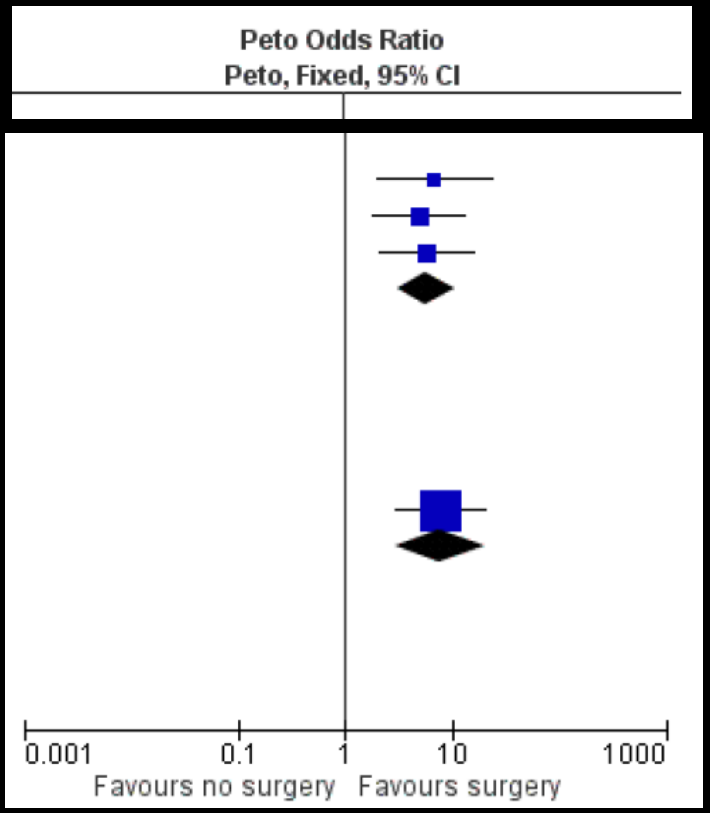
SlideLizard

Votes: 0

Meta-analysis of Laparoscopic Treatment Cochrane 2006

	+treatment	no treatment
6 months after surgery:		
Abbott 2004	16/20 (**80.0%**)	6/19 (31.6%)
Sutton 1994	20/32 (**62.5%**)	7/31 (22.6%)
Tutunaru 2006	34/41 (**82.9%**)	12/28 (42.9%)
12 months after surgery:		
Tutunaru 2006	30/41 (**73.2%**)	12/28 (42.9%)



Outcome= pain improved

OR= 5.72 (3.09, 10.60)

OR= 7.72 (2.97, 20.06)

In these studies, **60-80%** of patients who had laparoscopic treatment reported improvement in pain

PainWeek

Jacobson TZ, et al. The Cochrane database systematic reviews, 2006..

Meta-analysis of Laparoscopic Treatment, Odd of Improvement

Duffy JM, et al. Cochrane, 2014.

Population: Women with mild to moderate endometriosis
Settings: Any setting
Intervention: Laparoscopic ablation or excision
Comparison: Diagnostic laparoscopy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)
	Assumed risk	Corresponding risk		
	Diagnostic laparoscopy	Laparoscopic ablation or excision		
Overall pain better or improved at 6 month follow-up	321 per 1000	756 per 1000 (610 to 861)	OR 6.58 (3.31 to 13.10)	171 (3 Studies)
Overall pain better or improved at 12 month follow-up	214 per 1000	732 per 1000 (467 to 895)	OR 10.00 (3.21 to 31.17)	69 (1 Study)
Live birth or ongoing pregnancy	179 per 1000	297 per 1000 (207 to 408)	OR 1.94 (1.20 to 3.16)	382 (2 Studies)
Clinical pregnancy	186 per 1000	302 per 1000 (223 to 396)	OR 1.89 (1.25 to 2.86)	528 (3 Studies)
Miscarriage (per pregnancy)	190 per 1000	181 per 1000 (76 to 374)	OR 0.94 (0.35 to 2.54)	112 (2 Studies)

Laparoscopic Ablation vs. Diagnostic Laparoscopy + GnRH Agonist

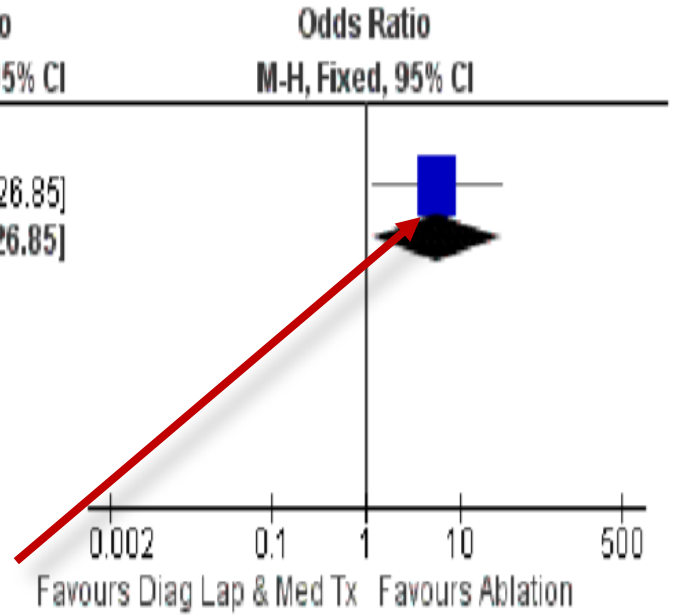
Figure 6. Forest plot of comparison: 2 Laparoscopic versus diagnostic laparoscopy and medical therapy, outcome: 2.1 Ablation versus diagnostic laparoscopy and GnRHa (and add-back therapy).

Study or Subgroup	Ablation Events	Ablation Total	Diag Lap & Med Tx Events	Diag Lap & Med Tx Total	Weight	Odds Ratio M-H, Fixed, 95% CI
2.1.1 Overall pain described as "Pain free" (12 months)						
Lalchandani 2005	9	17	3	18	100.0%	5.63 [1.18, 26.85]
Subtotal (95% CI)		**17**		**18**	**100.0%**	**5.63 [1.18, 26.85]**
Total events	9		3			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.17 (P = 0.03)

Test for subgroup differences: Not applicable



OR for 'pain free' at 12 months 5.63 (95%CI: 1.18-26.85)

Duffy JM, et al. Cochrane, 2014.

SlideLizard

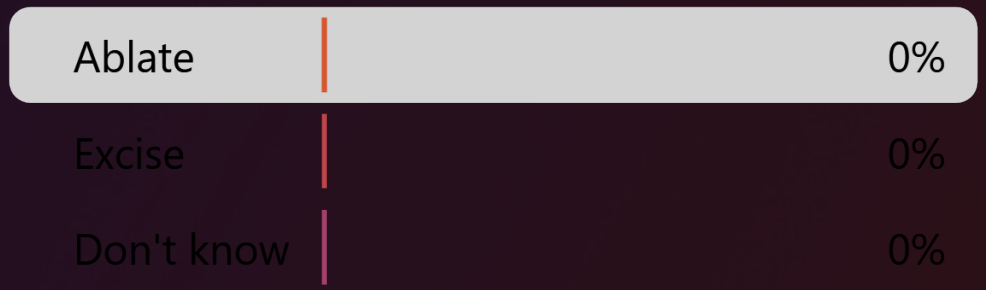
At the time of laparoscopy, is it better to ablate or excise the endometriosis?

Time left: 5

Vote at: **attend.sl/se47**

Votes: 0

At the time of laparoscopy, is it better to ablate or excise the endometriosis?



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Votes: 0

Review Article

Laparoscopic Excision Versus Ablation for Endometriosis-associated Pain: An Updated Systematic Review and Meta-analysis

Jyotsna Pundir, MD*, Kireki Omanwa, MRCOG, Elias Kovoor, MD, Vishal Pundir, MS, Gillian Lancaster, PhD, and Peter Barton-Smith, MD

Table 3

Quality of studies included in the systematic review of laparoscopic excision versus ablation for endometriosis-associated pain

Author	Method of randomization	Allocation concealment	Blinding	Intention-to-treat analysis	Follow-up rate (%)	Design
Barton – Smith 2010	Random sequence generation in blocks of 10	Yes	Double	Yes	77	Randomized double blind
Healey et. al., 2010	Computer-generated random numbers	Yes	Double	Yes	58	Randomized double blind
Wright et. al., 2005	Random sequence generation in blocks of 10	ND	ND	ND	100	Randomized double blind

‘The limited available evidence shows that at 12 months post surgery, symptoms of dysmenorrhea, dyschezia, and chronic pelvic pain secondary to endometriosis showed significantly greater improvement with laparoscopic excision compared with ablation.’

Pundir et al, Journal of Minimally Invasive Gynecology 2017

Endometriomas: Excise *or* Drain & Ablate?

