Bilaga till rapport

Endometrios – diagnostik, behandling och bemötande / Endometriosis – diagnosis, treatment and patients' experiences, rapport 277 (2018)

Bilaga 6 Tabellverk över ingående studier
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Included diagnostic studies in alphabetic order

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
Abrao et al 2007 Brazil [1]	**Study design; recruitment** Cross-sectional; consecutive enrolment **Target condition** Posterior DIE (recto-sigmoid and retro-cervical area) - separate anatomical sites **Setting** Tertiary university hospital, referral centre for endometriosis	**Population** n=104 Patients with clinically suspected endometriosis Mean age, years: 33.8±6.1, range 18–45 **No included in both tests** 104/104 **Clinical presentation** Dysmenorrhoea 53/104 Deep dyspareunia 66/104 Acyclical pelvic pain 17/104 Infertility 55/104 Cyclical bowel symptoms (pain/bleeding) 59/104, cyclical urinary symptoms14/104 **Prevalence** Pelvic endometriosis: 98/104 (91%), DIE: 63/104 (61%)	**Index test** • Transvaginal ultrasound, TVS • Pelvic MRI 1.5 Tesla, (T1/T2-weighted, gadolinium, gel in vagina) **Reference standard** Laparoscopy/laparoscopic surgery + histopathology **Examiners** TVS: one examiner; level of expertise unclear MRI-reader: one radiologist blinded to clinical data and to results of other imaging tests, level of expertise not reported Reference test: Not clearly reported (“results of surgery”)	**TVS** ***Rectosigmoid*** Sensitivity: 98% Specificity: 100% PPV: 100%, NPV: 98% ***Retrocervical*** Sensitivity: 95% Specificity: 98% PPV. 98%, NPV:97% **MRI** ***Rectosigmoid*** Sensitivity: 83% Specificity: 98% PPV: 98%, NPV: 84% ***Retrocervical*** Sensitivity: 76% Specificity: 68% PPV: 61%, NPV: 81%	Possible overlap of MRI data with Chamie 2009 [2] (study period November 2005 to July 2007)
Bazot 2001 France [3]	**Study design; recruitment** Prospective; consecutive enrolment **Target condition** Adenomyosis **Setting** Hospital	**Population** n=120 Patients referred for hysterectomy Mean age, years: 51, range 30–88 **No included in both tests** 120/120 **Symptoms/indications for surgery**	**Index test** Transvaginal ultrasonography, TVS **Reference standard** Gross and microscopic histopathological examinations **Examiners** Index test: examinations were interpreted blindly to histopathological findings.	**Adenomyosis** ***TVS 1*** Sensitivity 60% Specificity 99% ***TVS 2*** Sensitivity 38% Specificity 99% ***TVS 3*** Sensitivity 52% Specificity 90% ***TVS 4*** Sensitivity 30%	Sonography diagnostic criteria for adenomyosis: • TVS 1: myometrial cyst • TVS 2: focal abnormal myometrial echotexture • TVS 3: distorted heterogeneous

[1] Number of persons in the study that were included in both test the index test and reference test

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
		Menorrhagia and/or metrorrhagia 61/120 Post-menopausal bleeding 17/120 Adnexal masses 15/120 Cervical intraepithelial neoplasia 12/120 Pelvic pain 16/120 Genital prolapse 11/120 Premenopausal 69% Postmenopausal 31% **Prevalence** Adenomyosis 33%	Reference standard: Histopathological examinations were all performed by the same pathologist, who was blinded to sonographic	Specificity 96% ***TVS 5*** Sensitivity 65% Specificity 98%	myometrial echotexture • TVS 4: globular uterine configuration • TVS 5: criteria 'TVS 1 and 2'
Bazot et al 2009 France [4]	**Study design; recruitment** Longitudinal; consecutive enrolment **Target condition** DIE: separate anatomical sites; ovarian endometriosis **Setting** Tertiary care, referral centre for endometriosis and Surgical Centre	**Population** n=92 Women referred with clinical evidence of pelvic endometriosis Median age, years: 31.8, range 20–50 **No included in both tests** 92/92 **Clinical presentation** Dysmenorrhoea 79/92, Dyspareunia 63/92 Dyschezia 32/92 Dysuria 3/92 Infertility 21/92 History of surgery for endometriosis 31/92 **Prevalence** DIE 90/92 (97.8%) Ovarian endometriosis 36/92 (39.1%)	**Index test** • Transvaginal ultrasound, TVS • Rectal endoscopic sonography (RES) • MRI 1.5 Tesla (T1/T2-weighted +/- fat-supression/gadolinium contrast) **Examiners** All techniques interpreted independently and blindly by different physicians TVS: 1 radiologist with extensive experience in gynaecological imaging. Blinded Reference test: Not reported. RES: real time by the same gastroenterologist with 5 years' experience in endometriosis. MRI: according to a standardised protocol, retrospectively by 1 radiologist	**TVS** ***Uterosacral ligaments*** Sensitivity: 78% Specificity: 67% ***Rectosigmoid*** Sensitivity:94% Specificity:100% ***Vagina*** Sensitivity: 47% Specificity: 95% ***Rectovaginal septum*** Sensitivity: 9% Specificity: 99% ***Endometrioma*** Sensitivity: 95% Specificity: 84% **RES** ***Uterosacral ligaments*** Sensitivity: 48% Specificity: 44% ***Rectosigmoid*** Sensitivity: 89% Specificity: 93% ***Vagina***	Unclear if exclusion criteria were correct Readers informed of women's clinical history and symptoms, blinded to results of physical and previous imaging examinations.

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
			with 2 years' experience in gynaecological imaging. Reference test: not clearly reported (histology in all but 2 cases; surgery in 2 cases)	Sensitivity: 7% Specificity: 100% ***Rectovaginal septum*** Sensitivity: 18% Specificity: 95% ***Endometrioma*** Sensitivity: 65% Specificity: 93% **MRI** ***Uterosacral ligaments*** Sensitivity: 84% Specificity: 89% PPV:99%, NPV:38% ***Rectosigmoid*** Sensitivity: 87% Specificity: 93% PPV: 97%, NPV: 77% ***Vagina*** Sensitivity: 80% Specificity: 86% PPV: 73%, NPV: 90% ***Rectovaginal septum*** Sensitivity: 54% Specificity: 99% PPV: 50%, NPV: 89% ***Endometrioma*** Sensitivity: 92% Specificity: 88% ***Rectal endoscopic US*** ***Uterosacral ligaments*** Sensitivity:48% Specificity:44% PPV: 89%, NPV: 9% Accuracy: 47.8% ***Rectosigmoid*** Sensitivity:88.9% Specificity:93.1%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
				PPV: 97%, NPV:79% Accuracy: 90.2% ***Vagina*** Sensitivity: 7% Specificity: 100% PPV: 100%, NPV: 69% ***Rectovaginal septum*** Sensitivity: 18% Specificity: 95% PPV: 33%, NPV: 90%	
Bergamini et al 2010 Italy [5]	**Study design; recruitment** Prospective, multi-centre, observational; consecutive enrolment **Target condition** Posterior DIE/ rectosigmoid endometriosis **Setting** University Hospitals of Verona and Varese, referral centres for endometriosis treatment	**Population** n=61 women scheduled for surgery because of signs and symptoms of severe posterior DIE Mean age years: 33.1, range 28–37 **No included in both tests** 61/61 **Clinical presentation** Dyspareunia / catamenial rectal pain 61/61 History of intermittent bowel obstruction 4/61 Nulliparous 11/61, History of surgery for endometriosis 19/61 **Prevalence** Pelvic endometriosis 58/61 (95%) Rectosigmoid endometriosis 51/61 (84%)	**Index test** • Rectal-Water-Contrast transvaginal ultrasound, RWC-TVS • Transrectal Sonography (TRS) **Reference standard** Laparoscopy **Examiners** All scans performed by the same operator with extensive experience in ultrasonographic diagnosis of endometriosis. Operator blinded with respect to other diagnostic findings; unclear whether operator was aware of the results of an additional index test (same operator, different test times)	**TRS** ***Rectosigmoid*** Sensitivity: 88% Specificity: 80% **RWC-TVS** ***Rectosigmoid*** Sensitivity: 96% Specificity: 89%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
Biscaldi et al 2007 Italy [6]	**Study design; recruitment** Prospective, observational, unclear enrolment **Target condition** Bowel endometriosis/ rectosigmoid **Setting** Tertiary care university hospital	**Population** n=98 Women with typical symptoms caused by pelvic endometriosis and gastrointestinal symptoms suggestive of colorectal endometriosis Median age, years: 34, range 20 to 53 **No included in both tests** 98/98 **Clinical presentation** Dysmenorrhoea 87/98 Dyspareunia 73/98 Chronic pelvic pain 48/98 Infertility 23/98 Diarrhoea 20/98 Constipation 12/98 Bloating 5/98 Previous surgery for endometriosis 37/98 Previous medical treatment: oral contraceptive pill 81/98 GnRH-analogues 40/98 Norethisterone acetate 7/98 Letrozole 2/98 No patients with previous bowel surgery other than appendicectomy **Prevalence** Bowel endometriosis 76/98 (77.5%)	**Index test** MDCT-e (MSCTe) (CT-enterography) **Reference standard** Laparoscopy/laparscopic surgery 98/98 (100%) + histopathology **Examiners** Index test: independently reviewed by 2 observers; level of expertise not reported; radiologists not aware of clinical findings and patient history, knowing only that bowel endometriosis was suspected Reference test: a team of gynaecological and colorectal surgeons with extensive experience in the treatment of bowel endometriosis; unclear whether blinded to results of index test; Level of competence of pathologists not described; histological examination described	Sensitivity: 99% Specificity: 100%	Index test compared to reference test also regarding size, localization and degree of bowel wall infiltration. Unclear if lesions involving only the bowel serosa are included

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
Biscaldi et al 2014 Italy [7]	**Study design; recruitment** Prospective, observational, unclear enrolment **Target condition** Rectosigmoid endometriosis **Setting** Tertiary care university hospital, San Martino Hospital, referral centre for endometriosis.	**Population** n= 260 patients referred to (our) endometriosis centre Mean age, years: 32.6±4.3 **No included in both tests** 260/260 **Clinical presentation** Dysmenorrhoea 185/260 Dyspareunia 157/260 Chronic pelvic pain 142/260 Infertility 54/260 Diarrhoea 57/260 Constipation 85/260 Bloating 122/260 Dyschezia 130/260 Previous surgery for endometriosis 113/260 Previous medical treatment: oral contraceptive pill 79/260 Contraceptive vaginal ring 14/260 **Prevalence** Bowel endometriosis 176/260 (68 %)	**Index test** • MDCT-e (CT-enterography) • MRI-enema 1.5 T (T1/T2 weighted, +/- fat suppression, gadolinium contrast) **Reference standard** Laparoscopy 260/260 (100%) + histopathology **Examiners** Index test: 2 radiologists blindly reviewed images at a workstation; not aware of clinical findings and patient history, knowing only that the presence of bowel endometriosis was clinically suspected; level of expertise not reported Reference test: team of gynaecological and colorectal surgeons with extensive experience in the treatment of bowel endometriosis; surgeons aware of results of index tests; level of competence of pathologists not described; histological examination not described	**MDCT-e** ***Rectosigmoid*** Sensitivity: 98% Specificity: 99% **MRI** ***Rectosigmoid*** Sensitivity: 97% Specificity: 96%	Index test compared to reference test also regarding size of endometriotic nodules Lesions involving only the bowel serosa are probably not included (unclear)
Chamie et al 2009 Italy [2]	**Study design; recruitment** Prospective, cross-sectional; unclear enrolment **Target condition** DIE - separate anatomical sites	**Population** n=92 Women who had a history and findings of a physical exam consistent with endometriosis Mean age, years: 33, range 20–52 **No included in both tests** 92/92	**Index test** MRI 1.5 T (T1/T2-weighted +/- fat suppression/ Gadolinium contrast) **Reference standard** Laparoscopy 92/92 (100%) + histopathology	**Retrocervical** Sensitivity: 89% Specificity: 92% **Rectosigmoid** Sensitivity: 86% Specificity: 93% **Bladder** Sensitivity: 23% Specificity: 100%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
	Setting Tertiary university hospital, referral centre for endometriosis	**Clinical presentation** Dysmenorrhoea 89/92 Dyspareunia 54/92, Acyclical pain 72/92 Dysuria 8/92 Dyschezia 44/92 Infertility 40/92 Painful palpable nodules on examination 58/92 **Prevalence** Pelvic endometriosis 92/92 (100%) DIE 77/92 (83.7%)	**Examiners** MRI: images analysed prospectively by 2 radiologists (consensus agreement), blinded to each patient's history, physical findings and ultrasound results; level of expertise not reported. Reference test: numbers or level of expertise of surgeons or pathologists not reported; unclear whether blinded to results of index test.	**Ureteral** Sensitivity: 50% Specificity: 100% **Vagina** Sensitivity: 73% Specificity: 100%	
Dessole et al 2003 Italy [8]	**Study design; recruitment** Prospective, observational; unclear enrolment **Target condition** Posterior DIE (rectovaginal endometriosis) **Setting** University Hospital	**Population** n=46 Women scheduled for laparotomy or laparoscopy because rectovaginal endometriosis was suspected based on patient history and clinical examination Mean age, years: 30.3±4.2 **No included in both tests** 46/46 **Clinical presentation** Chronic pelvic pain, dysmenorrhoea or dyspareunia 38/46 Infertility 20/46 Gastrointestinal disorders 7/46 Urinary disorders 6/46 Endometriotic lesion detected on gynaecological examination 8/46	**Index test** • Transvaginal ultrasound, TVS • Sonovaginography, SVG **Reference standard** Laparoscopy 20/46 (43.5%) Laparotomy 26/46 (56.5%) + histopathology **Examiners** Index test: numbers of examiners, level of expertise and blinding to clinical data not reported Reference test: numbers or level of expertise of surgeons or pathologists not reported; no blinding to results of index test	**Rectovaginal** ***TVS*** Sensitivity: 44% Specificity: 50% ***SVG*** Sensitivity: 91% Specificity: 86%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
		No patients had undergone surgical pelvic procedure before entering the study **Prevalence** Pelvic endometriosis 40/46 (87%) Rectovaginal endometriosis 32/46 (69.5%) Peritoneal endometriosis 8/46 (17.4%)			
Dueholm 2001 Denmark [9]	**Study design; recruitment** Prospective, consecutive enrolment **Target condition** Adenomyosis **Setting** University medical school	**Population** n=106 Premenopausal patients undergoing hysterectomy for benign disease Mean age, years: 44.7±5.2, range 28–58 **No included in both tests** 106/106 **Symptoms:** Abnormal uterine bleeding 51/106 Symptomatic myomas 35/106 Lower abdominal pain or endometriosis 17/106 Dysplasia or prior borderline ovarian tumor 3/106 Abnormal bleeding 82/106 **Prevalence** Adenomyosis 22/106 (22%)	**Index test** • Transvaginal ultrasound, TVS • MRI 1.5T, T2 weighted **Reference standard** Histopathologic examination **Examiners** All hysterectomy specimens were examined by a single Pathologist (level of experience not reported), all MRI scans were evaluated by a single MRI specialist (level of experience not reported), and TVS was always performed by the same experienced gynaecologist (level of experience not reported). MRI, TVS, and pathologic examinations were performed independently and without knowledge of the other investigators' findings and the findings were evaluated consecutively.	**TVS** Sensitivity 59% Specificity 79% **MRI** Sensitivity: 64% Specificity: 88% **MRI + TVS** Sensitivity 73% Specificity 75%	Indefinite findings included as negative