Outcome	OR (95% CI)
Recurrence of Symptoms:	
Dysmenorrhea	0.15 (0.06, 0.38)
Non-menstrual pain	0.10 (0.02, 0.56)
Dyspareunia	0.08 (0.01, 0.51)
Recurrence of endometrioma	0.41 (0.18, 0.93)

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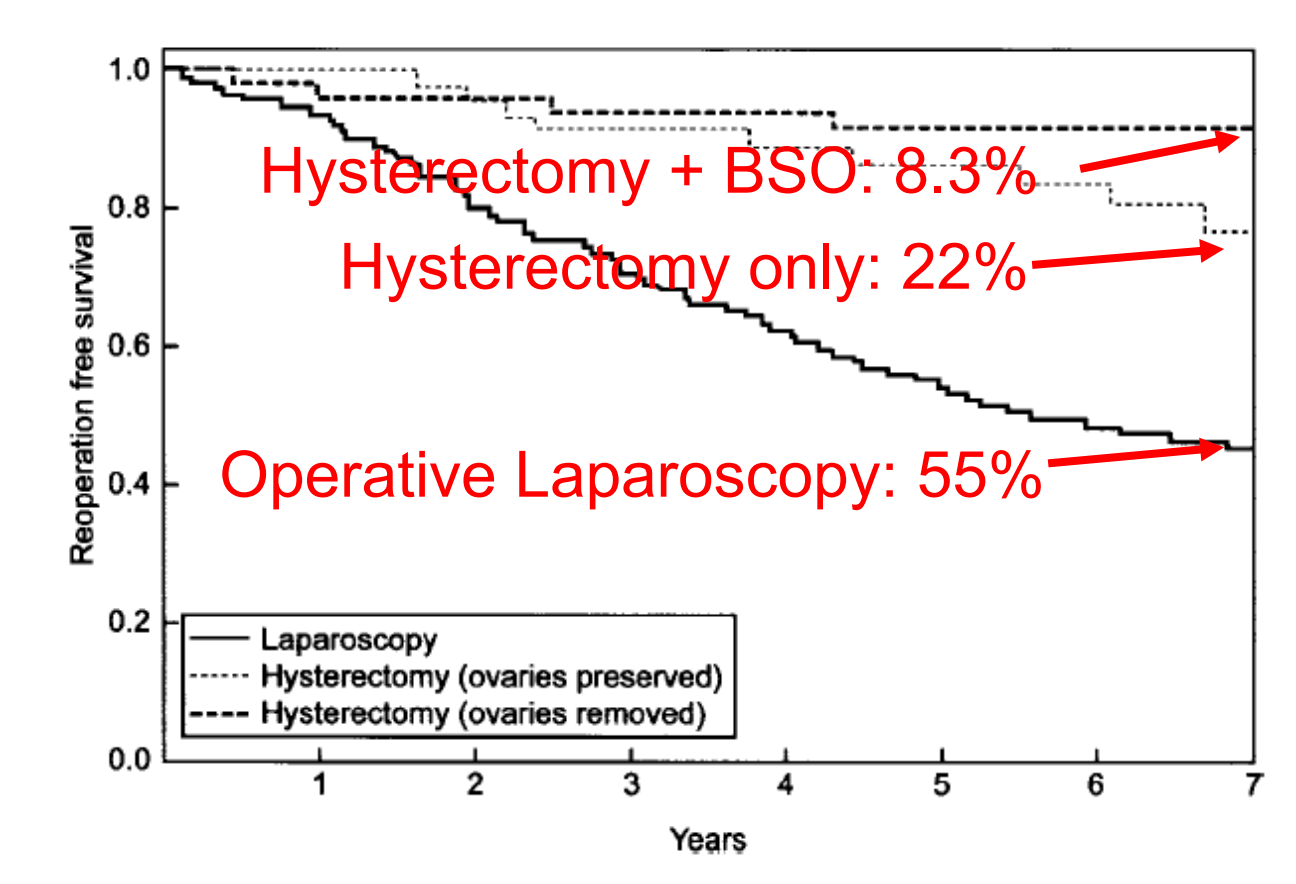
Hart RJ, Hickey M, Maouris P, Buckett W. Cochrane Database Syst Rev. 2008.

Hysterectomy for Endometriosis-Associated CPP

Likelihood of another surgery within 7 years of 1st surgery



Shakiba K, Bena JF, McGill KM, Minger J, Falcone T. Obstet Gynecol. 2008

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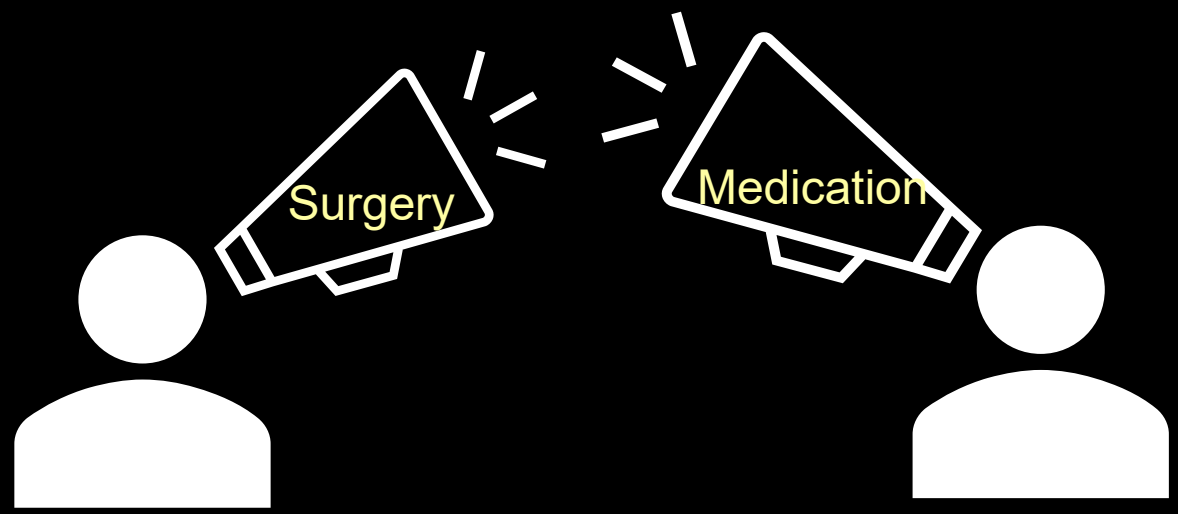
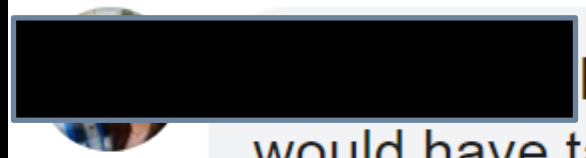
If we know so much about Endometriosis…

Why is there so much discussion / confusion?



[redacted] **MD - Endometriosis and Pelvic Pain**

I have patients/doctors asking about ablation versus excision. In my opinion, excision is the key. Not only for removing the disease (which can be accomplished in some patients with ablation), but to obtain estrogen and progesterone receptors on all of the specimens removed. In my 14 years of doing this, 75% of the receptors are positive for both estrogen and



[redacted] Birth control pills have ruined my life. I wish that I never would have taken them to control endo and cysts in the first place. 17 years of poison, and almost loss of life and now I get it! NO MORE!!

[redacted] **- Endometriosis and Pelvic Pain** is with

Heading home from my Second Look surgery. Dr said that it looked PERFECT when he went back inside. He told me only thing was a big adhesion that grew back connecting my left ovary to my side wall which hurt a lot. But it was detached and fixed. The good news? 70% that it won't come back. 🙈 Follow up in two weeks with pathology. 💗 I'll be trying for now.-

Hormones can't help me.

Is my endometriosis back? What else can I try?

I need to have another surgery.

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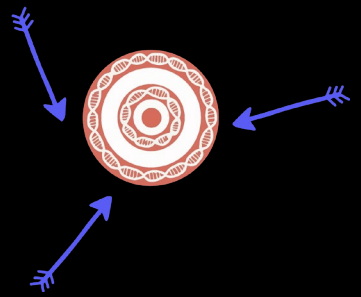
Difficulty in making the diagnosis

- There are no biological markers proven to reliably confirm presence of endometriosis. (Liu, Nisenblat et al. 2015, Gupta, Hull et al. 2016, Nisenblat, Bossuyt et al. 2016, Nisenblat, Prentice et al. 2016, Nisenblat, Sharkey et al. 2019, Anastasiu, Moga et al. 2020)

- Laparoscopy with pathologic confirmation is the only way definitively diagnose endometriosis.



- Even after laparoscopic confirmation, stage of endometriosis does not correlate to symptoms severity. (Schliep, Mumford et al. 2015, Vercellini, Trespidi et al. 1996, Fedele, Parazzini et al. 1990, Conroy, Mooney et al. 2021)

Treatment Recommendations For Endometriosis- North American Guidelines

ASRM (2014)

Establishing the correct diagnosis with laparoscopy before initiating therapy with medication that is associated with significant short-term and long-term side effects is the preferred approach, although further studies are warranted. (The Practice Committee ASRM, Fert Steril, 2014)

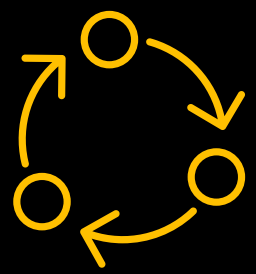
ACOG (2010)

The definitive diagnosis of endometriosis can only be made by histology of the lesions removed at surgery. After appropriate pretreatment evaluation and failure of COCs and NSAIDS, empiric therapy with a 3-month course of GnRH agonists is appropriate. (ACOG Practice Bulleting, Obstet Gynecol, 2010)

SOGC (2013)

The gold standard is direct visualization at laparoscopy and histologic study. Diagnostic laparoscopy is not required before treatment in all patients presenting with pelvic pain. (Leyland N. et.al. J Obstet Gynaecol Can, 2010)

- Patients may present with pain (dysmenorrhea, dyspareunia, CPP) and have no obvious endometriosis on laparoscopic examination. (Walter, Hentz et al. 2001, Ling 1999)



- Other conditions (IC/Bladder Pain Syndrome (BPS), IBS) may present with similar symptoms, 70-80% of women with endometriosis have BPS.(Chung, et al. 2002, Chung, et al. 2005, Tirlapur, Kuhrt et al. 2013)

Treatment Effectiveness

A second look at the data…

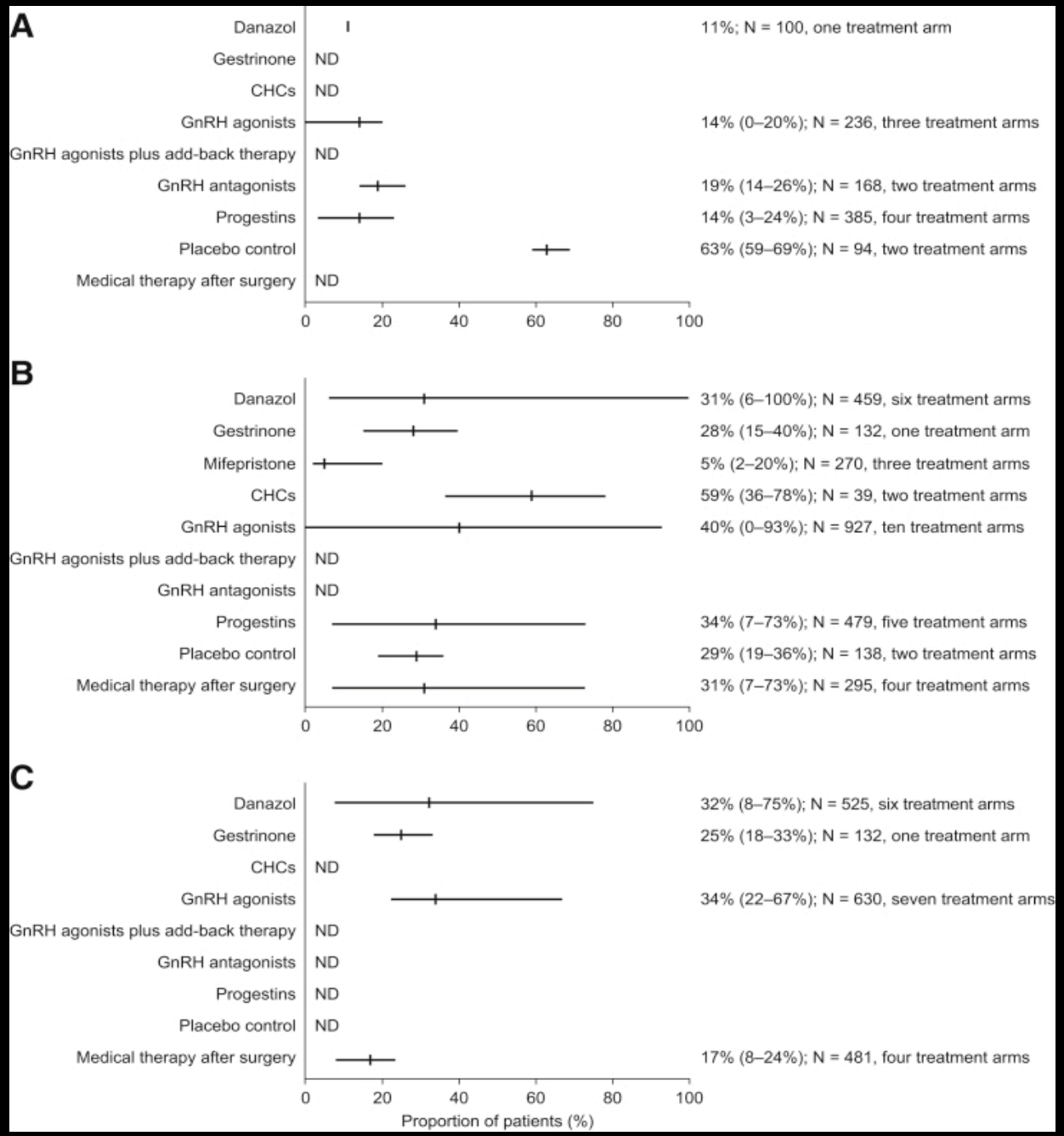
Response to medical therapy and symptom recurrence after treatment cessation. **Becker, Gattrell et al. 2017: Systematic Review**

Proportions of patients with

(**A**) no reduction in pain symptoms,

(**B**) pain symptoms remaining at end of treatment, and

(**C**) recurrence of pain symptoms after treatment cessation.



Results are presented as median (range). ND = no data; CHC = combined hormonal contraceptive

Meta-analysis of Laparoscopic Treatment Cochrane 2006

	+treatment	no treatment
6 months after surgery:		
Abbott 2004	16/20 (80.0%)	6/19 (31.6%)
Sutton 1994	20/32 (62.5%)	7/31 (22.6%)
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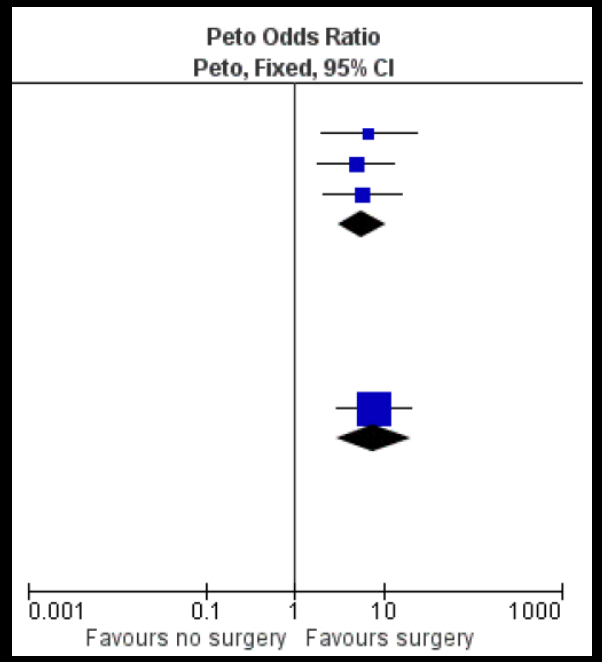


Outcome= pain improved

OR= 5.72 (3.09, 10.60)

OR= 7.72 (2.97, 20.06)

Limitations: Few studies, small sample size, Wide confidence intervals

Not all patients respond, 18%-38% do not respond
Placebo rate is high, 22-43% in diagnostic laparoscopy alone report improvement

PainWeek

Jacobson TZ, et al. 2006.

Laparoscopic surgery for endometriosis: Systematic Review Bafort C, et al. Cochrane 2020

- 14 RCTS, 1563 women with endometriosis

Main conclusion

– Laparoscopic treatment vs. diagnostic laparoscopy, very low-quality evidence insufficient evidence to determine whether laparoscopy helps pain

– Not enough evidence to show that excision favors ablation

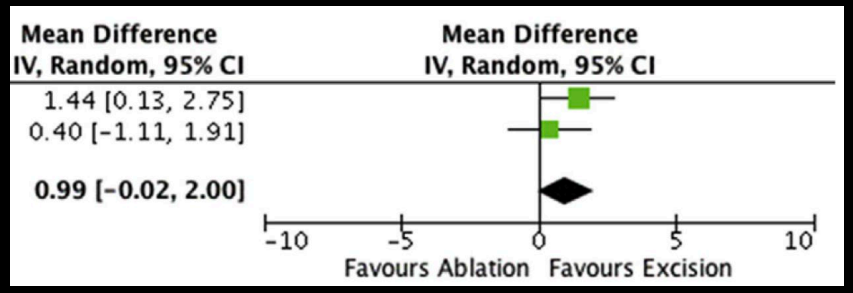
Review Article

Laparoscopic Excision Versus Ablation for Endometriosis-associated Pain: An Updated Systematic Review and Meta-analysis