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
Exacoustos 2011 Italy [10]	**Study design; recruitment** Prospective, consecutive enrolment **Target condition** Adenomyosis **Setting** University hospital	**Population** n=72 Premenopausal patients scheduled for hysterectomy Mean age, years: 46.7, range 38–52 **No included in both tests** 72/72 **Symptoms/indications for surgery:** Benign pelvic pathology: Menorrhagia or abnormal uterine bleeding 55/72 (76%) Uterine prolapse 7/72 (10%) Ovarian pathology 10/72 (14%) **Prevalence** Adenomyosis 44.4%	**Index test** 2D & 3D transvaginal ultrasound, TVS **Reference standard** Histopathologic examination after hysterectomy **Examiners** TVS: Each scan (2D and 3D) was performed by one of three expert sonographers. All 2D and 3D ultrasound evaluations and measurements were done during the same examination period and by the same operator. Histopathological examination: performed by a single pathologist, who was blinded to the sonographic data	**Adenomyosis** ***2D-TVS*** Sensitivity 75% Specificity 90% ***3D-TVS*** Sensitivity 91% Specificity 88%	
Ferrero et al 2011 Italy [11]	**Study design; recruitment** Prospective, observational; unclear Enrolment **Target condition** Bowel and rectosigmoid endometriosis **Setting** Single centre, University Hospital	**Population** n=96 Patients referred to the endometriosis centre, suspicion of deep pelvic endometriosis mean age: 33.4±5.2 years **No included in both tests** 96/96 **Clinical presentation** Dysmenorrhoea 72/96 Deep dyspareunia 49/96 Chronic pelvic pain 61/96 Dyschezia 39/96 Infertility 32/96 Diarrhoea 28/96 Constipation 39/96 Intestinal cramping 40/96 Abdominal bloating 53/96 Mucus in the stools 13/96	**Index test** • Rectal-Water-Contrast transvaginal sonography, RWC-TVS • MDCT-e (CT-enterography) **Reference standard** Laparoscopy 96/96 (100%) + histopathology **Examiners** Index test: independently and blindly performed by different investigators, blinded to the clinical data, level of expertise not reported. Reference test: team of gynaecological and colorectal surgeons with extensive experience in the treatment of	**RWC-TVS** ***Rectosigmoid*** Sensitivity: 94% Specificity: 98% ***Bowel endometriosis*** Sensitivity: 88% Specificity: 98% **CT** ***Rectosigmoid*** Sensitivity: 96% Specificity: 100.0% ***Bowel endometriosis*** Sensitivity: 96% Specificity: 100%	CT-enterography was associated with more intense pain than Rectal Water Contrast transvaginal sonography Index test compared to reference test also regarding size and number of endometriotic nodules For rectosigmoid it is unclear if lesions involving only the bowel serosa are included; for bowel

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
		Rectal bleeding 2/96 Previous live birth 27/96 Previous surgery for endometriosis 39/96 Hormonal therapy at time of study 34/96 **Prevalence** Pelvic endometriosis 96/96 (100%) Bowel endometriosis 51/96 (53.1%) Rectosigmoid endometriosis 48/96 (50%)	pelvic and bowel endometriosis, aware of index test results. The same pathologist histologically evaluated all biopsies, level of expertise not reported.		endometriosis serosal lesions are not included
Ferrero 2017 Italy [12]	**Study design; recruitment** Prospective observational **Target condition** Intestinal endometriosis **Setting** Single centre, University Hospital	**Population** n=70 Women scheduled for laparoscopy with strong suspicion of intestinal endometriosis Mean age, years 35.7±5.1 **No included in both tests** 70/70 **Clinical presentation** Dysmenorrhea 64/70 (91 %) Non-menstrual pelvic pain 55/70 (79 %) Dyspareunia 52/70 (74 %) Dyschezia 44/70 (63 %) Persistent constipation 25/70 (36 %) Constipation during menstruation 14/70 (20%) Diarrhea 20/70 (29 %) Diarrhea during menstruation 22/70 (31 %) Intestinal cramping 40 (57 %) Abdominal bloating 43 (61 %)	**Index test** • Rectal-Water-Contrast transvaginal sonography, RWC-TVS • Computed tomographic colonography (CTC) **Reference standard** Laparoscopy 70/70 (100%) + histopathology **Examiners** Index test: TVS: A sonographer with extensive experience in the diagnosis of intestinal endometriosis (>500 scans) performed all the examinations. CTC: A radiologist with more than 5 years' experience in virtual colonoscopy scans (>500 cases) and in the diagnosis of intestinal endometriosis monitored each	**RWC-TVS** ***Rectosigmoid*** **RWC-TVS** ***Rectosigmoid*** Sensitivity 93% Specificity 97% **CTC** ***Rectosigmoid*** Sensitivity 93% Specificity 87%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
		Feeling of incomplete evacuation 23 (33%) Passage of mucus 27 (39 %) Cyclical rectal bleeding 11 (16%) **Prevalence** Rectosigmoid endometriosis 40/70 (57 %)	scan on the main console to ensure that the quality of the scans were adequate for postprocessing. Reference test: the same pathologist examined all specimens excised at surgery, level of expertise not reported. The surgeons examined the reports and the images of CTC and RWC-TVS prior to laparoscopy.		
Goncalves et al 2010 Brazil [13]	**Study design; recruitment** Prospective observational; consecutive enrolment **Target condition** Recto-sigmoid endometriosis **Setting** 2 University Hospitals	**Population** N=194 Women submitted to laparoscopy on suspicion of endometriosis Mean age, years: 34.2±4.9 **No included in both tests** 194/194 **Clinical presentation** Severe dysmenorrhoea 109/194 Deep dyspareunia 120/194 Cyclical bowel complaints 112/194 Chronic pelvic pain 39/194 Infertility 97/194 Cyclical urinary complaints 18/194 Mean time between onset of symptoms and diagnosis 5.2 years (range 0.4–10) **Prevalence** Pelvic endometriosis 194/194	**Index test** Transvaginal ultrasound, TVS with bowel preparation (TVS-BP) **Reference standard** Laparoscopy 194/194 + histopathology **Examiners** TVS: 1 radiologist, level of expertise not reported Reference test: same team; surgical specimens evaluated by 1 pathologist; level of expertise not reported	**Rectosigmoid** Sensitivity: 98% Specificity: 100% **Presence of at least two rectosigmoid lesions** Sensitivity: 81% Specificity: 99% **Lesions affecting the submucosal/mucosal layer of the bowel** Sensitivity: 83% Specificity: 94%	Maybe diagnosis of endometriosis was made before enrolment in this study, but the information is not clear enough for the study to be excluded

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
		Stage I to II 71/194 (37%), stage III to IV 123/194 (63%), Rectosigmoid endometriosis 81/194 (42%)			
Grasso et al 2010 Italy [14]	**Study design; recruitment** Prospective observational; unclear enrolment **Target condition** DIE **Setting** Single centre, University Hospital	**Population** n=33 MRI=33 3D-TVS=24 Patients with clinical suspicion of pelvic endometriosis Mean age, years: 35, range 22–53 **No included in both tests** 24 (3D-TVS); 33 (MRI) **Clinical presentation** Pain (dysmenorrhoea, dyspareunia, chronic pelvic pain) 18/33 Infertility 5/33 Adnexal masses and/or tenderness at physical examination 10/33 **Prevalence** Pelvic endometriosis 33/33 DIE 26/33 (78.7%)	**Index test** • Three-dimensional transvaginal ultrasound, 3D-TVS • MRI 1.5 T (T1/T2-weighted +/- fat-suppression/gadolinium contrast) **Reference standard** Laparoscopy 33/33 (100%) + histopathology **Examiners** TVS: 1 gynaecologist with 20 years' experience, blinded to the patient's clinical history, symptoms and MR results MRI: One radiologist, blinded to clinical/sonographic findings level of expertise not reported. Reference test: numbers or level of expertise of surgeons not provided; 2 different pathologists with level of expertise not reported analysed the specimens, unclear if blinded to results of the index tests	**3D-TVS** ***Deep infiltrating pelvic endometriosis*** Sensitivity: 79% Specificity: 60/70% (in the table in the article 70% is reported, but the numbers in the text give a specificity of 60%) **MRI** ***Deep infiltrating pelvic endometriosis*** Sensitivity: 96% Specificity: 86% ***Bladder*** Sensitivity: 83% Specificity: 100%	Too little information was given in the article for all locations reported except for pelvic DIE in general and bladder. Therefore, only these locations are included in the analysis.

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
Guerriero et al 2007 Italy [15]	**Study design; recruitment** Prospective observational; consecutive enrolment **Target condition** Posterior DIE, ovarian endometriosis **Setting** University Hospital	**Population** n=50 Women scheduled for laparoscopic surgery for rectovaginal endometriosis, suspected on the basis of patient history of pelvic pain and/or clinical examination Mean age, years:33±5, range 22–41 **No included in both tests** 50/50 **Clinical presentation** Pelvic pain: 50/50 Dyspareunia 19/50 Dysmenorrhoea 42/50 Infertility 5/50 All had previous medical treatment for persistent pelvic pain for ≥2 years **Prevalence** Pelvic endometriosis 43/50 (86%) DIE: 31/50 (62%)	**Index test** Transvaginal ultrasonography, TVS **Reference standard** Laparoscopy + histopathology **Examiners** TVS: 1 investigator, ≥15 years' experience with TVUS, blinding to clinical data not reported- Reference test: numbers or level of expertise of surgeons or pathologists not reported. Unclear whether blinded to results of the index test	**Rectovaginal** Sensitivity: 90% Specificity: 95% **Endometrioma** Sensitivity: 100% Positivity: 100%	Selection criteria: not specified
Guerriero et al 2008 Italy [16]	**Study design; recruitment** Prospective observational; consecutive enrolment **Target condition** DIE **Setting** University Hospital	**Population** n=88 Women scheduled for laparoscopic surgery for clinically suspected endometriosis on the basis of patient history of pelvic pain and/or clinical examination **No included in both tests** 88/88 **Clinical presentation**	**Index test** Transvaginal ultrasound, TVS, tenderness guided **Reference standard** Laparoscopic surgery + histopathology **Examiners** TVUS: 1 investigator, ≥15 years' experience with TVUS, blinding to clinical data not reported	**Vaginal involvement** Sensitivity: 91% Specificity: 89% **Recto-sigmoid involvement** Sensitivity: 67% Specificity: 92% **Uterosacral ligaments** Sensitivity: 50% Specificity: 94% **Rectovaginal septum** Sensitivity: 74% Specificity: 88%	Selection criteria: not specified

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
		Pelvic pain: 100% Dyspareunia 40/88 Dysmenorrhoea 71/88 Infertility 10/88 All had previous medical treatment for persistent pelvic pain for ≥2 years. Mean age, years: 33±5, range 20–45 **Prevalence** DIE 72/88 (82%)	Reference test: numbers or level of expertise of surgeons or pathologists nor reported, unclear whether blinded to results of the index test	**Anterior pouch** Sensitivity; 33% Specificity: 100% **Bladder** Sensitivity: 100% Specificity: 100%	
Guerriero et al 2014 Italy [17]	**Study design; recruitment** Prospective observational; consecutive enrolment **Target condition** Posterior DIE-different sites **Setting** University Hospital	**Population** n=2202 Premenopausal women with clinical suspicion of deep endometriosis scheduled for surgery **No included in both tests** 202/240 **Clinical presentation** Chronic pelvic pain 101/202 Dyspareunia 51/202 Dysmenorrhoea 132/202 Previous surgery for pelvic pain 20/202 Hormonal treatment at the time of ultrasound examination 43/202 Mean age, years: 34±6, range 18–52 **Prevalence** DIE: 129/202 (64%) Participants: single nodule 75/129 (58%) ≥1 location endometriosis 54/129 (42%) Posterior DIE 122/129 (95%)	**Index test** TVS 2 types (2D-TVS, tenderness guided and 3D-TVS) **Reference standard** Laparoscopy 194/202 Laparotomy 8/202 + histopathology **Examiners** TVS: 1 investigator with ≥20 years' experience Reference test: Same group of surgeons with ≥10 years' experience.	**Recto-sigmoid** ***2D-TVS*** Sensitivity: 95% Specificity: 93% ***3D-TVS*** Sensitivity: 91% Specificity:97% **Other posterior locations** ***2D-TVS*** Sensitivity: 71% Specificity: 88% ***3D-TVS*** Sensitivity. 87% Specificity: 94%	Blinding to clinical data not reported Unclear if surgeons blinded to imaging results

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
		Rectosigmoid endometriosis 77/129 (60%) Complete obliteration of POD 51/129 (40%)			
Holland et al 2010 UK [18]	**Study design; recruitment** Prospective observational, consecutive enrolment **Target condition** Pelvic endometriosis; DIE - overall and separately for anterior and posterior compartments; POD obliteration **Setting** Multicentre, University Hospital	**Population** n=211 Women with clinically suspected/proven pelvic endometriosis **No included in both tests** 201/211 **Clinical presentation** Dysmenorrhoea 142/201 Chronic pelvic pain 104/201 Dyspareunia 78/201 Infertility 38/201 Dyschezia 7/201 Cyclical rectal bleeding 2/201 Mean age, years: 34.9±6.79, range 19–51 **Prevalence** Pelvic endometriosis 139/201 (69.2%) DIE 71/201 (35.3%)	**Index test** Transvaginal ultrasound, TVS **Reference standard** Laparoscopy, histology not on all persons included in the study **Examiners** TVS: 4 ultrasound operators, all gynaecologists with a high level of expertise, no significant difference found in overall accuracy between examiners Reference test: 4 different laparoscopic surgeons (experienced)	**DIE in bladder/uterovesical** Sensitivity: 56% Specificity: 100% **DIE rectovaginal/sigmoid** Sensitivity: 45% Specificity: 100% **POD-obliteration** Sensitivity: 72% Specificity: 97% **DIE (any of the above)** Sensitivity: 61% Specificity: 96%	Examiners: blinded to previous surgical findings Surgeons blinded to detailed TVS findings
Hottat et al 2009 Belgium [19]	**Study design; recruitment** Prospective observational study, consecutive enrolment **Target condition** DIE - overall and separately for specific anatomical locations **Setting**	**Population** n=106 Women referred for pelvic MR imaging due to clinical suspicion of endometriosis **No included in both tests** 41/106 **Clinical presentation** Dysmenorrhoea 19/41 Chronic pelvic pain 29/41 Dyspareunia 5/41	**Index test** MRI 3.0T, T1/T2 weighted +/- fat suppression, no gadolinium contrast (with or without jelly in rectum for assessment of colon wall) **Reference standard** Laparoscopy 34/41or laparotomy 7/41 with histopathology (100%)	**Endometriomas** Reader 1: Sensitivity: 96% Specificity: 98% Reader 2: Sensitivity: 93% Specificity: 98% **Ovarian hemorrhagic foci** Reader 1: Sensitivity: 67% Specificity: 92% Reader 2:	MRI readers were blinded to clinical findings Colon wall infiltration was graded (none, serosa, muscularis, submucosa, mucosa) It is unclear, if results for other locations than the