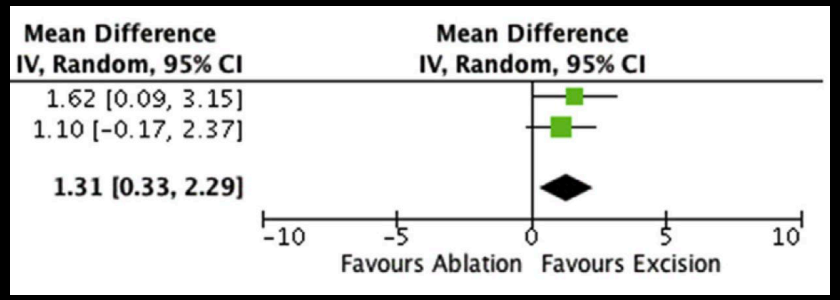
Jyotsna Pundir, MD*, Kireki Omanwa, MRCOG, Elias Kovoor, MD, Vishal Pundir, MS, Gillian Lancaster, PhD, and Peter Barton-Smith, MD

Pundir et al, Journal of Minimally Invasive Gynecology 2017

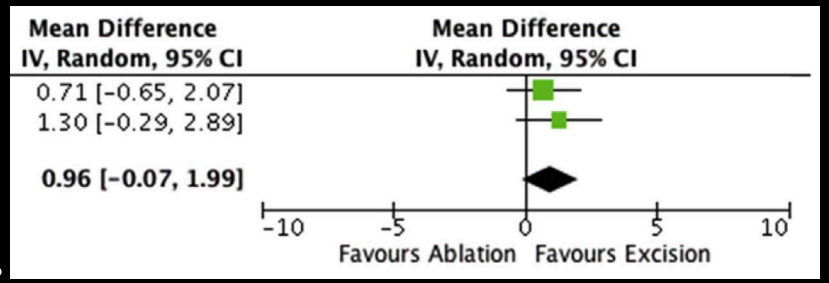
Dysmenorrhea no benefit



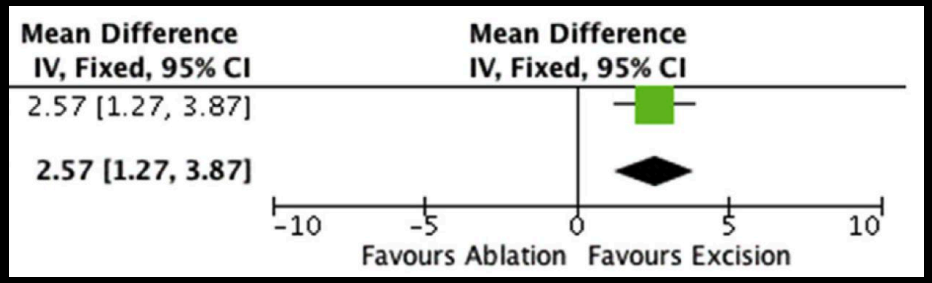
Dyschezia favors excision



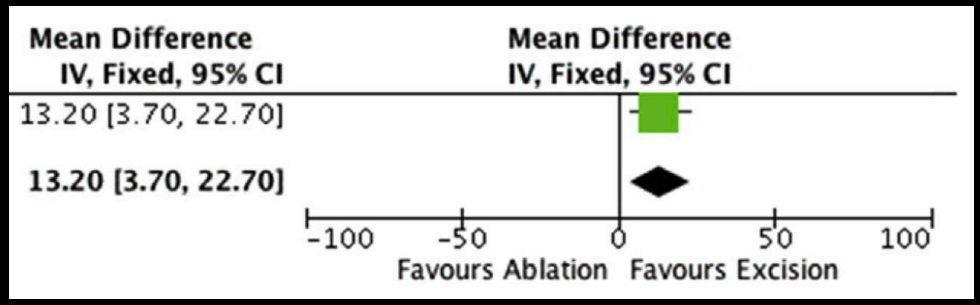
Dyspareunia no benefit



CPP favors excision, one study only



Quality of life favors excision, one study only



Same or worse at 12 months:

- Excision 14.6%
- Ablation 27.2%

P=0.13

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Significant Study Limitations

- Small sample sizes
- Large loss to follow-up
- Conflict of interest not stated: members of the authorship team were 1) related and 2) authors on one of the papers evaluated as favoring excision
- Overall, this was a poor meta-analysis and **conclusions cannot be made in favor of either technique**

Recurrence in Deep Infiltrating Endometriosis: A Systematic Review

- Inconsistencies and heterogeneity in data reporting, case definition, and outcome definition; could not complete a meta-analysis
- Recurrence rate 2%-43.5%
- Risk factors for recurrence: young age, weight, and incomplete resection

Ianieri, M, Mautone D, Ceccaroni M, J Minim Invasive Gynecol, 2018

Pain Recurrence After 1st Conservative Surgery

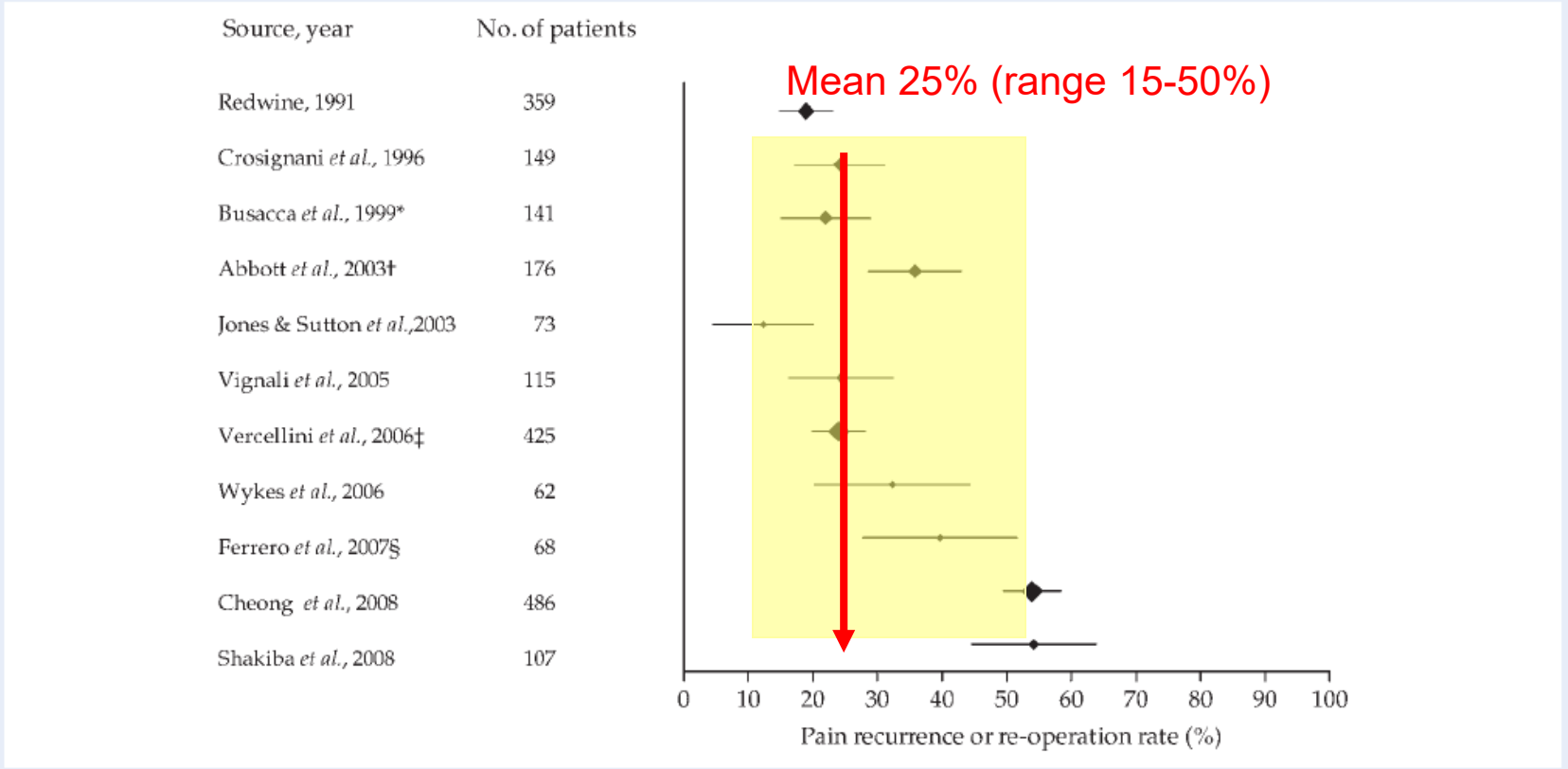


Figure 1 Pain recurrence or re-operation rates reported after first-line conservative surgery for symptomatic endometriosis. Literature data, 1991–2008, observational and retrospective studies. Diamonds represent percentage point estimates and horizontal lines 95% confidence intervals. *Cumulative dysmenorrhoea recurrence rate after surgery at laparotomy; †Cumulative re-operation rate; ‡Only subjects with moderate to severe dysmenorrhoea are considered; §Dyspareunia recurrence rate at intention-to-treat analysis.

Vercellini et al. Hum Repro Update 2009.

Time to Recurrent Pain after 1st Surgery

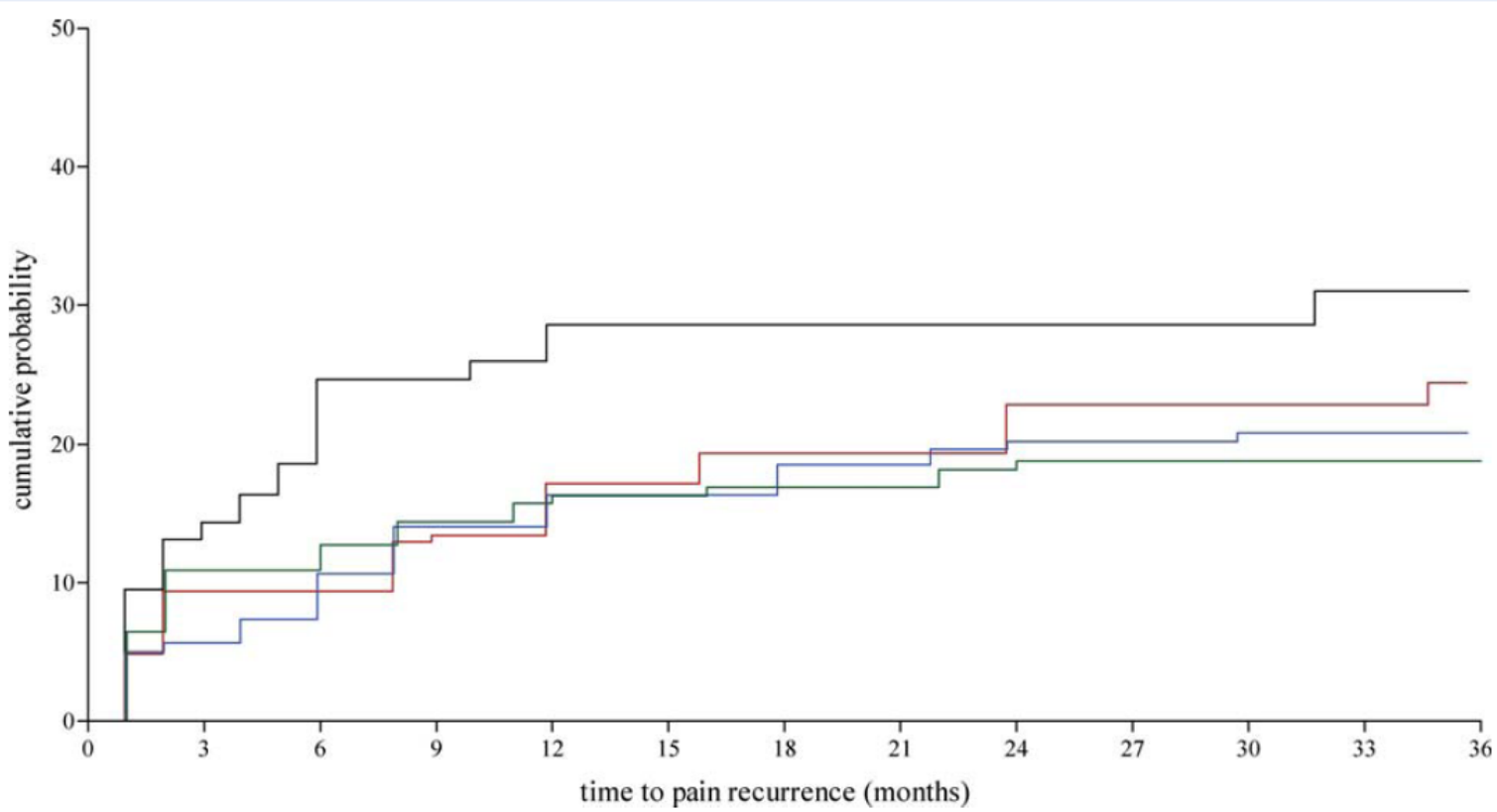


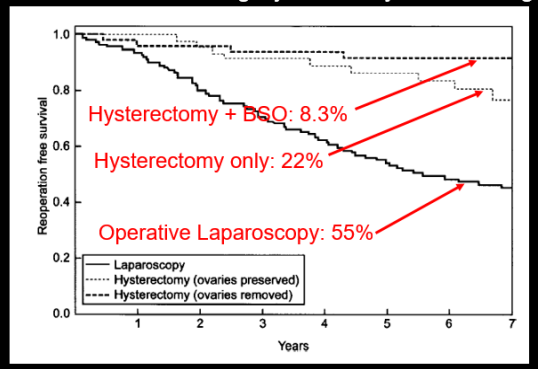
Figure 2 Cumulative 36 month probability of recurrence of moderate or severe dysmenorrhoea by disease stage in 425 symptomatic women who underwent conservative surgery for endometriosis (black line, stage I; red line, stage II; blue line, stage III; green line, stage IV). From Vercellini *et al.* (2006a), reproduced with permission of the publisher.

Vercellini et al. Hum Repro Update 2009.

Hysterectomy Likelihood of Success (No Re-operation) Depends on Age and Ovarian Preservation

Surgery for Endometriosis-Associated CPP

Likelihood of another surgery within 7 yrs of 1st surgery



Shakiba K, Bena JF, McGill KM, Minger J, Falcone T. Obstet Gynecol. 2008.

	Hysterectomy Only		Hysterectomy + BSO
Age 30-39	89.6 (76.0–100.0)	=	85.7 (70.7–100.0)
≥ 40 yrs old	64.3 (33.0–95.7)	<	96.0 (88.3–100.0)

Preserve ovaries in younger women (when feasible), because removal of ovaries does not reduce reoperation

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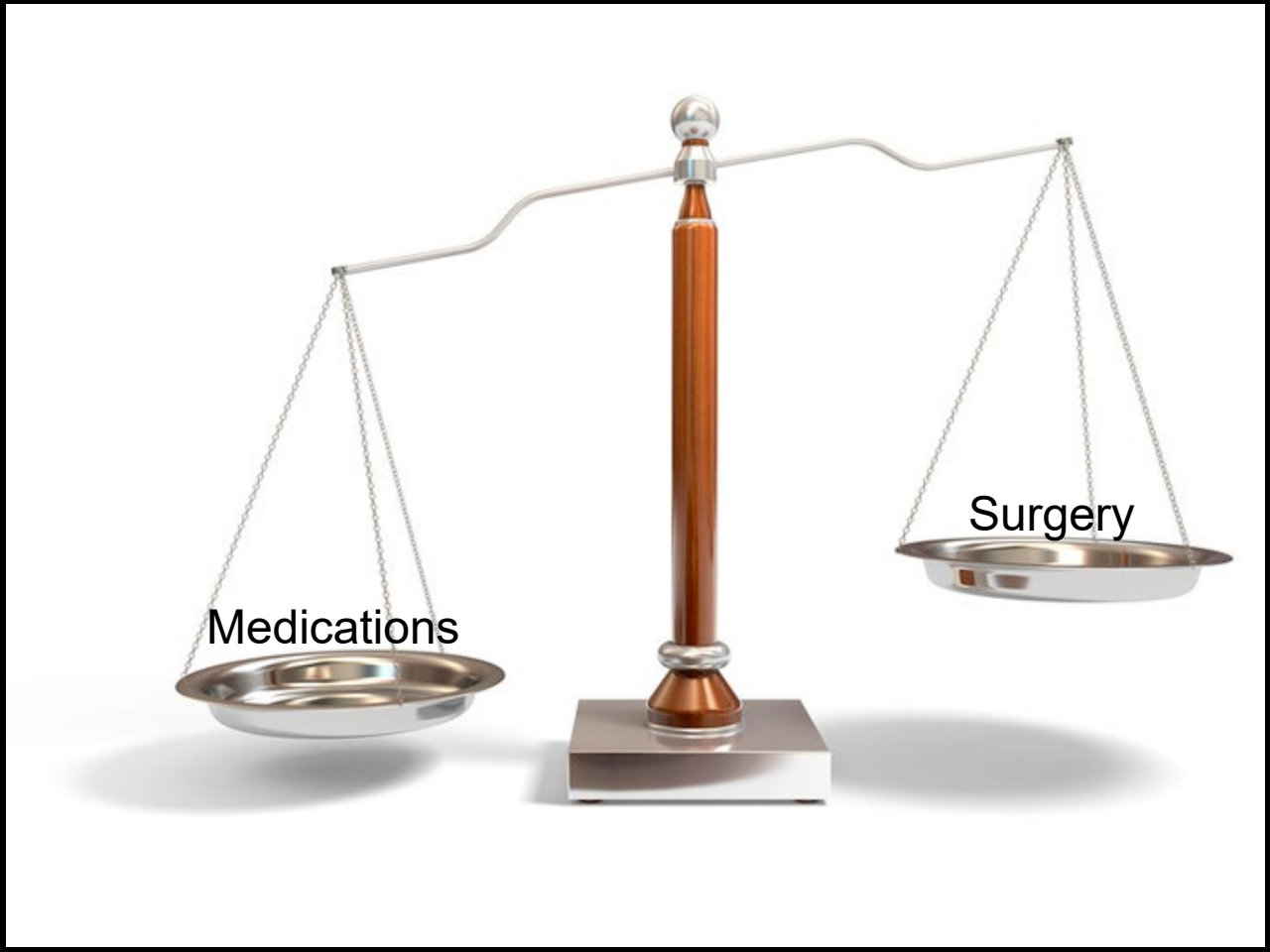
Shakiba K, Bena JF, McGill KM, Minger J, Falcone T. Obstet Gynecol. 2008 Jun;111(6):1285-92

Nearly 50% of women with endometriosis have recurrent symptoms within 5 years, regardless of the treatment approach. (Zondervan, Becker et al. 2020, Becker, Gattrell et al. 2017)

So how do we win the war of endometriosis?