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
	University hospital, endometriosis referral centre	Suspicious clinical examination 15/41 History of endometriosis 7/41 Mean age 33 years (range 20–46) **Prevalence** DIE 27/41 (66%) USL 21/41 (51%), POD 22/41 (54%), vaginal 11/41 (27%), colon 13/41 (31%)	**Examiners** MRI: 2 investigators with 8 years' and 1 year experience in MRI; independently and prospectively analysed all images. level of agreement between the 2 readers reported for each site of endometriosis Reference test: both surgeon and pathologist with more than 10 years' experience in evaluation of endometriosis; same team for all cases	Sensitivity: 67% Specificity: 81% **POD involvement** Reader 1: Sensitivity: 95% Specificity: 100% Reader 2: Sensitivity: 95% Specificity:100% **Utero-sacral ligaments** Reader 1: Sensitivity: 80% Specificity: 96% Reader 2: Sensitivity: 90% Specificity: 79% **Vesico-uterine pouch** Reader 1; Sensitivity: 75 % Specificity: 100 % Reader 2: Sensitivity: 63% Specificity: 100% **Bladder** Reader 1: Sensitivity: 50% Specificity:100% Reader 2: Sensitivity: 50% Specificity: 100% **Vagina** Reader 1: Sensitivity: 82% Specificity: 97% Reader 2: Sensitivity: 55% Specificity: 100% **Colon wall with gel** Reader 1:	colon wall are for MRI with or without gel in the colon

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
				Sensitivity: 100% Specificity: 100% Reader 2: Sensitivity: 100% Specificity: 96% **Colon wall without gel** Reader 1: Sensitivity: 100% Specificity: 96% Reader 2: Sensitivity: 100% Specificity:96%	
Hudelist et al 2011 UK [20]	**Study design; recruitment** Prospective, observational, multi-centre; unclear enrolment **Target condition** DIE - separate anatomical sites; ovarian endometriosis **Setting** 3 tertiary referral service Hospitals	**Population** n=153 Women with suspected endometriosis attending 1 of 3 pelvic pain clinics, referred to the pelvic pain clinic for laparoscopy because of suspected endometriosis on the basis of clinical history and the referring physician's clinical findings, or were self-referred Mean age, years: 32.2±5.4, range 17–44 **No included in both tests** 129/153 **Clinical presentation** Dysmenorrhoea 111/129 Dyspareunia 72/129 Dyschezia 39/129 Dysuria 6/129 Chronic pelvic pain 45/129 Subfertility 20/129	**Index test** Transvaginal ultrasound, TVS **Reference standard** Laparoscopy 129/129 (100%) + histopathology **Examiners** Index test: 1 experienced examiner, blinded to results of the vaginal examinations but aware that women were being investigated for chronic pelvic pain; therefore, endometriosis was suspected Reference test: 3 surgeons performed laparoscopy, all had ≥10 years' experience in radical laparoscopic surgery for DIE, blinded to results of the vaginal examination and TVS at 1 of the centres but were aware of the vaginal examination and TVS results at the other 2 centres; numbers and level of expertise of pathologists not reported	**Ovary (endometrioma)** Sensitivity: 96% Specificity: 96% **Uterosacral ligaments** Sensitivity: 63% Specificity: 98% **POD involvement** Sensitivity: 76% Specificity: 92% **Vagina** Sensitivity: 64% Specificity: 99% **Urinary bladder** Sensitivity: 50% Specificity: 98% **Rectosigmoid** Sensitivity: 90% Specificity: 99% **Rectovaginal** Sensitivity: 78% Specificity: 100%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
		Prevalence Pelvic endometriosis 83/129 (64.3%) DIE 52/129 (40.3%) Ovarian endometriosis 27/129 (16.2%)			
Hudelist et al 2013 Austria [21]	**Study design; recruitment** Prospective observational, consecutive enrolment **Target condition** DIE of rectum **Setting** Multicentre, pelvic pain clinic	**Population** n=142 Women with suspected endometriosis and scheduled for laparoscopy on the basis of clinical examination and TVS findings **No included in both tests** 117/142 **Clinical presentation** Dysmenorrhoea 116/117 Dyspareunia 74/117 Dyschezia 31/117 Dysuria 9/117 Chronic pelvic pain 32/117 Subfertility 22/117 Mean age: 31.6±6.5 **Prevalence** Pelvic peritoneum endometriosis 62/117 RS DIE 34/117	**Index test** Transvaginal ultrasound, TVS **Reference standard** Laparoscopy (117/117) + histopathology **Examiners** TVS: 1 experienced examiner, not blinded to clinical data Reference test: 2 experienced surgeons	**DIE in rectum** Sensitivity: 85% Specificity: 96%	25 patients excluded because they did not meet the inclusion criteria: Surgeons not blinded to TVS results
Kepkep Turkey 2007 [22]	**Study design; recruitment** Prospective, consecutive enrolment **Target condition** Adenomyosis	**Population** n=70 Patients planned for hysterectomy Mean age, years: 49.03±5.58, range 37–63 **No included in both tests** 70/70	**Index test** Transvaginal ultrasound, TVS **Reference standard** Histopathologic examination after hysterectomy **Examiners** TVS: preoperative	**Adenomyosis** Sensitivity 81% Specificity 61%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
	Setting Educational and Research Hospital	**Symptoms/indications for surgery** Leiomyoma of the uterus 28/70 Endometrial hyperplasia 18/70 Adnexal tumors 8/70 Premenopausal abnormal uterine bleeding 8/70 Uterine prolapse 4/70 Cervical dysplasia 2/70 Postmenopausal bleeding 2/70 Premenopausal 74.3% Postmenopausal 25.7% **Prevalence** Adenomyosis 37.1%	transvaginal ultrasound examinations performed by one of the four authors who had 20, 16, 15 and 5 years' experience in female pelvic sonography, respectively. All printed sonographic images were re-evaluated and the results confirmed by one of the authors. All histopathological examinations were performed by the same pathologist, who was blinded to the sonographic findings.		
Leon et al 2014 Chile [23]	**Study design; recruitment** Prospective, observational; unclear enrolment **Target condition** DIE - separate anatomical sites **Setting** Single centre	**Population** n=110 Women with clinical suspicion of DIE based on clinical symptoms or physical pelvic examination findings Mean age, years: 32.9±4.7 years, range 23–43 **No included in both tests** 51/51 **Clinical presentation** Dysmenorrhoea 51/51 Dyspareunia 39/51 Dyschezia 34/51 Chronic pelvic pain 46/51 Hematochezia 5/51 Suspicious bimanual vaginal examination 26/51 **Prevalence** DIE 39/51 (77%) POD obliteration 27/39 (69%)	**Index test** Extended transvaginal ultrasound, TVS **Reference standard** Laparoscopy surgery 51/51 (100%) + histopathology **Examiners** Index test: 1 operator, ≥10 years' experience in gynaecological sonography and 3 years' experience in assessment of DIE, unclear whether operator was blinded to clinical data Reference test: 1 surgeon, expert in endometriotic surgery, aware of index test results	**POD-obliteration** Sensitivity: 89% Specificity: 92% **Rectosigmoid** Sensitivity: 100% Specificity: 93% **Retrocervical** Sensitivity: 84% Specificity: 96% **Bladder** Sensitivity: 20% Specificity: 100% **Vaginal fornix** Sensitivity: 60% Specificity: 98%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
Leone Roberti Maggiore et al. 2017 [24]	**Study design;** **Recruitment** Prospective, consecutive enrolment **Target condition** Rectosigmoid endometriosis **Setting** Single centre, University Hospital	**Population** n=286 Women in reproductive age and suspicion of deep pelvic endometriosis based on gynaecological symptoms and vaginal examination and/or presence of gastrointestinal symptoms Mean age, years: 31.9±4.8 years **No included in both tests** **Prevalence** 286/286 **Clinical presentation** Dysmenorrhea 85% Non-menstrual pelvic pain 82% Dyspareunia 80% Dyschezia 58% Persistent constipation 37% Constipation during menstruation 20% Diarrhea 28% Diarrhea during menstruation 33% Intestinal cramping 63% Abdominal bloating 59% Feeling of incomplete evacuation 37% Cyclical rectal bleeding 46% **Prevalence** 53%	**Index test** • Magnetic resonance enema (MR-e) • Rectal water-contrast transvaginal sonography (RWC-TVS) • **Reference standard** Laparoscopy 96/96 (100%) + histopathology **Examiners** MR-e: one radiologist performed all the exams RWC-TVS: one physician performed the exams. The radiologist and the sonographer knew the clinical data and that rectosigmoid endometriosis was suspected; however, each was blinded to the findings of the other imaging technique. Reference test: performed by a team of gynaecological and colorectal surgeons with extensive experience in the surgical treatment of pelvic and rectosigmoid endometriosis.	**MR-e** Sensitivity 95% Specificity 98% **RWC-TVS** Sensitivity 93% Specificity 97%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
Luciano 2013 Italy [25]	**Study design; recruitment** Prospective **Target condition** Adenomyosis **Setting** Private practice associated with a university program	**Population** n=54 Symptomatic premenopausal patients scheduled to undergo hysterectomy Mean age, years: 42.1±5.1, range (34–54) **No. included in both tests** 54/54 **Symptoms/indications for surgery:** ***In the endometrial ablation group*** Pain 6/12 Dysmenorrhea 4/12 Abnormal bleeding 2/12 ***In the medical group*** Pain 5/10 Dysmenorrhea 4/10 Abnormal bleeding 1/10 ***For the other patients*** Dysmenorrhea 17/32 Pelvic pain 9/32 Menometrorrhagia 17/32 Dyspareunia 2/32 **Prevalence** Adenomyosis 66.6%	**Index test** 2D transvaginal ultrasound and 3D-TVS (2D in combination with 3D) **Reference standard** Histopathologic examination after hysterectomy **Examiners** TVS: All scanning was performed by 2 expert sonographers. All 2D and 3D ultrasound measurements and evaluations were performed during the same TVS examination and by the same operator. Histopathological examination: the pathologist was blinded to sonographic findings	**Adenomyosis** ***All patients (n=54***) Sensitivity 92% Specificity 44% ***No previous ablation or medical therapy (n=32)*** Sensitivity 92% Specificity 83% ***Previous ablation (n=12)*** Sensitivity 80% Specificity 29% ***Previous medical treatment (n=10)*** Sensitivity 100% Specificity 20%	
Milone et al 2015 Italy [26]	**Study design; recruitment** Prospective observational; Unclear enrolment **Target condition** Bowel endometriosis	**Population** n=174 Women with a clinical and radiological diagnosis of deep pelvic endometriosis whit suspected bowel endometriosis.	**Index test** Colonoscopy **Reference standard** Laparoscopy **Examiners** Colonoscopy by an expert operator with >10 years of	Sensitivity: 8% Specificity: 99%	Video laparoscopy within 4 wk of the colonoscopic examination.

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
	Setting University hospital, single centre	**No included in both tests** 174/174 **Prevalence** Intestinal endometriosis: 76/174 DIE: 74/74	experience endoscopist was blinded about the previous radiological diagnosis. Reference test: expert laparoscopic surgeons.		
Pascual et al 2010 Spain [27]	**Study design; recruitment** Prospective observational; consecutive enrolment **Target condition** RVS endometriosis (deep rectovaginal septum endometriosis) **Setting** University Hospital	**Population** n=39 Women with clinically suspected endometriosis based on patient history of pelvic pain and/or clinical examination Mean age, years: 35.6±5.7, range 25–44 **No included in both tests** 38/39 **Prevalence** Pelvic endometriosis 38/38 Deep rectovaginal septum endometriosis 19/38	**Index test** Introital three-dimensional (3D) ultrasound **Reference standard** Laparoscopy + histopathology **Examiners** 3D ultrasound: 3 experienced examiners, stored 3D volumes analysed by 1 examiner; Reference test: numbers or level of expertise of surgeons or pathologists not provided;	**Recto-vaginal septum DIE** Sensitivity: 90% Specificity: 95%	Unclear whether blinded to clinical data Unclear whether blinded to results of the index test
Pateman et al 2015 UK [28]	**Study design; recruitment** Prospective observational **Target condition** Ureteric endometriosis **Setting** Teaching hospital	**Population** n=848 Patients with chronic pelvic pain Mean age, years: 36.1±7.8 308 had previous surgery for endometriosis **No included in both tests** 164/848 **Prevalence** 335/848 (39.5%) of which 14/335 had ureteric endometriotic lesions and 6/335 had bladder lesions	**Index test** Transvaginal ultrasound, TVS **Reference standard** Surgery + histology and/or CT or MRI **Examiners** Not specified	**Ureteric endometriosis** Sensitivity: 92% Specificity: 100%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
Piessens et al 2014 Australia [29]	**Study design; recruitment** Prospective observational, consecutive enrolment; retrospective analysis **Target condition** DIE at specific anatomical sites, ovarian endometrioma **Setting** University Hospital	**Population** n=205 Patients with clinically suspected endometriosis referred to TVS **No included in both tests** 85/205 **Clinical presentation** Dysmenorrhoea (63%) Dyschezia (53%) Dyspareunia (44%) Infertility (22%) Abnormal bleeding (20%) Chronic pain (21%) Rectal bleeding (8%) Past history of endometriosis (72%) Age, years: 18 to 48 **Prevalence** Bowel endometriosis 24/85 (7%) POD obliteration 34 (40%) Vaginal endometriosis 15/85 (18%) Ovarian endometrioma 17/85 (20%)	**Index test** Transvaginal ultrasound after minimal bowel preparation, TVS-BP **Reference standard l** Laparoscopy + histopathology **Examiners** TVS: 1 gynaecologist with a subspecialty degree in ultrasound ≥10 years' experience no prior experience in detecting DIE	**Ovary (endometrioma)** Sensitivity: 100% Specificity: 93% **POD-obliteration** Sensitivity: 88% Specificity: 90% **Vagina** Sensitivity: 80% Specificity: 100% **Bladder** Sensitivity: 33% Specificity: 100% **Bowel** Sensitivity: 88% Specificity: 93%	Selection criteria: not specified Operator was not blinded to symptoms and history of women
Reid et al 2013 Australia [30]	**Study design; recruitment** Prospective observational, consecutive enrolment **Target condition** Posterior DIE - separate anatomical sites **Setting**	**Population** n=100 Women with a history of chronic pelvic pain and/or endometriosis and scheduled for operative laparoscopy Mean age, years: 32.78±6.28 years, range 19–48 **No included in both tests**	**Index test** Transvaginal ultrasound, TVS with sliding sign **Reference standard** Laparoscopy + histopathology **Examiners**	**Recto-sigmoid** Sensitivity: 85% Specificity: 91% **Uterosacral ligaments** Sensitivity: 40% Specificity: 96% **Rectovaginal septum/vagina** Sensitivity: 25% Specificity: 100%	Unclear whether blinded to results of the index test