- Pay attention to the evidence
- Don’t pooh pooh medical therapy
- Don’t over-promise surgical therapy



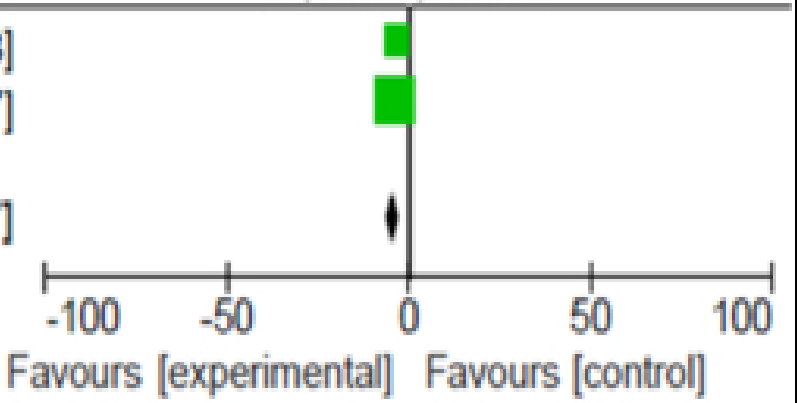
How can we improve outcomes?

Hormonal Suppression

- Progestins are preferred to COCs, and continuous suppression of menstruation is preferred over cyclic. (Seracchioli R et al. *Fertil Steril*. 2010; Muzii L et al. *Am J Obstet Gynecol*. 2016)

	Continuous			Cyclic				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Momoeda 2017	11.9	9.4	105	15.3	11.8	107	35.5%	-3.40 [-6.27, -0.53]	
Strowitzki 2012	10.6	6.7	112	14.9	8.9	102	64.5%	-4.30 [-6.43, -2.17]	
Total (95% CI)			217			209	100.0%	-3.98 [-5.69, -2.27]	

Heterogeneity: Chi² = 0.24, df = 1 (P = 0.62); I² = 0%
Test for overall effect: Z = 4.57 (P < 0.00001)

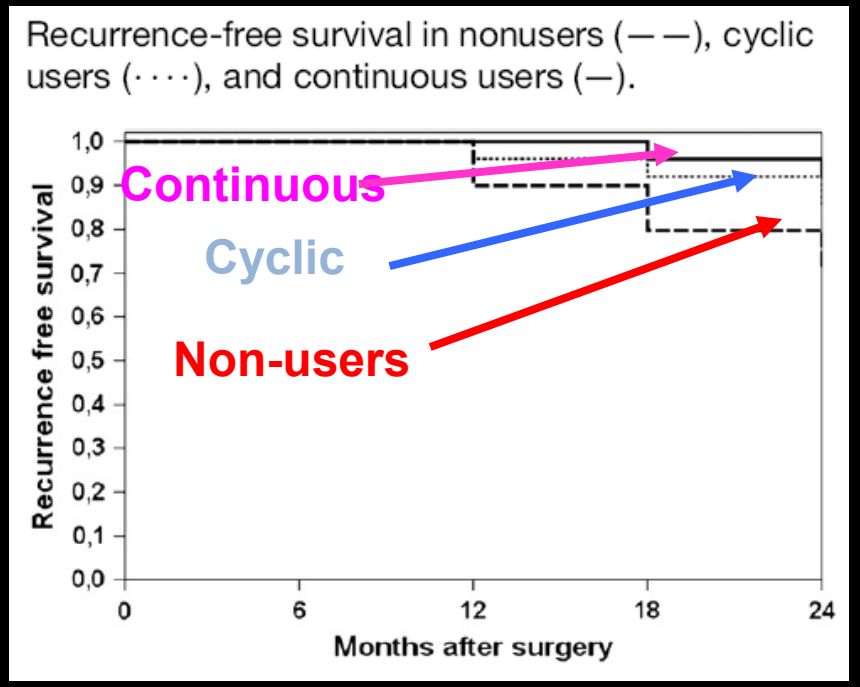


Damm, T., Lamvu, G., Carrillo J., Ouyang, C., Feranec, J., Contraception X, 2019

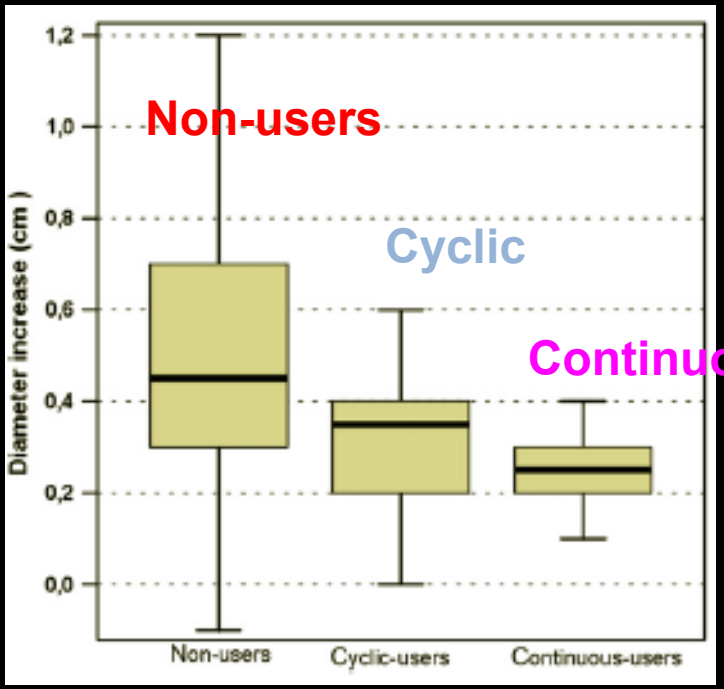
Post Cystectomy Medical Therapy Reduces Rate and Size of Recurrent Endometrioma

RCT, n=239, 24 month follow-up.

Seracchioli R et al, Fertility and Sterility, 2010.



Recurrence free survival is higher in OCP users vs. non-users.



In those with recurrent endometriomas, users of OCPs had smaller cysts.