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
	Multicenter, 4 university teaching hospitals, tertiary referral centres	100/100 **Clinical presentation** Cyclical pain 70/100 Pain requiring strong analgesia 49/100 Pain affecting life despite analgesia 53/100 Pain preventing daily activities 55/100 Dyspareunia 56/100 Dyschezia 51/100 Constant pain 2/100 (2%) Non-cyclical pain 2/100 Median duration of pelvic pain 18 months; history of in vitro fertilisation (13%) Use of contraception (30%) History of infertility (30%) History of endometriosis (60%) **Prevalence** Pelvic endometriosis 84/100 Posterior DIE 33/100	TVUS: 1 examiner; level of expertise and blinding to clinical data not reported Reference test: 7 advanced laparoscopic surgeons, all experienced in excision of DIE; data on numbers or level of expertise of pathologists not reported	**POD-obliteration** Sensitivity: 83% Specificity: 97%	
Reid et al 2014 Australia, UK [31] Reid 2015 [32]	**Study design; recruitment** Prospective observational; consecutive enrolment **Target condition** Posterior DIE-overall and separate anatomical sites (USL, RVS, vagina, bowel including anterior rectum and recto-sigmoid) POD obliteration **Setting**	**Population** n=220 Women who presented to pelvic pain clinic with symptoms suggestive of endometriosis Mean age: 32.2±7.5 **No included in both tests** 189/220 **Clinical presentation** Chronic pelvic pain, dysmenorrhoea, dyspareunia, dyschezia; mean duration of pain 39.7±47.5 months	**Index test** Transvaginal ultrasound, TVS Sonovaginography, SVG **Reference standard** Laparoscopy **Examiners** TVS: Same person who performed the gynaecological examination, level of expertise not reported SVG: 2 operators, 1 expert gynaecological sonologist with experience in diagnosis of DIE;	**TVS** ***POD-obliteration*** Sensitivity: 85% Specificity: 98% **SVG** ***Bowel*** Sensitivity: 88% Specificity: 93% ***Recto-sigmoid*** Sensitivity: 85% Specificity: 96% ***Anterior rectum*** Sensitivity: 72% Specificity: 95%	Same person who performed SVG performed the gynaecological examination and TVS. Operators were not blinded to clinical history Surgeons not blinded to patient data, including results of the index test

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
	Multicentre, University teaching hospitals, tertiary referral centres	History of infertility 44/220 History of endometriosis 92/220 History of bowel DIE 10/220 **Prevalence** POD obliteration 47/189	the other a gynaecological ultrasound fellow supervised by an experienced operator. Reference test: Surgery performed by 13 laparoscopic surgeons: 9 advanced laparoscopic surgeons and 4 general gynaecological surgeons.	***Posterior vaginal wall*** Sensitivity: 18% Specificity: 99% ***Rectovaginal septum*** Sensitivity: 18% Specificity: 100% ***Uterosacral ligaments*** Sensitivity; 40% Specificity: 97.8%	
Ribeiro et al 2008 Brazil [33]	**Study design; recruitment** Prospective observational; consecutive enrolment **Target condition** Recto-sigmoid endometriosis **Setting** University hospital, gynaecological endoscopy and endometriosis clinic/ referral centre for endometriosis	**Population** N=37 Women with clinically suspected DIE Mean age: 35.8±4.4, range 28–48 years **No included in both tests** 37/37 **Prevalence** DIE 37/37 Recto-sigmoid endometriosis 27/37 (73%)	**Index test** • Double-contrast barium enema, DCBE • TRUS (Tr EUS) **Reference standard** Laparoscopy + histopathology **Examiners** Both tests in a non-randomised sequence, by 2 blinded examiners: DCBE - 1 operator under supervision of a radiologist technician; images were then reviewed by a skilled radiologist; TrEUS - performed by 1 senior echographer, Reference test: numbers or level of expertise of surgeons NR. All biopsies studied by same pathologist; level of expertise NR	**Intestinal DIE** ***DCBE*** Sensitivity: 78% Specificity: 70% ***Tr EUS*** Sensitivity: 100% Specificity: 90%	Unclear whether examiners were blinded to clinical data Not blinded to results of the index tests
Ros et al 2017 Spain, Brazil [34]	**Study design; recruitment** Prospective observational; consecutive enrolment **Target condition** Rectosigmoid deep infiltrating endometriosis	**Population** n=40 Women awaiting surgery for endometriosis. Mean age: 36.8±5.0 **No included in both tests** 40/40	**Index test** Transvaginal ultrasound, TVS, with or without bowel preparation (BP) **Reference standard** Laparoscopy + histopathology	**TVS** Sensitivity 73% Specificity 88% **TVS-BP** Sensitivity 100% Specificity 96%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
	Setting A tertiary university hospital	**Prevalence** 45%	**Examiners** Index test: All the TVS studies were performed by the same trained gynaecologist who was blinded to the clinical data and the results of the first TVUS during the second examination with BP. Reference test: surgical interventions were performed by expert endometriotic surgeons. Histologic evaluation was performed by a single pathologist.		
Savelli et al 2011 Italy [35]	**Study design;** **recruitment** Prospective observational; consecutive enrolment **Target condition** Posterior DIE, recto-sigmoid endometriosis **Setting** University hospital tertiary care referral	**Population** n=94 Women with results of pelvic examination or symptoms suggestive of DIE of the posterior compartment Median age, years: 33.6±5.9 **No included in both tests** 69/94 **Clinical presentation** Infertility 30/69 Dysmenorrhoea 64/69 Dyspareunia 59/69 Dyschezia 45/69 Nulliparous 49/69 Previous surgery for endometriosis 18/69 Oestrogen-progestin therapy before surgery 22/69 **Prevalence** Posterior DIE 67/69 (97%) Recto-sigmoid endometriosis 56/69 (81.2%)	**Index test** Transvaginal ultrasound, TVS Double-contrast barium enema, DCBE **Reference standard** Laparoscopy+ histopathology **Examiners** Both DCBE and TVS performed by 2 groups of physicians specialising in endometriosis with training and expertise in gynaecological imaging studies reference test: laparoscopy performed by 1 skilled gynaecological surgeon specialising in endometriosis; data on numbers or level of expertise of pathologists NR	**TVS** Overall posterior DIE Sensitivity: 85% Specificity: 100% Bowel DIE Sensitivity: 91% Specificity: 100% **DCBE** Overall posterior DIE Sensitivity: 36% Specificity: 100% Bowel DIE Sensitivity: 43% Specificity: 100%	Image examiners: were aware of each patient's history, symptoms and pelvic examination but were blinded to the results of other index tests Surgeon: was aware of TVS and DCBE findings

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
Sayasneh et al 2015 Belgium, UK [36]	**Study design; recruitment** Prospective observational, cross sectional, consecutive enrolment **Target condition** Endometrioma **Setting** Multicentre	**Population** n=1279 ≥one adnexal mass, ≥16 years of age (mean age: 47 years) Women with at least one adnexal mass operated ≤120 days after ultrasound examination **No included in both tests** 313/1276 **Prevalence** Endometrioma 55 (17.6%)	**Index test** Transvaginal ultrasound, TVS **Reference standard** Laparoscopy + histopathology **Examiners** Index test: level II examiners according to EFSUMB Reference test: histological examination carried out at each of three local centres	Sensitivity:75% Specificity: 99%	
Stabile et al 2013 Italy [37]	**Study design; recruitment** Prospective observational, consecutive enrolment **Target condition** Recto-sigmoid endometriosis **Setting** University Hospital	**Population** n=37 Women suspected to have deep pelvic endometriosis (DPE) and bowel endometriosis based on history and findings at physical examination Mean age, years: 31.5±3, range 24–39 **No included in both tests** 33/37 **Prevalence** Pelvic endometriosis 33/33 DPE 26/33 (79%) Recto-sigmoid endometriosis 23/33 (69%)	**Index test** MDCT-e (water enema CT) (CT-enterography) **Reference standard** Laparoscopy + histopathology **Examiners** Index test: 2 radiologists with 15 years' and 5 years' experience in abdominal imaging, almost perfect agreement was found between the 2 readers (kappa = 0.84) Reference test: 1 surgeon with 15 years' experience in abdominal video laparoscopy; data on numbers or level of expertise of pathologists not reported; histological examination not described	Sensitivity: 87% Specificity: 100%	Radiologists blinded to clinical data and to other results Unclear whether surgeons blinded to results of the index test Lesions involving only bowel serosa are included.
Stamatopoulos 2012 Greece [38]	**Study design; recruitment** Prospective cohort, consecutive enrolment	**Population** n=135 Mean age, years: 46.7±11.2 (95% CI 44.93 to 48.65) **No. included in both tests**	**Index test** MRI 1.0 T, T1/T2 weighted, gadolinium contrast, fat-suppression not stated	**Adenomyosis** Sensitivity: 46% Specificity: 99%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
	Target condition Adenomyosis **Setting** Tertiary academic hospital	135/135 **Symptoms/indications for surgery** Heavy menstrual bleeding 78/135 Postmenopausal bleeding 12/135 Abdominal heaviness, bloating, and suprapubic pain 24/135 Pelvic mass 9/135 **Prevalence** Adenomyosis 26/135 (19%)	**Reference standard** Histopathologic examination after hysterectomy **Examiners** All hysterectomy specimens were examined by a single pathologist; all MRI images were evaluated by a single radiologist with special interest in pelvic MRI and extensive experience in the diagnosis of adenomyosis and myomas		
Takeuchi et al 2005 Japan [39]	**Study design; recruitment** Prospective, observational; unclear enrolment **Target condition** Posterior DIE POD obliteration (CDSO, Cul-de-Sac obliteration) **Setting** Single centre, university hospital	**Population** n=31 Women scheduled to undergo laparoscopy for suspected rectovaginal endometriosis Mean age, years: 32.1±4.2 **No included in both tests** 31/31 **Clinical presentation** Dysmenorrhoea 31/31 Dyspareunia 10/31 Chronic pelvic pain 7/31 Sonography suggestive for endometrioma 25/31 None had a history of previous pelvic surgery, and had received hormonal therapy within 6 months preceding the study **Prevalence** Posterior deep pelvic endometriosis 17/31 (55%) CDSO 22/31 (71%)	**Index test** MRI 1.5 T (T1/T2-weighted +/- fat-suppression, no gadolinium contrast, jelly in vagina and rectum) **Reference standard** Laparoscopy 31/31 (100%) + histopathology **Examiners** Index test: one radiologist who was blinded to clinical findings; level of expertise not reported Reference test: numbers or level of expertise of surgeons or pathologists not reported; surgeon blinded to MRI findings	**Recto-vaginal** Sensitivity: 94% Specificity: 100% **Obliterated POD** Sensitivity: 91% Specificity: 78%.	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
Thomeer et al 2014 Netherlands [40]	**Study design; recruitment** Prospective observational; consecutive enrolment **Target condition** Pelvic endometriosis **Setting** University hospital	**Population** n=40 Women with clinical suspicion of endometriosis scheduled to undergo laparoscopy Median age, years: 25, range 18–39 **No included in both tests** 40/40 **Prevalence** Pelvic endometriosis 37/40 (93%) r-AFS stage I to II 20/37 (54%) r-AFS stage III to IV 17/37 (46%) POD obliteration 10/40 (25%)	**Index test** MRI 3.0T (2D T2 weighted, 3D fat-suppressed T1 weighted, no contrast) **Reference standard** Laparoscopy (not histology) **Examiners** MRI: 2 experienced radiologists (blinded), with 13 years' and 12 years' experience in abdominal MRI, analysed independently and blindly data, disagreements were sorted by consensus, perfect per-patient interobserver agreement (kappa =1); substantial per-lesion interobserver agreement (kappa =0.65) Reference test: operative videos reviewed by 2 gynaecologists with extensive experience with laparoscopy and detecting endometriosis; interobserver agreement with consensus reading performed	**Pelvic endometriosis any type** Sensitivity: 81% Specificity: 100% **POD-obliteration** Sensitivity: 100% Specificity: 100%	MRI examiners: had no information regarding clinical data; Surgeons blinded to MRI findings; no data provided on the team performing surgery (number of surgeons, level of expertise)
Valenzano et al 2008 Italy [41]	**Study design; recruitment** Prospective, observational; unclear enrolment **Target condition** Rectovaginal endometriosis **Setting**	**Population** n=90 Women with suspected rectovaginal endometriosis on the basis of pain symptoms and/or gynaecological examination Median age, years: 32, range 18–42 years **No included in both tests** 90/90	**Index test** • Transvaginal ultrasound, TVS • Rectal-Water-Contrast-TVS, RWC-TVS **Reference standard** Laparoscopy, laparotomy (number in each group not specified) 90/90 (100%) + histopathology	**TVS** ***Rectovaginal*** Sensitivity: 91% Specificity: 97% ***Infiltration of the muscularis of the rectum*** Sensitivity: 57% Specificity: 93% **RWC-TVS** ***Rectovaginal*** Sensitivity: 97%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
	Single centre, University Hospital	**Clinical presentation** Dysmenorrhoea 84/90 Dyspareunia 68/90 Chronic pelvic pain 62/90 Infertility 32/90 Diarrhoea and/or constipation 61/90 Bowel movement pain or cramping 69/90 Pain on defecation 32/90 Rectal bleeding 16/90 Lower back pain 57/90 Previous medical treatments for endometriosis 82/90 **Prevalence** Pelvic endometriosis 81/90 (90%) Rectovaginal endometriosis 69/90 (76.7%) Rectal infiltration 29/90 (32.2%)	**Examiners** Index test: 1 experienced ultrasonographer, not aware of the findings of vaginal examination, and not informed of the findings of previous radiological examinations and results of other index tests Reference test: a team of gynaecological and colorectal surgeons, extensive experience in the treatment of pelvic and bowel endometriosis; expertise of pathologists not reported	Specificity: 100% ***Infiltration of the muscularis of the rectum*** Sensitivity: 96% Specificity: 100%	
Van Holsbeke et al 2009 Belgium, UK, Italy, Poland, Sweden [42]	**Study design; recruitment** Prospective observational, IOTA database **Target condition** Endometrioma **Setting** Multicentre; 21 centres in 9 countries	**Population** n=3511 Patients with adnexal mass, surgically removed ≤120 days after ultrasound examination Mean age: 45 years; postmenopausal: 39% **No included in both tests** 3511/3511 **Prevalence** Endometrioma 713 (20.3%) 2560 masses benign (73%) 951 malignant (27%)	**Index test** Transvaginal ultrasound, TVS **Reference standard** Laparoscopy+ histopathology **Examiners** Index test: expert sonologists, following a strict research protocol	**Ovarian (endometrioma)** Sensitivity: 81% Specificity: 97%	

First author Year Country Reference	Study design; recruitment Target condition Setting	Population No included in both tests[1] Clinical presentation Prevalence	Index test(s) Reference standard(s) Examiners	Results Sensitivity Specificity PPV, NPV	Comments
Zannoni 2017 Italy [43]	**Study design;** **Recruitment** Prospective cross-sectional **Target condition** Deep infiltrating endometriosis of the posterior compartment of the pelvis **Setting** Single centre, University Hospital	**Population** n=47 Women with clinical suspicion of posterior DIE Mean age 37±5.3 **No included in both tests** 47/47 **Clinical presentation** Dysmenorrhoea 77% Dyspareunia 66% Chronic pelvic pain 64% Dyschezia 70% Dysuria 28% **Prevalence** DIE nodule in the posterior compartment 96%	**Index test** • Transvaginal ultrasound, TVS • Computed tomography–colonography with contrast media and urographic phase, CTCU • **Reference standard** Laparoscopy + histopathology **Examiners** Index tests: TVS was performed by one gynaecologist with more than 5 years of experience in gynaecological ultrasound. Radiological images were evaluated by two radiologists with more than 10 years of experience in abdominal radiology. Reference standard: Laparoscopy performed by the same experienced surgeon	**TVS** ***Intestinal DIE*** Sensitivity 98% Specificity 33% ***Right ureter*** Sensitivity 10% Specificity 95% ***Left ureter*** Sensitivity 29% Specificity 96% **CTCU** ***Intestinal DIE*** Sensitivity 78% Specificity 50% ***Right ureter*** Sensitivity 60% Specificity 70% ***Left ureter*** Sensitivity 57% Specificity 77%	

3D-TVS = Three-dimensional transvaginal ultrasound; **CDSO** = Cul-de-Sac obliteration; **CTCU** = Computed tomography–colonography with contrast media and urographic phase; **DCBE** = Double-contrast barium enema; **DIE** = Deep infiltrating endometriosis; **MDCT-e (MSCTe)** = Multidetector computed tomography enteroclysis; **MRI** = Magnetic resonance imaging; **NR** = Not reported; **RES** = Rectal endoscopic sonography; **RWC-TVS** = Rectal-Water-Contrast tranvaginal ultrasound; **POD** = Pouch of Douglas; **SVG** = Sonovaginography; **TAS** = Transabdominal ultrasonography; **TVS** = Transvaginal ultrasonography; **TVS-BP** = Transvaginal ultrasound with bowel preparation; **TRS** = Transrectal Sonography; **TRUS** = Transrectal endoscopic ultrasonography; **TVUS** = Transvaginal ultrasound; **USL** = Uterosacral ligaments

Interventions studies except for surgery

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Gestrinone Italian Study Group [44]	**Study design** RCT, double blind, double dummy **Setting/recruitment** Multicentre/referred for chronic pelvic pain to the outpatient clinics **Population** n=55 Mean age: 30 years Stage III and IV: 29% **Inclusion criteria** Aged 18–40 years, laparoscopically diagnosed endometriosis, moderate–severer pelvic pain, no treatment for endometriosis other than nonsteroid anti-inflammatory drugs in previous 6 months, **Follow up time** 6 months after end of treatment	**Intervention** Oral gestrinone 2.5 mg twice a week, beginning on the first day of the menstrual cycle **Duration** 6 months **Participants** n=27 **Dropout** 4 (15%)	**Comparison** Leuprolide acetate (LA) 3.75 mg depot IM injections every 4 weeks **Duration** 6 months **Participants** n=28 **Dropout** 2 (7%)	**Pain symptoms, mean ±SD** ***Dysmenorrhea*** *VAS, 0–10* BL; I: 6.23±3.03, C: 6.71±3.20 Post; I: 0.87±1.77, C: 0.05±0.24 6 months; I: 1.76±3.12, C: 4.76±3.63 *VRS* BL; I: 2.07±0.83, C: 2.29±0.76 Post; I: 0.39±0.58, C: 0.04±0.20 6 months; I: 0.65±0.86, C: 1.59±1.23 ***Deep dyspareunia*** *VAS* BL; I: 4.01±3.57, C: 4.53±3.12 Post; I: 0.44±1.11, C: 1.61±2.12 6 months; I: 0.30±0.44, C: 2.64±3.41 *VRS* BL; I: 1.19±1.06, C: 1.46±1.03 Post; I: 0.10±0.30, C: 0.43±0.68 6 months; I: 0.13±0.34, C: 0.67±0.98 ***Non-menstrual pelvic pain*** *VAS* BL; I: 4.07±2.86, C: 4.67±2.87 Post; I: 1.23±2.65, C: 1.64±2.46 6 months; I: 1.11±1.54, C: 3.41±3.45 *VRS* BL; I: 1.22±0.93, C: 1.68±0.90 Post; I: 0.35±0.71, C: 0.50±0.59 6 months; I: 0.29±0.47, C: 1.12±0.99 **BMD, mean change % ±SD** (BL; I: 20.9±2.1, C: 21.4±3.1) Post; I: +0.88±2.12, C: –3.04±4.77 6 months; I: +2.06±2.51, C: –1.08±3.26	**Comments** 1:1 randomization Randomization performed by allocating consecutively numbered anonymous packages containing indistinguishable active drug and placebo capsules and vials. Sealed envelopes

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				Tolerability (Safety), % Amenorrheic; I: 52%, C: 96% Any side effects; I: 56%, C: 68% Weight gain (kg); I: 0.9±4.6, C: –0.4±2.6	
Abd Rabbo et al 2012 Egypt [45]	**Study design** RCT **Setting** Single centre **Population** n=60 Mean age: 29 years **Inclusion criteria** Age <35 years, basal serum FSH <10 IU, minimal/mild endometriosis diagnosed by laparoscopy classified with rASRM, no previous ovarian surgery or potentially poor responder **Follow up time** Unclear	**Intervention** Luteal long agonist protocol at day 21, with triptorelin (0.1mg), and aromatase inhibitor (letrozole, 5 mg/day) 5 days after the start of the agonist for 10 days **Participants** n=30 **Dropout** 3 (10%)	**Comparison** Luteal long agonist protocol at day 21 with triptorelin (0.1 mg) **Participants** n=30 **Dropout** 2 (7%)	**Pregnancy** C: 9/28 (32%) pregnant cases of 28 I: 8/27 (29.6%).	**Comments** Moderate risk of bias Unclear randomization and allocation In both groups stimulation started using combined human menopausal gonadotrophin and purified FSH after complete suppression (300 IU).
Acien et al 2003 Spain [46]	**Study design** RCT, double blind **Setting/recruitment** Single centre, consecutive enrolment **Population** n=24 Mean age: 31.8±4.8 Mean size of endometrioma: 5.7 (4–12)	**Intervention** GnRH analogue depot every 4 weeks, 24/25 days later transvaginal US-guided puncture of endometriomas + 15 ml 5% dextrose solution containing 600 000 IU of r IL-2 in the aspirated endometrioma **Duration** 3 months	**Comparison** GnRH analogue depot every 4 weeks,24/25 days later transvaginal US-guided puncture of endometriomas+15 ml of a 5% dextrose solution in the aspirated endometrioma **Duration** 3 months	**Pain symptoms (VAS, 0–10),** Score, mean ±SD BL: 6.7±1.1 FU; I: 2.9±1, C: 3.9±1.9 No with severity of symptoms ≥4, n (%) I: 3 (27%), C: 5 (42%) Recurrence of symptoms I: 4 (36%), C: 9 (75%) **Endometriomas** Size of endometriomas, cm, mean BL: 5.7±1.8 cm FU; I: 3.1±1, C: 4.1±2.1 No with cysts ≥3 cm, n (%)	**Comments** If several endometriomas in same ovary; aspiration via same puncture, 5–6 ml solution was left in each Afterwards: 10 laparotomies (41.6% all patients) with conservative surgery (6 in the analogue plus

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Inclusion criteria Age ≤40 years, severity of symptoms ≥4 (VAS), endometriomas >3 cm, high values of CA-125 (≥35 U/ml) and absence of other gynaecological pathology. **Follow up time** >6 months	**Participants** n=12 **Dropout** 1 (8%)	**Participants** n=12 **Dropout** 0	I: 5 (45%), C: 8 (67%), ns Recurrence I: 9 (75%), C: 10 (83%) **Good clinical outcome, n (%)** I: 11 (92%), C: 4 (33%)	dextrose group and 4 in the analogue plus rIL-2 group) was performed due to reactivation of the symptoms & endometriomas in a similar state to those before GnRH analogues and drainage
Adamson 1994 USA [47]	**Study design** RCT double blind **Setting/recruitment** Single centre/ enrolment unclear **Population** N=90 (58% of eligible??) **Inclusion criteria** Age 18–48 years, laparoscopically confirmed pelvic endometriosis and dysmenorrhoea, dyspareunia or pelvic pain, no hormonal treatment ≤6 months. **Follow up time** Post treatment (6 moths)	**Intervention** Nafarelin acetate 400 μg twice daily, intranasal + placebo **Duration** 6 months **Participants** n=45 **Dropout** 0	**Comparison** Nafarelin acetate 200 μg twice daily, intranasal + placebo **Duration** 6 months **Participants** N=45 **Dropout** 0	**Pain report (scale none-severe), present %** ***Dysmenorrhoea,*** BL; I: 100%, C: 100% Post; I: 0%, C: 2% 6 months; I: 64%, C: 67% ***Dyspareunia*** BL; I: 100%, C:100% Post; I: 31%, C: 32% 6 months; I: 35%, C: 29% ***Pelvic pain*** BL; I: 100%, C: 100% Post; I: 35%, C: 43% 6 months; I: 55%, C: 51%	**Comments** The group receiving danazol was excluded since no longer in use in Sweden No surgical procedures performed during diagnostic laparoscopy,

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Agarwal et al 1997 [48] Agarwal 2002 [49] Zhao et al 1999 [50] USA	**Study design** RCT, double-blind, double-placebo **Setting/recruitment** Multicentre/enrolment unclear **Population** n=208, 192 analysed Stage III/IV: 39% Complaints of infertility: 36% ***Endometriosis severity*** Mild: 10% Moderate: 46% Severe: 17% **Inclusion criteria** Laparoscopically diagnosed endometriosis ≤18 months, age 19–44 years, clinical symptoms and signs, normal age BMD-range **Follow up time** 3, 6 months (posttreatments) and at 3–6 months after end of treatment	**Intervention** Nafarelin 200 μg twice daily, intranasal + placebo every 4 weeks intra muscular **Duration** 6 months **Participants** n=105 **Dropout** 6 (5.7%)	**Comparison** Leuprolide acetate depot 3.75 mg every 4 weeks intra muscular + placebo BD intranasal **Duration** 6 months **Participants** n=103 **Dropout** 10 (9.7%)	**Pain (0–3 scale)** ***Dysmenorrhoea,*** absent, n (%) BL; I: 1%, C: 3% FU; I: 77 (78%), C: 77 (83%) mean score: I: 0.35, C: 0.34, p=0.87 ***Dyspareunia,*** absent n (%) BL; I: 27%, C: 25% FU; I:52 (60%), C: 44 (55%) mean score; I: 0.83, C: 0.73, p=0.052 ***Pelvic pain,*** absent, n (%) BL; I: 11%, C: 6% FU; I: 49 (49%), C: 44 (47%) mean score; I: 0.74, C: 0.75, p=0.39 ***Tenderness,*** absent, n (%) BL; I: 9%, C: 15% FU; I: 53 (54%), C: 58 (62%) mean score; I: 0.56, C: 0.47, p=0.55 ***Induration,*** absent, n (%) BL; I: 42%, 45% FU; I: 73 (74%), C: 74 (1%) Mean score; I 0.28, C: 0.21, p=0.19 **Improvement rate, %** Post; I: 87%, C: 88% 6 months; I: 74%, C: 71% ***QoL,*** total score BL; I: 4.9±2.04, C: 4.7±1.96, ns FU: no significant differences between groups at 3 or 6 months. Patients with severe symptoms of endometriosis at BL showed a significantly greater improvement in QOL with nafarelin than leuprolide at the last posttreatment visit; 3.67 vs. 2.04, respectively; p=0.0074. **BMD, mean decrease ±SE** Post: I: 3±0.3%, C: 5±0.3%, p=0.002 6 months; I: 1±0.4%, C: 2±0.3%, p=0.07	**Comments** Unclear allocation concealment Restoration of ovarian function was rapidly restored

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				Adverse effects (mean %±SD) ***Hot flushes*** 3 months; I: 33±35, C: 53±41, p=0.02 6 months; I: 35±41, C: 52±43, p=0.009 3 months FU; I: 0.8±5, C: 5±15, p=0.052 ***Vaginal dryness*** 3 months; I: 8.4±23, C: 12±30, ns 6 months; I: 10±27, C: 5±35, ns 3 months FU; I: 0.4±2, C: 6±19, p=0.053 ***Mood swings*** 3 months; I: 18±26, C: 21±30, ns 6 months; I: 17±27, C: 22±32, ns 3 months FU; I: 7±12, C: 11±19, ns ***Headache*** 3 months; I: 16±24, C: 10±18, ns 6 months; I: 13±24, C: 11±22, ns 3 months FU; I: 7±17, C: 7±12, ns ***Sleep problem*** 3 months; I: 34±30, C: 38±34, p ns 6 months; I: 34±32, C: 32±34, ns 3 months FU; I: 12±20, C: 13±22, ns ***Joint aches*** 3 months; I: 13±24, C: 14±24, ns 6 months; I: 16±30, C: 19±31, ns 3 months FU; I: 11±19, C: 8±19, ns	
Alborzi et al 2011 Iran [51]	**Study design** RCT, open labelled **Setting/recruitment** Single centre, participants were selected from those referred to infertility clinics **Population** n=144 Mean age: 30 years **Inclusion criteria**	**Intervention 1** Laparoscopy+ Letrozole-aromatase inhibitor, one tablet 2.5 mg/day **Duration** 2 months **Participants** n=58 **Dropout** 11 (19%)	**Comparison** Laparoscopy **Participants** n=59 **Dropout** 2 (3%)	**Recurrence rate, n (%)** I1: 3 (6%), I2: 2 (5%), C: 3 (5%), ns All in stage II-IV group **Cyst formation, functional, %** I1: 24%, I2: 2.5%, C: 0, p<0.001 **Pregnancy rate** No conceived I1: 11 (23%), I2: 11 (28%), C: 16 (28%), ns	**Comments** Random computer-generated lists. Unclear allocation concealment