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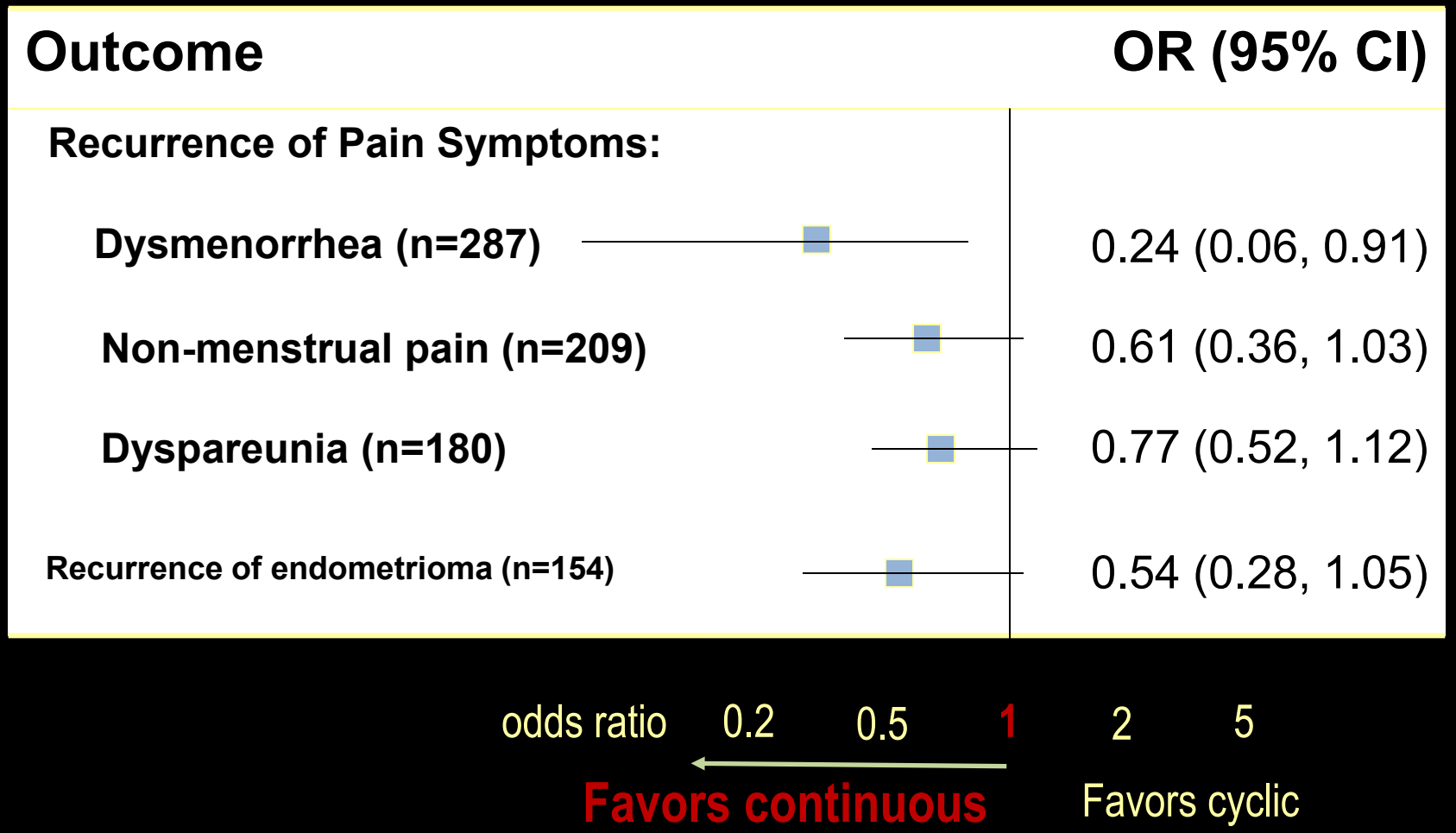
Post-operative OCPs Following Excision of Ovarian Endometrioma: Continuous or Cyclic?



Muzii L, et al. Continuous versus cyclic oral contraceptives after laparoscopic excision of ovarian endometriomas: a systematic review and metaanalysis. Am J Obstet Gynecol. 2016 Feb;214(2):203-11.

Hormonal Suppression Following Surgery

Endometriosis recurrence following post-operative hormonal suppression: a systematic review and meta-analysis.

‘When hormonal suppression (CHC, progestin, LNG-IUS, GnRH agonist) is initiated within 6 weeks of endometriosis surgery, there is a significant reduction in endometriosis recurrence and pain scores at up to 1 year post-operatively. Medical suppression should be considered and discussed with patients not seeking pregnancy immediately after surgery. As various hormonal agents have been shown to be effective, the choice of treatment should be individualized according to each woman’s needs’

Zakhari, A, et.al. Human Reproductive Update, 2021.

Risk of radiologic or clinical endometriosis recurrence with post-operative hormonal suppression compared to expectant management

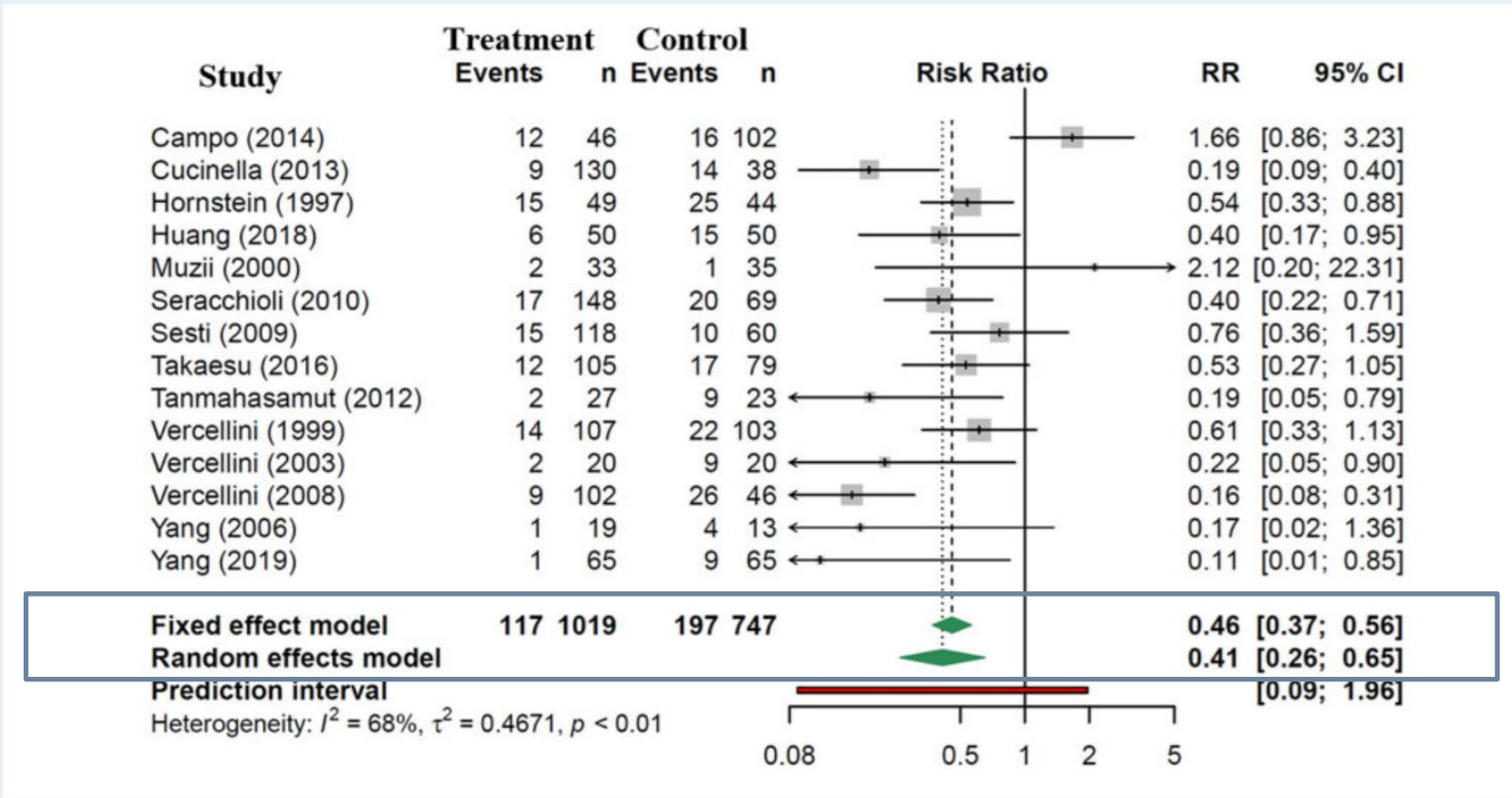


Figure 2. Risk of radiologic or clinical endometriosis recurrence with post-operative hormonal suppression compared to expectant management.

Zakhari, A, et.al. Human Reproductive Update, 2021.

Risk of endometriosis recurrence by hormonal method

	Studies	Patients	I^2	Relative Risk (95% CI)
CHC	6	854	67%	0.36 (0.15 – 0.87)
Progestin*	1	32	NA	0.17 (0.02 – 1.36)
LNG-IUS	2	90	0.0%	0.21 (0.07 – 0.57)
GnRH-a	7	929	52%	0.62 (0.35 – 1.13)

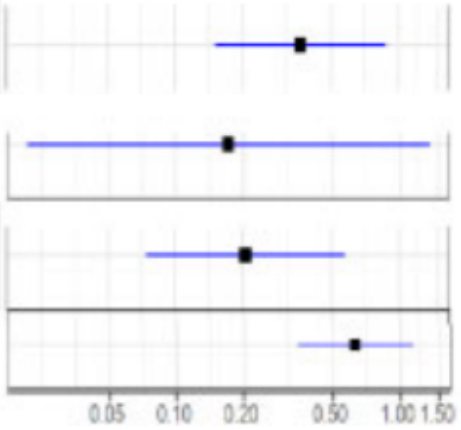


Figure 3. Relative risk of endometriosis recurrence by hormonal intervention (random effects). CHC, combined hormonal contraceptive; CI, confidence interval; LNG-IUS, levonorgesterel intra-uterine system. *Single study—fixed effect model.

Zakhari, A, et.al. Human Reproductive Update, 2021.