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Laparoscopical and histological diagnosis of endometriosis, infertile ≥1 year conservative surgery **Follow up time** 1 year (3 months intervals)	**Intervention 2** Laparoscopy+ Triptorelin 3.75 mg, IM every 4 week **Duration** 2 months **Participants** n=58 **Dropout** 18 (31%)			
Alkatout et al 2013 Germany [52]	**Study design** RCT, open label **Setting/recruitment** Single centre/ unclear enrolment **Population** n=450 **Inclusion criteria** Aged 18–44 years, symptomatic endometriosis in whom 2 consecutive laparoscopic interventions were to be assessed, no previous surgery or hormone therapy for endometriosis, no DIE with bladder or rectum excision. **Follow up time** 2 months and 1 year after end of treatment	**Intervention 1** Leuprorelin acetate depot SC, 3.75 mg monthly **Duration** 3 months **Participants** n=150 **Dropout** 25 (16.7%) **Intervention 2** Laparoscopy+ Leuprorelin acetate depot SC, 3.75 mg Monthly **Duration** 3 months **Participants** n=150 **Dropout** 2 (1.3%)	**Comparison** Laparoscopy **Participants** n=150 **Dropout** 13 (8.7%)	**Recurrent Symptoms (scale unclear)** ***Dysmenorrhea, n (%)*** BL; I: 75 (60), I2: 80 (54), C: 78 (57) 1 year; I: 35 (28), I2: 24 (16), C:27 (20), ns ***Dyspareunia, n (%)*** BL; I: 70 (56), I2: 75 (51), C: 69 (50) 1 year; I: 28 (22), I2: 12 (8), C: 21 (15), p=0.007 ***Abdominal Pain, n (%)*** BL; I: 60 (48), I2: 62 (42), C: 58 (42) 1 year; I: 33 (26), I2: 25 (17), C: 33 (24), ns **Pregnancy rate, n (%)** I: 81 (65), I2: 89 (60), C: 75 (55) **Live birth n (%)** I: 69 (55), I2: 74 (50), C: 62 (45)	**Comments** Randomization via random principle Unblinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Angioni et al 2014 Italy [53]	**Study design** RCT **Setting/recruitment** Single centre, Chronic Pelvic Pain Clinic/ unclear enrolment **Population** N=159 (66% of eligible), Mean age: 26 years **Inclusion criteria** Age >40 years old, laparoscopic diagnosis of DIE with complete or incomplete surgical treatment, patient total symptoms score before surgery ≥6 (of max 15), no previous medical or surgical therapy for endometriosis, no infiltration of the rectum >3 cm and/or rectal stenosis **Follow up time** Post and 6 months FU	**Intervention 1** Complete excision + triptorelin acetate 3.75 mg, IM injection every 4 weeks **Duration** 6 months **Participants** n=40 **Dropout** 0 **Intervention 2** “incomplete" resection + triptorelin acetate 3.75 mg, IM injection every 4 weeks **Duration** 6 months **Participants** n=39 **Drop-out** 0	**Comparison 1** Complete excision **Participants** n=40 **Dropout** 0 **Comparison 2** “Incomplete" resection **Participants** n=40 **Drop-out** 0	**Pain score** Post; patients treated with complete excision of DIE (groups I1 and C1) showed highest reduction of cumulative pain scores for chronic pelvic pain, dysmenorrhea and dyspareunia. No significant difference between these 2 groups. Similar data in I2 group. I1, C1, I2 significantly lower, p<0.01, pain scores than C2 (incomplete resection). 6 months: pain scores returned to pre-surgical levels in patients undergoing the groups with incomplete resection. Significant difference between C2 and I1 and C1 (p<0.01). **QoL, SF-36, mean ±SD,** 6 months FU General health; I1: 63.1±13, C1: 60±11.5, I2: 46±18, C2: 43.2±11, P<0.01 in favour or complete resection Pain; I1: 67±11, C1: 68±12, I2: 42.1±16, C2: 45.1±11.2, P<0.01 in favour or complete resection	**Comments** Randomized 1:1 computer-generated randomization sequence to receive allocation unclear Unclear if participants and assessors were blinded.
Audebert et al 1998 France [54]	**Study design** RCT, double blind **Setting/recruitment** Multicentre/unclear enrolment **Population** n=53 Mean age: 33 years Endometriosis already diagnosed: 22 (39%)	**Intervention 1** Laparoscopy + Nafarelin, 200 mg intranasal, twice daily **Duration** 6 months **Participants** n=28	**Comparison** Nafarelin, 200 mg intranasal, twice daily+ Laparoscopy **Duration** 6 months **Participants** n=25	**Symptoms, n (%)** ***Dysmenorrhea diminution*** I: 28 (100), C: 25 (100), ns ***Dyspareunia diminution*** I: 27 (89), C:19 (76), ns ***Pelvic pain diminution*** I: 18 (64), C 16 (64), ns ***Pelvic tenderness*** I: 15 (54), C: 14 (56), ns ***Pelvic induration diminution*** I: 17 (62), C: 9 (36), ns	**Comments** Unclear randomization and allocation Assessor blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Inclusion criteria Aged 24–40 years, laparoscopic diagnosis, stage III–IV endometriosis **Follow up** Post treatment	**Drop-out** 0	**Dropout** 0	***Amenorrhea*** I: 26 (92.8), C: 25 (100) **AFS score,** ***Global;*** BL; I: 40, C: 52 Post; I: 6, C:0, p=0.007 ***Adhesion;*** BL; I: 7.5, C: 12 Post; I: 2, C: 0 ***Endometriosis;*** BL; I: 31, C:42 Post; I: 4, C: 0, p=0.05 **Adverse events, n (%)** ***Hot flashes;*** I: 27(96), C: 23 (92) ***Vaginal dryness;*** I: 12 (43), C: 8 (32) ***Decreased libido;*** I: 10 (36), C: 9 (36) ***Headache;*** I: 6 (21), C: 5 (20) ***Insomnia;*** I: 1 (4), C: 1 (4) ***Weight gain (kg):*** I: +0.5, C: +2	
Badawy et al 2012 Egypt [55]	**Study design** RCT, open-labelled **Setting/recruitment** A university hospital and a private practice setting /unclear enrolment **Population** n=32 Mean age: 36 years Symptoms: 16% **Inclusion criteria** Aged 18–42 years, adenomyosis with abnormal uterine bleeding, unexplained infertility, pelvic pain, dysmenorrhea or pressure effects, no hormonal therapy within the past month	**Intervention** Letrozole, orally, 2.5 mg/day (aromatase inhibitors) **Duration** 12 weeks **Participants** n=16 **Dropout** 1 (6.3%)	**Comparison** Goserelin, 3.6 mg, SC **Duration** 12 weeks **Participants** n=16 **Dropout** 0	**Symptoms improvement, n (%)** ***Chronic pain*** BL; I: 7 (46.7), C: 8 (53), ns 3 mo; I: 10 (83), 13 (93), p=0.04 ***Dysmenorrhea*** BL; I: 8 (53.3%), C: 7 (46.7%) 3 mo; I: 4 (57%), C: 8 (100%), ns ***Dyspareunia*** BL; I: 8 (53.3%), C: 7 (46.7%) 3 mo; I: 2 (33%), C: 6 (75%), ns ***Subfertility*** BL; I: 5 (33.3%), C: 7 (46.7%) 3 mo; I: 2 (25%), C: 0, ns ***Menorrhagia*** BL; I: 4 (26.7%), C: 4 (26.7%) 3 mo; I: 3 (60%), C: 7 (100%), ns ***Metrorrhagia*** BL; I: 6 (40%), C: 8 (50%) 3mo; I: 1(25%), C: 2 (75%), ns	**Comments** Computer-generated random table An assessor-blind design

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Follow up time Post treatment (12 weeks)			**Side effects** Hot flushes; I: 0, C: 13 (81%)	
Bayoglu et al 2011 Turkey [56]	**Study design** RCT, open labelled **Setting/recruitment** Single centre, reproductive endocrinology unit of a tertiary, research and education hospital /unclear enrolment **Population** n=40 Mean age: 37 years Mean rAFS: 46 **Inclusion criteria** Age 18–45, surgically and histologically proven severe endometriosis and CPP, no hormonal therapy ≤3 months prior surgery **Follow up time** 1 year	**Intervention** Conservative laparoscopic surgery + gosareline acetate, unclear dose, every 4 weeks **Duration** 6 months **Participants** n=20 **Dropout** 0	**Comparison** Conservative laparoscopic surgery + levonorgestrel-releasing intrauterine system (LNG-IUS) **Participants** n=20 **Dropout** 0	**Symptoms** ***Chronic pain (VAS score)*** No statistical difference between groups at 1 year ***Total endometriosis severity profile (TESP)*** No statistical difference between groups at 1 year **Side effects, n (%), 1 year** ***Irregular bleeding*** I: 0, C:13 (65%), ***One sided lower abdominal pain*** I: 0, C: 8 (40%) ***Weight gain*** I: 1 (5%), C: 2 (10%), ***Amenorrhea*** I: 6 (30%), C: 0 ***Vasomotor symptoms*** I: 10 (50%), C: 0 ***Simple ovarian cyst*** I: 0, C: 11 (55%)	**Comments** A computer-generated system, sealed envelopes Intervention group: 9 underwent unilateral cystectomy (45%), 8 bilateral cystectomy (40%), 3 unilateral salpingoophorectomy (15%) Control group: 8 underwent cystectomy (40%), 6 bilateral cystectomy (30%), 6 unilateral salpingo-ophorectomy (30%).
Bergqvist and the SCANDET group 2001 Sweden, Norway, Finland, Denmark [57]	**Study design** RCT, open parallel group **Setting/recruitment** Multicentre (28 centres)/ unclear enrolment **Population** n=252 Median age: 31 years **Inclusion criteria**	**Intervention** Goserelin, 3.6 mg, SC, every 28 days **Duration** 6 months **Participants** n=130 **Dropout** 11 (8%)	**Comparison** Nafarelin, 200 µg nasally twice daily **Duration** 6 months **Participants** n=122 **Dropout** 17 (14%)	**Total pain score (scale 0–3), %** Reduced; I: 45%, C: 43%, ns Pelvic tenderness, reduced; I: 49%; C: 75%, ns Pelvic induration, reduced; I: 41%, C: 66%, ns **R-AFS score** ≥50% I: 37%, C: 34% **ADI >50%** ADI score at BL: I: 50.8±49.6, C: 44.6±45.1 FU; I: 39%, C: 39%	**Comments** Unclear allocation and if assessors were blinded **Surgery required** I: 40%, C: 40%

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Aged 18–45 years, laparoscopy or laparotomy conformed diagnosis, symptomatic endometriosis, no sex hormones within 2 months of treatment, no GnRH agonist therapy previous 6 months and not for more than 3 months altogether **Follow up time** 12 weeks post treatment			**New lesion** I: 43/113 (38%), C: 30/100 (30%) **Adverse events, n (%)** Any; I: 97%, C: 93% Hot flashes; I: 91 (81), C: 74 (74) Headache; I: 61 (54), 45 (45) Sweating; I: 27 (24), C: 27 (27) Vaginal dryness; I: 24 (21), C: 11 (11) Vaginal bleeding; I: 0, C: 8 (8) Irritation nasal mucosa; I: 15%, C:23%	
Bergqvist et al 1997 Sweden, UK [58]	**Study design** RCT, double-blind **Setting/recruitment** Single centre/unclear enrolment **Population** n=49, 47 were analysed Median age: 30 (21–46) **Inclusion criteria** Laparoscopically diagnosed endometriosis, no hormonal preparations during study, no hormone treatment ≤3 months, no GnRH ≤12 months, no steroid therapy ≤12 months **Follow up time** Post treatment: 6 months	**Intervention 1** Nafarelin 400 μg daily intranasal + placebo **Participants** n=12 **Dropout** 0 **Intervention 2** Nafarelin 200 μg daily intranasal + nore-thisterone 1.2 mg daily **Participants** n=25 **Dropout** 2 (8%) **Duration** 6 months	**Comparison** Nafarelin 200 μg daily intranasal + placebo **Participants** n=12 **Dropout** 0	**AFS score median (range)** BL: I1: 6 (2–21), I2: 6 (1–60), I2: C: 3.5 (1–19) 6 months; I1: 1 (0–6), I2: 0 (0–10) C: 1 (0–40), ns **Total symptom score, median (range)** BL; I1: 6 (2–29), I2: 9 (1–81), C: 12 (2–42), ns 6 months; I1: 1 (0–14), I2: 0 (0–38), C:7 (0–80), ns sign reduced in all 3 groups compared to BL **Irregular bleedings** C: 42%, I1: 58%, I2: 48%, ns	**Comments** Unclear randomization and allocation. Unclear whether assessor was blinded Randomly allocated in a 1: 1: 2 ratio

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Bergqvist et al 1998 Sweden [59]	**Study design** RCT, placebo-controlled, double-blind **Setting/recruitment** Departments of Obstetrics and Gynecology at two universities and one general hospital/ unclear enrolment **Population** n=49 Mean age: 31 years Stage: most mild to moderate (IV n=1) **Inclusion criteria** Menstruating regularly ≤3 months, clinical symptoms, no OC or oral steroid therapy ≤3 months, no gestagens or GnRHas ≤6 months, not pregnant in prior 3 months, no history of osteoporosis or coagulation disorders **Follow up time** Post treatment (24 weeks)	**Intervention** Triptorelin 3.75 mg IM depot every 4 weeks **Duration** 6 months **Participants** n=24 **Dropout** 1 (4%)	**Comparison** Placebo IM every 4 weeks **Duration** 6 months **Participants** n=25 **Dropout** 2 (8%)	**Pain, total score (VAS)** 2 months: statistical significant difference, favour I, p<0.01 6 months: I: 3.5 (95% CI, 2.58 to 4.44) C: 35% ***Dyspareunia, n (%)*** BL; I: 13, C: 20 6 months; I: 3 (13 %), C: 11 (48%) ***Pelvic tenderness, n (%)*** BL; I: 20 (mild-moderate, 18), C: 23 (mild moderate: 19) 6-monts; I:4, C: 19 **Adverse effects** Major AE: 0 reported ***Hot flushes*** BL; I: 2, C:6 2 months; I: 14, C:9 ***Sleeping disturbances*** BL; I: 9, C:9 2 months; I:20, C:9	**Comments** Unclear randomization and allocation. Unclear whether assessor was blinded
Bianchi et al 2009 Brazil [60]	**Study design** Prospective cohort study **Setting/recruitment** Infertility clinic and private hospital. Consecutive recruitment **Population** n=179	**Intervention** IVF/ICSI **Participants** n=105 **Dropout** 0	**Comparison** Laparoscopy before IVF/ICSI **Participants** n=66 **Dropout** 2 (3%) 10 (5,6%) total study dropout	**Clinical pregnancy rate** I: 24%, C: 41%, p=0.004 **Live birth rate** I: 87.5%, C: 94.4%, ns	**Comments** Unclear if assessor was blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Age range: 24–38 years Mean infertility duration: 32 months ***Inclusion criteria*** Age 21–38 years, infertility with clinical and TVS-bp evidence of DIE, presence of at least 1 functional ovary, presence of a standard indication for IVF or ICSI, anatomically normal uterine cavity, early follicular phase (day 2 or 3) FSH levels of ≤15 IU/, estradiol levels ≤60 pg/Ml, absence of untreated endocrinologic disorder; male partner ejaculated spermaatozoa having 1% or greater strict morphology **Follow up time** 3–18 months				
Bulletti et al 1996 Italy [61]	**Study design** Prospective CCT **Setting/recruitment** Single centre/unclear **Population** n=516, 453 continued after laparoscopy Thirty women did not undergo the second laparoscopy and another 60 were excluded from the analysis to balance the case-control design (total 90 excluded) ***Stage***: 1 to 3	**Intervention 1** Depot GnRH agonists at 28-day intervals,according to a) goserelin 3.6 mg SC n=51 women b) triptorelin 3.75 mg IM n=50 women c) leuprorelin 3.75 mg IM n=50 women Age 27.3±6.0 years, range 19–42 years, median 27 years **Participants** n=151	**Comparison** No treatment between the first and second laparoscopies, or from the second laparoscopy to the end of follow-up. Age 27.4±5.3 years, range 18–39 years, median 28 years **Duration** **Participants** n=151	**No with decreased AFS score, n (%)** I: 61 (56%), C: 14 (13%)	**Comments** Patients were progressively classified according to case-control criteria into three groups, and stratification was performed for age (±3 years) and AFS score during the first laparoscopy Study participants were asked not to take any drugs for the duration of the study; severe dysmenorrhea

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Age 18–43 years, Mean ± SD 27.3±5.6 year **Inclusion criteria** Endometriosis confirmed by laparoscopy, no steroids in the 6 months before study. After biopsy, laparoscopic surgery was performed to remove possible residual disease and to stop blood loss at the biopsy site(s). **Follow up time** Unclear	**Dropout** After correcting for women dropped from the analysis, subgroups 3a, 3b, and 3c consisted of 37, 35, and 38 patients, respectively			was treated only with paracetamol 50 mg rectal suppositories The group with Danazol is excluded
Busacca et al 2001 Italy [62]	**Study design** RCT, open-label **Setting/recruitment** Single centre/unclear enrolment **Population** n=89 (92% of eligible) Age range: 21–38 Stage IV: 33.5% **Inclusion criteria** Reproductive age, age ≤40 years, laparoscopic diagnosis of endometriosis stage III–IV, no previous medical or surgical therapy for endometriosis **Follow up** 6–36 months	**Intervention** Laparoscopic surgery + leuprolide acetate 3.75 mg IM every 4 weeks **Duration** 8 weeks **Participants** n=44 **Dropout** 0	**Comparison** Laparoscopic surgery + expectant management **Participants** n=45 **Dropout** 0	**Symptoms** ***Cumulative pain recurrence (Biberoglu and Behrman),*** 18 months; I: 23%, C: 29%, ns ***Moderate/severe pain recurrence*** I: 10 (23%), C: 11 (24%) **Objective disease recurrence** I: 4 (9%), C: 4 (9%), ns **Cumulative pregnancy rate** I:38%, C: 40%, ns **Second surgery** I: 2 (5%), C: 0, ns **Adverse events** Case withdrawal: I: 1 (2%)	**Comments** Randomization: computer generated, unclear concealment. Physicians blinded ITT analysis

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Carbonell et al 2016 Cuba, Spain [63]	**Study design** RCT, double blind **Setting/recruitment** Singe centre (hospital)/ unclear enrolment **Population** n=360 (96.5% of eligible) Mean age: 32 years Infertility: 68/360 (18.9%) Hysterectomies (n): 15 **Inclusion criteria** Age 18–45, laparoscopic confirmed endometriosis, patients with dysmenorrhea or pelvic pain not attributable to other gynaecological illness, no hormonal or surgical therapies ≥4 months before study **Follow up time** Post treatment (6 months)	**Intervention** Mifepristone, orally, 1 tablet/day Group I: 2.5 mg Group II: 5 mg Group III: 10 mg **Duration** 6 months **Participants** n=90/group **Dropout** 2.5 mg: 4 (4.7%) 5 mg: 4 (4.4%), 10 mg: 5 (5.7%)	**Comparison** Placebo **Duration** 3 months **Participants** n=90 **Dropout** 17 (19.1%)	**Prevalence of symptoms, n (%)** ***Dysmenorrhea*** BL: 2.5 mg: 82 (91.1), 5 mg: 88 (97.8) 10 mg: 85 (94.4), C: 97 (96.8) 6 months; 2.5 mg: 4 (5), 5 mg: 5 (6), 10 mg: 4 (5), p=0.867 ***Dyspareunia*** BL; 2.5 mg: 55 (61.1), 5 mg: 53 (70), 10 mg: 56 (62.2), C: 59 (65.6) 6 months; 2.5 mg: 6 (7), 5 mg: 1(1), 10 mg: 2 (2), p=0.089 ***Pelvic pain*** BL; 2.5 mg: 51 (56.7), 5 mg: 59 (65.6), 10 mg: 61 (67.8), C: 46 (51.1) 6 months: 2.5 mg: 10 (12),5 mg: 7 (8), 10 mg: 2 (2), p<0.001 ***Urinary*** BL; 2.5 mg: 18 (20), 5 mg: 16 (17.8), 10 mg: 19 (21.1), C: 16 (17.8) 6 months; 2.5 mg: 3 (4), 5 mg: 1 (1), 10 mg: 0, p=0.202 ***Intestinal*** BL; 2.5 mg: 23 (25.6), 5 mg: 30 (33.3) 10 mg: 35 (38.9), C: 29 (32.2) 6 months; 2.5 mg: 7 (8), 5 mg: 1 (1), 10 mg: 0 **Adverse events, n (%)** ***Amenorrhea;*** 2.5 mg: 67 (8586), 5 mg 78 (89), 10mg: 77 (88), ns ***Hot flushes;*** 2.5 mg: 13 (15), 5 mg: 15 (17), 10 mg: 19 (22), ns ***Nausea;*** 2.5 mg: 2 (2), 5 mg: 1 (1), 10 mg: 1 (1), ns ***Vomiting;*** 2.5 mg: 1 (1.2), 5 mg: 0, 10 mg: 1 (1.1), ns ***Fatigue, tiredness***; 2.5 mg: 6 (7.0), 5 mg: 0, 10 mg: 13 (14.8), p<0.001	**Comments** Random list obtained from the MEDSTAT 2.1 program and opaque sealed envelopes 15 subjects had received hysterectomies as part of their treatment for endometriosis

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				AFS score All intervention groups significant improvement compared to placebo	
Cheewadhanaraksa et al 2013 Thailand [64]	**Study design** Prospective cohort study **Setting/recruitment** Single centre/consecutive enrolment **Population** n=161 Mean age: 41 years Stage III/IV: 82% Endometrioma: 52% Previous treatment for endometriosis; Medical: 49% Surgery: 18.5% **Inclusion criteria** Endometriosis-associated pain, had undergone a total abdominal hysterectomy with bilateral salpingo-ophorectomy (BSO) and in whom the foci of endometriosis had been removed without taking the risk of damaging the involved visceral organs, pre-menopausal women **Follow up time** Every 6 months, >20 months	**Intervention** Definitive surgery for endometriosis + continuous oral conjugated equine estrogen 0.625 mg+ MPA, 2.5 mg per day, orally. **Duration** >20 months **Participants** n=68 **Dropout** 12 (17.6%)	**Comparison** Definitive surgery for endometriosis + continuous oral conjugated equine estrogen 0.625 mg **Duration** >20 months **Participants** n=93 **Dropout** 8 (8.6%)	**Recurrence of pain** Pain: I: 1 (1%), C: 9 (10%) Deep dyspareunia: 0 in both groups Crude recurrence, 36 months; I: 1 (2%), C: 6 (7%) Cumulative pain recurrence rate 12 months; I: 0, C: 4%, ns 24 months; I: 3%, C: 6%, ns 36 months; I: 3%, C: 8%, ns **Side effect** Causing withdrawal: none Breast tenderness; I: 3 (4%), C: 2 (2%)	**Comments** Patient pre-treatment characteristics differ between the two groups

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Cheewadhanaraksa et al 2012 Thailand [65]	**Study design** RCT, open labelled **Setting/recruitment** Single centre/unclear enrolment **Population** n=84 VAS score ≥5 for at least one type of pain Mean age: 31 Stage III/IV: 55% **Inclusion criteria** Age 18–40 years, surgical diagnosis of endometriosis, endometriosis-associated pain for ≥6 months, did not wish to conceive in the next ≥18 months, no medical treatments for endometriosis other than non-steroid anti-inflammatory drugs within the previous 6 months, no other pelvic pathology **Follow up time** Post treatment (24 weeks)	**Intervention** Conservative surgery + DMPA ,150 mg IM every 12 weeks **Duration** 24 weeks **Participants** n=42 **Dropout** 3 (7%)	**Comparison** Conservative surgery + continuous OC pills; Ethinyl estradiol 0.03 mg and gestodene 0.075 mg, daily **Duration** 24 weeks **Participants** n=42 **Dropout** 4 (9.5%)	**Symptoms** ***Non-menstrual pain*** ***VAS score, medians (IQR)*** BL; I: 2.5 (0–6.8), C: 2 (0–6.4), ns Post: I: 0 (0–0), C: 0 (0–0.4), ns VRS, n (%) Score 0; I: 30 (78%), C: 28 (74%) Score 1; I: 7 (18%), C: 10 (26%) Score 2; 2 (5%), C: 0 ***Dysmenorrhea*** ***VAS score, medians (IQR)*** BL; I: 9 (7–10), C: 8.2 (7–10), ns Post: I: 0 (0–0), C: 0 (0–3), p=0.039 VRS scale, n (%) Score 0; I: 32 (81%), C: 24 (63%) Score 1; I: 7 (18%), C: 14 (37%) ***Deep dyspareunia*** ***VAS score, medians (IQR)*** BL; I: 3 (0–5), C: 4.5 (0–7), ns Post: I: 0 (0–0), C: 0 (0–0), ns VRS, n (%) Score 0; I: 12 (71%), C: 13 (81%) Score 1; I: 4 (24%), C: 3 (19%) Score 2; I: 1 (6%), C: 0 **Patient satisfaction** Post: I: 39 of 42 (93%), C: 37 (88%) **Side effects n (%)** ***Drop out due to AE; I: 2/42, C: 1/42*** ***Spotting;*** I: 28 (72), C: 24 (63) Break through bleeding; I: 4 (18), C: 11 (29) Amenhorrea; I: 7 (20), C: 3 (8) I: weight gain, oily skin (38.5%), irritability (30.8%) C: breakthrough bleeding, mastalgia (50.0%), nausea (35.7%)	**Comments** Computer generated randomization sequence with the use of numbered, opaque, sealed envelopes ITT analysis Patients with minimal–moderate endometriosis underwent conservative surgery via laparoscopy, patients with severe disease via laparotomy. Subjects were permitted to take acetaminophen when needed

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Chen et al 2017 Taiwan [66]	**Study design** RCT, single blind **Setting/recruitment** Tertiary medical centre **Population** n=80 Mean age: 34 years Stage III: 31% **Inclusion criteria** Women aged 20–42, with dysmenorrhea and a sonographic diagnosis of endometrioma, moderate and severe symptomatic endometriosis (stages 3 and 4, ASRM), with a chocolate-containing cyst observed during laparoscopic surgery scheduled for elective laparoscopic ovarian cystectomy surgery, no desire to become pregnant within 30 months, no hormonal therapy within the 3 months preceding surgery, no history of previous surgery for endometriosis, the use of GnRHas **Follow up time** 1, 3, 6, 12, 15, 18, 21, 24, 27, and 30 months	**Intervention** Laparoscopic ovarian cystectomy + postoperative leuprorelin acetate 3.75 mg, IM, every 4 weeks + levonorgestrel-releasing intrauterine system **Duration** GnRHa: 6 months **Participants** n=40 **Dropout** 1 (2.5%)	**Comparison** Laparoscopic ovarian cystectomy + postoperative leuprorelin acetate 3.75 mg, IM every 4 weeks **Duration** GnRHa: 6 months **Participants** n=40 **Dropout** 0	**Endometrioma recurrence rate, n (%)** **30 months** I: 10/40 (25.0%), C: 15/40 (37.5%), p=0.228 **Dysmenorrhea recurrence, 30 months, n (%)** I: 6/40 (15%), C: 15/40 (37.5%), HR: 0.32 (0.12–0.83), p=0.019 **Pain Symptom (VAS, mm) score, 30 moths, median (IQR).** ***Dysmenorrhea (n40/40)*** BL; I: 82.5 (73.5–95.8), C: 75.5 (67.5–92.3) Mean reduction±SD, 30 months; I: 60.8±25.5, C: 38.7±25.9, p<0.001, MD: 22.1 (10.7–33.5) ***Noncyclic pelvic pain (n27/26)*** BL: I: 42.2±12.4, C: 43.8±11.7, p=0.634 Mean reduction ±SD, 30 months; I: 39.1±10.9, C: 30.1±14.7, p<0.001, MD (95% CI): 9.0 (1.9–16.1) **Side effects, n (%)** Overall; C: 18 (45%), I: 29 (72.5%) RD= –27.5% (–48.2, –6.8%) Bloating; C: 9 (22.5), I: 10 (25), RD= –2.5% (–21.1,16.1) Acne; C: 4 (10), I: 5 (12.5), RD= –2.5% (–16.3,11.3) Vaginal spotting; C: 2 (5), I: 11 (27.5), RD= –22.5% (–37.9, –7.1) Leukorrhea; C:5 (12.5), I: 7 (17.5), RD= –5.0% (–20.6, 10.6) Oily skin; C:3 (7.5), I: 6 (15.0), RD= –7.5% (–21.3, 6.3) Nausea; C: 6 (15), I: 5 (12.5),	**Comments** Computer-generated random numbers in sequentially sealed opaque envelopes. The surgeons and participants were not blinded to study allocation. (NCT01125488). Laparoscopy was performed under general anesthesia using the 4-puncture technique, Adhesions were dissected and the ovaries were completely mobilized.

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				RD= 2.5% (12.6, 17.6) Headache; C: 11 (27.5), I: 13 (32.5), RD= –5 (25.1, 15.1) Weight gain; C: 7 (17.5), I: 8 (20), RD= –2.5(–19.6, 14.6) Breast tenderness; C: 12 (30), I: 15 (37.5), RD= –7.5% (–28.2, 13.2) Amenorrhe; C: 0, I: 6 (15), RD= –15 (–26.1, –3.9)	
Cheng et al 2005 China [67]	**Study design** RCT, double blind **Setting/recruitment** Single centre (university hospital)/unclear enrolment **Population** n=50 Mean age: 35 years **Inclusion criteria** Women with significant endometriosis remaining after laparoscopic/open surgery **Follow up time** 6 weeks after last GnRH dose	**Intervention** Triptorelin, 3.75 mg, SC every 6 weeks, 4 doses + 2 mg E2 and 1 mg NETA start at second dose of GnRH **Duration** 19 weeks (12 weeks) **Participants** n=25 **Dropout** 3 (12%)	**Comparison** Triptorelin, 3.75 mg, SC every 6 weeks, 4 doses + 2 mg E2 and 5 mg norethindrone, start at second dose of GnRH **Duration** 19 weeks (12 weeks) **Participants** n=25 **Dropout** 0	**BMD (g/cm^2)** ***Lumbar; mean±SEM*** I: 0.95±0.02, C: 0.98±0.019 % change; I: –0.9, C: 0.004 ***Total BMD, mean ±SEM*** I: 0.76±0.03, C: 0.803±0.027 % change; I: –0.64, C: 1.53 **Modified Kupperman index, mean** I: 11.6, C: 11 Change, median (IQR) I: –4 (–10.5, –2.3), C: –3 (–10.5, –0.5)	**Comments** Unclear randomization and allocation Assessors blinded
Cheung et al 2000 China [68]	**Study design** RCT, crossover, double blind **Setting/recruitment** Single centre, teaching hospital/unclear enrolment **Population** n=54 recruited, 44 participated Mean age: 34 years	**Intervention** Triptorelin, 3.75 mg, 3 doses IM followed by leuprorelin acetate 3.75 mg, 3 doses, IM at 4-week intervals **Duration** 6 months **Participants** n=27	**Comparison** Leuprorelin acetate, 3.75 mg IM, 3 doses, followed by triptorelin, 3.75 mg, 3 doses IM at 4-week intervals **Duration** 6 months **Participants** n=21	**Adverse events** 4 weeks, time of cross over Hot flushes & sweating; I: 63%, C: 67% Paraesthesia; I: 22v, C: 38% Insomnia; I: 37%, 38% Anxiety; I: 37%, C: 29% Depression; I: 22%, C: 19% Vertigo and dizziness; I: 19%, C: 10% Fatigue; I: 30%, C: 29% Arthralgia; I: 52%, C24% Headache; I: 26%, C: 24%	**Comments** Unclear randomization and allocation Unclear if assessor was blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Inclusion criteria Patients diagnosed having pelvic endometriosis after surgery and indications for GnRH-a therapy **Follow up** Post treatment (6 months)	**Dropout** 0	**Dropout** 0	Palpitation; I: 26%, C: 29% Formication; I: 19%, C: 19% Vaginal dryness; I: 22%, C: 14%	
Cobellis et al 2011 Italy [69]	**Study design** RCT, double blind **Setting/recruitment** Single centre/ND **Population** n=61 in total, 41 included in this report **Inclusion criteria** Age 24–41, diagnosis of endometriosis according to the ESHRE guideline, stage I and II **Follow up time** Post treatment (3 months)	**Intervention 1** Laparoscopy + N-Palmitoylethanolamine 400 mg + transpolydatin 40 mg twice a day **Duration** 3 months **Participants** n=21 **Dropout** 0	**Comparison** Laparoscopy + Placebo **Duration** 3 months **Participants** n=20 **Dropout** 0	**Pain (VAS)** Decrease in dysmenorrhoea, dyspareunia and pelvic pain in all groups, N-Palmitoylethanolamine and transpolydatin more effective than placebo (P<0.001) **Patients' satisfaction** Very satisfied; I: 9, C: 4 Satisfied; I: 7, C: 4 Uncertain; I: 4, C: 5 Dissatisfied; I: 1, C: 3 Very dissatisfied; I: 0, C: 4 **Recurrence** I: 1, C: 2 **Side effects** No significant side effects reported	**Comments** Random Allocation Software The arm that received Celecoxib (NSAID) is not included due to irrelevant treatment period
Cosson et al 2002 France [70]	**Study design** RCT, open, phase III **Setting/recruitment** Multicentre/ Volunteer patients **Population** n=142 Mean age: 29 years	**Intervention** Dienogest (DNG), 1 mg orally twice a day **Duration** 16 weeks **Participants** n=74	**Comparison** Triptorelin, 3.75 mg IM every 4 weeks **Duration** 16 weeks **Participants** n=68	**Change in rAFS score, median (IQR)** **Spontaneous pregnancy,** 12 months FU; DNG; 15/45 (33%), GnRH: 12/41 (29%), p=0.71 **Satisfaction with treatment,** Very; I: 34.5%, C: 30% Satisfied; I: 51.7%, C: 50%	**Comments** Unclear concealment