Change in pain scores with post-operative hormonal suppression compared to expectant management

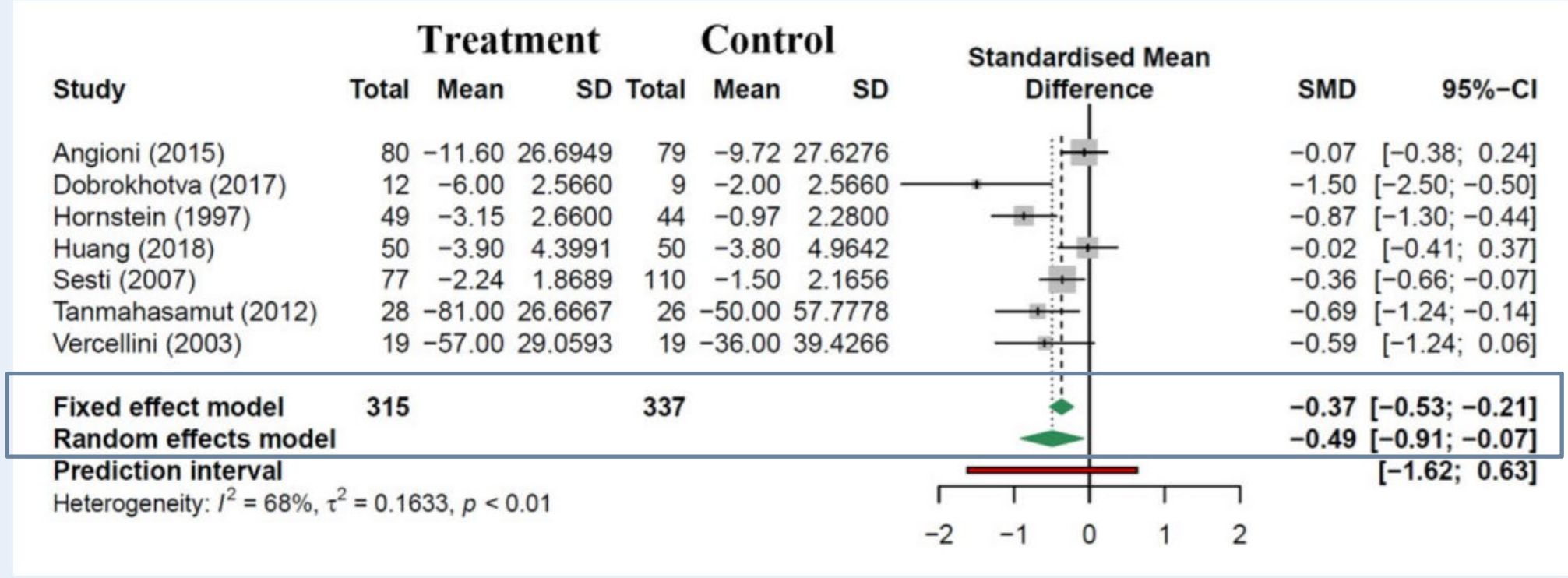


Figure 4. Change in pain scores with post-operative hormonal suppression compared to expectant management.

Zakhari, A, et.al. Human Reproductive Update, 2021.

Other Factors Matter: Influence of Depression on Risk of Persistent Pain

Table 4. Pain, Sexual Function, and Satisfaction With Outcome of Surgery by Preoperative Depression and Pain Status

Outcomes	n	Preoperative status			
		Pain only	Depressed only	Depressed with pain	Not depressed without pain (referent group)
Pelvic pain as a problem*†‡§					
6 months	1,080	2.39 (1.43–4.02)	1.78 (0.96–3.30)	4.49 (2.63–7.69)	1.00
24 months	1,031	2.22 (1.17–4.23)	1.42 (0.65–3.10)	4.91 (2.63–9.16)	1.00

"Women with pelvic pain (OR 2.22), depression (OR 1.42) and both pain + depression (OR 4.91) fared less well 24 months after hysterectomy than women who have neither."

Hartmann KE, Ma C, Lamvu GM, et. Al. Obstet Gynecol. 2004 Oct;104(4):701-9.

Summary: Evidence on Endometriosis-Associated Chronic Pelvic Pain

- All treatments, except hysterectomy, are considered ***suppressive*** rather than curative; endometriosis is a chronic disease requiring sustained treatment and suppression of menstruation[1-3]

- Can have significant physical, sexual, psychological, and social effects requiring long-term treatment.[1-5] ***Biopsychosocial evaluation and treatment is needed***[6]

- In many cases, endometriosis is not the only contributor to pain, thus ***multiple causes of pain must be considered…even in patients with surgically confirmed endometriosis*** (especially if the pain persists after surgery). [1,9]

1. https://www.nice.org.uk/guidance/ng73/chapter/Recommendations. 2. https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Endometriosis-guideline. 3. Abou-Setta AM et al. *Cochrane Database Syst Rev*. 2013; 4. Falcone T, Flyckt R. *Obstet Gynecol*. 2018. 5. Vercellini P et al. *Hum Reprod Update*. 2009; 6.Allaire C et al. *J Endometr Pelvic Pain Disord*. 2017;7. Seracchioli R et al. *Fertil Steril*. 2010;94:856-861. 8. Muzii L et al. *Am J Obstet Gynecol*. 2016;214:203-211. 9. Falcone T, Flyckt R, 2018;

Summary: Evidence on Endometriosis-Associated Chronic Pelvic Pain

- When using medical therapy
  - Full suppression of menstruation with continuous regimens is recommended in women with endometriosis associated pain and / or dysmenorrhea
  - Progestins are preferred over E/P hormonal regimens
  - Expect that therapies will not be effective long term (~ every 2 years)

- When using surgical therapy
  - Up to 40% of patients do not respond, recurrence rates are high; 15%-50% have recurrent pain or reoperation within 2 years
  - Medical suppression with progestins, LNG-IUD, GnRH analogues or combination contraceptives delays recurrence of pain after conservative surgery

- Hysterectomy is beneficial for pain relief; however, ovarian preservation is recommended in women aged <40 years as oophorectomy is associated with severe menopausal symptoms and increased all-cause mortality

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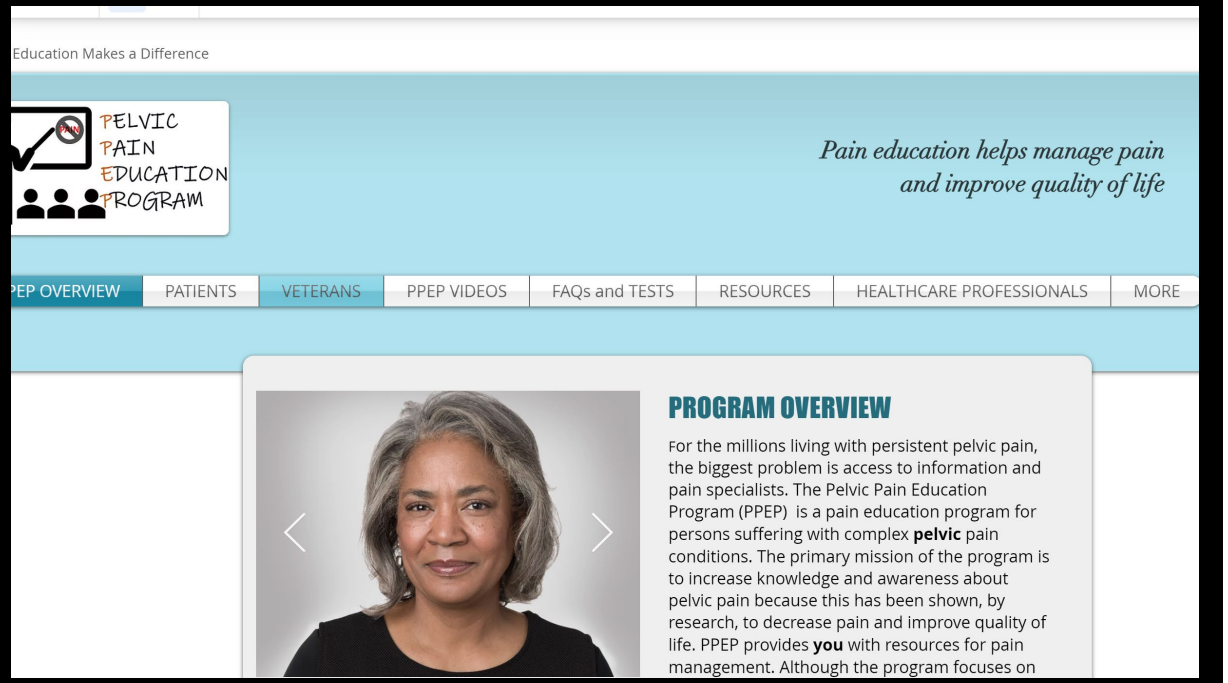
All women with endometriosis should be counseled that:

- Stage is not predictive of symptoms or outcome and not all endometriosis is the same… endometriomas respond to therapy, but wide-spread endometriosis is more complex.

- Medical (before and after surgery) *AND* surgical excision (or ablation) will likely be needed to control severe symptoms long-term and that neither option is a ‘cure’ for endometriosis.

Patient Education Resources

- www.pelvicpaineducation.com



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24th Annual Scientific Meeting on Pelvic Pain
www.pelvicpain.org

- Attend face-to-face or virtual
- Foundations course on October 21 for new HCPS
- Trigger point injections, and myofascial manipulation course on October 24

PainWeek

Thank you

- Contact Email:
  Georgine.Lamvu@va.gov

- Submit additional questions and evaluation at