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Previous diagnose of endometriosis: 32% Previous medical treatment: 86% Laparoscopic treatment: 80% **Inclusion criteria** Age:18–40 years, laparo-scopic diagnosis, no therapy for ≥3 months prior study, operative laparoscopy, stage II–IV rAFS (score ≥70) **Follow up time** 12 months	**Dropout** 15 (20%)	**Dropout** 7 (10%)	Total satisfied; I: 86.2%, C: 80.0% satisfied patients. **Function of response in each group** Favourable to Dienogest, OR=1.35, not statistically significant (p=0.39) **Side effects, %** Spotting; DNG: 61.6%, GnRH: 25.4% Hot flushes; DNG: 9.6%, GnRH: 61.2%	
Crosignani et al 2005 Europe, Asia, Latin America and New Zealand [71]	**Study design** RCT, phase III, evaluator blinded **Setting/recruitment** Multicentre/unclear enrolment **Population** n=299 (300 randomized) Mean age: 31 years **Inclusion criteria** Aged 18–49 years, laparo-scopically diagnosed endometriosis, recently diagnosed with signs and symptoms that fulfilled endometriosis pain criteria and with 3 months of persistent symptoms if surgery had been performed during laparoscopy, or they could have had a diagnostic laparoscopy within	**Intervention** Leuprolide acetate (LA) 3.75 mg monthly or 11.25 mg every 3 months **Duration** 6 months **Participants** n=146 **Dropout** 12 months: 36 (25%)	**Comparison** Medroxyprogesterone acetate (DMPA), 104 mg/0.65 ml, SC, every 3 months **Duration** 6 months **Participants** n=153 **Dropout** 12 months: 39 (25%)	**Pain improvement, Biberoglu & Behrman scale** Statistical equivalence for dysmenorrhoea, pelvic pain, pelvic tenderness, induration between the groups **BMD, median % change from BL** ***Femur;*** 6 months: DMPA: –0.5, LA: –2.1, p<0.001 18 months; DMPA: –0.2, LA: –1.1, p<0.006 ***Spine*** 6 months; DMPA: –1, LA: –4, p<0.001 18 months: DMPA: –0.4, LA: –1.3, p<0.08 **Productivity;** **Hours of employment productivity lost at 6 months** ***Due to absenteeism*** DMPA: 4.88±17.11, LA: 1.36±6.54	**Comments** Block-randomization, 1:1 ratio ITT analysis

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	the past 42 months and persistent or recurrent symptoms for ≥3 months for which they had not received pharmacotherapy with medication **Follow up time** Post treatment and 12 months later			***Due to presenteeism,*** 6 months: DMPA: 26.62±41.72, LA: 26.90±35.25 Total hours of productivity lost at employment; DMPA: 30.32±43.79, LA: 26.75±35.09 **Hours of housework** lost at 6 months ***Due to absenteeism;*** DMPA: 3.88±14.81, LA: 2.80±9.77, 6 months ***Due to presenteeism;*** DMPA: 7.32±12.68, LA: 12.31±21.48 Total hours of productivity lost at housework; DMPA: 10.98±20.12, LA: 14.08±22.38 **Adverse events, n (%)** ***Patient reported at least 1 AE*** DMPA: 69.7%. LA: 65.0% ***Drug-related adverse events*** DMPA: 50.7%, LA: 39.2%, p=0.047 ***Nausea*** DMPA: 17 (11.2%), LA: 10 (7%) ***Headache*** DMPA: 5 (3.3%), LA: 9 (6.3%) ***Breast pain*** DMPA: 8 (5.3%), LA: 5 (3.5%) ***Intermenstrual bleeding*** DMPA:19 (12.55), LA: 1 (0.7%) ***Hot flushes*** DMPA: 9 (5.9%), LA: 24 (16.8%)	
Daru et al 2011 Hungary [72]	**Study design** Prospective controlled study **Setting** Single centre **Population** n=119	**Intervention** Laparoscopy + GnRH+ Controlled ovarian hyperstimulation-intrauterine insemination (COH-/IUI) GnRH: 3.75 mg triptoreline or leuprolelin acetate IM monthly for 6 months	**Comparison** Surgery and 3.75 mg triptoreline or leuprolelin acetate IM monthly for 6 months **Participants** n=55	**Pregnancy rate (PR)** stage I–II I: 16 (62%), C: 13 (52%) Stage III–IV I: 17 (45%), C: 10 (33%) All stages I: 33 (51.6%), C: 23 (42%)	**Comments** Assessor not blinded. Baseline characteristic poorly described.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Endometriosis stages I–IV Age between 23–36 (average age: 32.4) **Inclusion criteria** Patients who had infertility associated with endometriosis for at least one year, women with additional infertility factors were excluded **Follow up time** 1–10 years	COH: monofollicular protocol; briefly 50 IU FSH daily for 2 days, day 3 75 IU FSH, 75 IU LH IM. When follicle reached 20 mm in size, and the endomelrium was >9 mm, 10 000 IU hCG for luteinization after the serum level of the estradiol was determined. IUI performed 36 hours later. **Participants** n=64 **Dropout** 0	**Dropout** 0		
Dawood et al 1997 USA [73]	**Study design** RCT, phase II, double blind **Setting/recruitment** Single centre/unclear enrolment **Population** n=11 Mean age: 29.7±1.3 years **Inclusion criteria** Aged 20–30 years, regularly menstruating, pelvic endometriosis diagnosed at laparoscopy, stage II and III **Follow up** Post treatment (6 months)	**Intervention** Gestrinone, 1.25 mg twice a week **Duration** 6 months **Participants** n=5 **Dropout** 0	**Comparison** Gestrinone, 2.5 mg twice a week **Duration** 6 months **Participants** n=6 **Dropout** 0	**r-AFS score, mean ±SEM** Before; I: 18.6±4.5, C: 16.8±4.3 6 months; I: 16.6±7.8, C: 15.0+5.8 **Endometriosis implants, score** I: 10.0±3.9, C: 3.8±0.8 **Symptom,** categoric rating scale of none, mild, moderate, or severe on the basis of clearly delineated clinical experience, limitation, or functional impediment All patients improved in dysmenorrhea and pelvic pain, no sign difference between groups **BMD, % decrease** I: –7.1%, C: +7.1%, p=0.02 **Side effects, n** Hot flushes: 10	**Comments** Computer-generated order and code supplied by the sponsor of the study.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				Weight gain: 10, Acne: 9, Headache: 7, Nausea: 5, Oily skin: 3, Nervousness and shaking sensations: 3, Increase or firmness of breast: 2, Leg swelling: 2, Decrease in breast size: 1, Leg cramps: 1, Weight gain: 4	
Decleer et al 2017 Belgium [74]	**Study design** RCT, open label trial **Setting/recruitment** Single centre, consecutive enrolment **Population** n=120 (79% of screened) Mean age: 31±4 years Mean duration of infertility: 2.7±1.87 years **Inclusion criteria** Age <38 years, with indication for IVF-treatment, mild peritoneal endometriosis, stage I–II (AFS). No ovarian endometriosis, **Follow up time** 2 years	**Intervention** A 3-month pituitary suppression with a long-acting GnRH agonist, 3.6 mg, in the abdominal subcutaneous fat tissue on a monthly basis. Ten days after the last dose of the ovarian stimulation was initiated with Menopurw, giving three ampules of 75 IU s.c. daily **Duration** GnRH: 3 months **Participants** n=61 **Dropout** 0	**Comparison** IVF straight away: Menopurw, giving three ampules of 75 IU s.c. daily (no hormonal treatment) To avoid possible bias from comparing long protocol stimulation with short protocol stimulation, the patients were given a long protocol schedule, using buserelin nasal spray (3×3 puffs/day), from Day 20 of the pre-treatment cycle. **Participants** n=59 **Dropout** 1 (1.7%)	**The pregnancy rates** I: 39.3%, C: 39.7% (p=0.972) Logistic regression model adjusted for the baseline covariates p=0.693	**Comments** Randomization via computer program by the study coordinator, who did not come in contact with the individual patients.
Dlugi et al 1990 USA [75]	**Study design** RCT, Phase III, double-blind **Setting** Multicentre study	**Intervention** Leuprolide acetate (LA) 3.75 mg IM depot every 4 weeks	**Comparison** Placebo 2 ml IM every 4 weeks **Duration**	**Pain symptoms (Biberoglu & Behrman), mean change** ***Dysmenorrhoea*** 3 months; I: –2.3, C: –0.3, p<0.001 4 weeks; I: –2.2, C: –0.1, p<0.001	**Comments** Unclear allocation and concealment

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Population n=63 Mean age: 30 years (range 19–44) Stage: I to IV **Inclusion criteria** Laparoscopically diagnosed endometriosis ≤3 months, pain secondary to endometriosis, age >18 years, no previous treatment with GnRHas, ≥1 ovary intact, no treatment for endometriosis ≤3 months **Follow up** During treatment and 4 weeks FU	**Duration** 20 weeks **Participants** n=32 **Dropout** 4 (12.5%)	20 weeks **Participants** n=31 **Dropout** 7 (22.6%) 27 prematurely, 24 because their symptoms worsened	***Pelvic pain*** 3 months; –1.2, C: –0.2, p<0.005 4 weeks; I: –1.2, C: –0.3, p<0.001 ***Dyspareunia*** 3 months; I: –0.2, C: 0.1, ns 4 weeks; I: –0.4, C: 0.1, ns ***Pelvic tenderness*** 3 months; I: –0.9, C: –0.3, ns 4 weeks; I: –1, C: –0.3, p=0.001 **Pelvic Induration** 3 months; p<0.01 Final visit (4 weeks FU): p<0.05, in favour for I group	Due to large drop out in control group after 3 months, between group analysis was performed only for months 3 and the final visit because of the selection bias in placebo group After 12 weeks of treatment, if significant pain was present, the patient was considered a treatment failure, and the blind was broken.
Donnez et al. 2004 France, Belgium, UK, Germany, Spain, and Italy [76]	**Study design** RCT, phase II, open label **Setting/recruitment** Multicentre/unclear enrolment **Population** n=152 Mean age: 29 years Stage III/IV: 70% **Inclusion criteria** Age: 18–40, laparoscopy confirmed recurrent or newly diagnosed, regular cycles between 25–35 days the last 6 months, use an effective barrierier method of contraception for 1 month after the first injection, no treatment	**Intervention** Single IM injection of 3-month triptorelin sustained-release (SR) **Duration** 12 weeks **Participants** n=75 **Dropout** 3 (4%)	**Comparison** One IM injection of 28-day triptorelin SR every 28 days **Duration** 12 weeks **Participants** n=77 **Dropout** 6 (8%)	**Adverse events** ***Prevalent AE/body system*** Reproductive; I: 33%, C: 36% Gastrointestinal; I: 13%, C: 14% Psychiatric; I: 19%, C: 12% Respiratory system; I: 11%, C: 11% General: I: 10%, C: 8% **Expected side effects** Hot flushes; I: 90, C: 93% Headache; I: 63%, C: 57% Asthenia; I: 50%, C: 51% Vaginal dryness; I: 42%, C: 46% Local reaction; I: 1%, C: 4% **Other AE** Withdrawal bleeding; I: 25%, C: 27% Insomnia; I: 8%, C: 5% Depression; I: 6%, C: 4 Nausea; I: 6%, C: 3% Back pain; I: 6%, C: 1%	**Comments** Assessor not blinded ITT analysis

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	with GnRH analogues in previous 3 months or concomitant treatment with coumarin or indanedione derivatives, no other hormonal treatment during the previous month **Follow up** 12 weeks after end of treatment			Dizziness; I: 6%, C: 1% Pharyngitis; I: 3%, C: 5% Menstrual disorder; I: 3%, C: 5% Vertigo; I: 0%, C: 5% Dysuria; I: 0%, C: 5%	
Donnez et al 1994 Belgium [77]	**Study design** RCT **Setting** Single centre **Population** n=80 Mean age: 27/28 years **Inclusion criteria** Age <35 years, with laparoscopically confirmed ovarian endometriotic cysts (AFS moderate; n=41; severe, n=39) **Follow up time** Post treatment: 12 weeks	**Intervention** Laparoscopic drainage of the ovarian cyst + gosereline SC every 4 week (4 I total) **Duration** 12 weeks **Participants** n=40 **Dropout** 0	**Comparison** Laparoscopic drainage of the ovarian cyst + no therapy **Participants** n=40 **Dropout** 0	**Ovarian Cyst Diameter, mean± SD** I: 15.1±6.0, C: 33.2±5.1 mm **Active endometriosis (%)** I: 46%, C: 83% **Total scores r- AFS classification, mean ±SD** BL: I: 42.5±3.8, C: 44.1±4.2 2nd look: I: 34.5±1.1, C: 44.1±4.2	**Comments** Moderate risk of bias Unclear if assessors were blinded Official randomization tables Unclear allocation The degree of endometriosis was assessed by the same two observers
Fawzy et al 2015 Egypt [78]	**Study design** Prospective CCT **Setting** Outpatient Gynecologic Clinic and a private practice **Population** n=41	**Intervention** Oral dienogest (DNG) 2 mg once daily on days 2–5 of menstruation without a break **Duration** 16 weeks	**Comparison** Triptorelin acetate (TA) SC, 3.75 mg every 4 weeks, on days 2–5 of menstruation **Duration** 16 weeks	**Pain, VAS 0–100, mean ±SD** ***Dysmenorrhea*** DNG: 30.6±18.4, TA: 0, p<0.0001 ***Dyspareunia,*** DNG: 20.7±16.5, TA: 25.8±19.1, p=0.39 ***Chronic pelvic pain*** DNG: 21.7±1.6, TA: 24.5±13.8, p=0.51	**Comments** Transvaginal sonography (TVS) evaluation was carried out by the same physician. Analysis was done on the recruited women

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Mean age: 40 years **Inclusion criteria** Aged 35–45 years, married premenopausal with uterine adenomyosis, complaining of menorrhagia, dysmenorrhea, dyspareunia, and chronic pelvic pain. No hormonal therapy in the preceding 3 months, no myoma, endometriosis or chronic pelvic inflammatory disease **Follow up** Post treatment (16 weeks)	**Participants** n=22 **Dropout** 3 (14%)	**Participants** n=19 **Dropout** 1 (6%)		who continued the study Unclear if patients and assessors were blinded
Fedele et al 1999 Italy [79]	**Study design** RCT **Setting** Single centre **Population** n=21 Previous hysterectomy: 80% **Inclusion criteria** Age 35–46, symptomatic patients with deeply infiltrating endometriotic nodules that recurred after one or more previous operations. Patients had bilateral oophorectomy with or without hysterectomy. The disease was not completely eradicated after the surgery **Follow up time** Post treatment (12 months)	**Intervention** Hormone replacement therapy (HRT): Nonstop tibolone 2.5 mg/day **Duration** ≥12 months **Participants** n=11 **Dropout** 0	**Comparison** Nonstop transdermal 17β-estradiol 0.05 mg/day, combined with cyclic MPA 10 mg daily for 12 days/month **Duration** ≥12 months **Participants** n=10 **Dropout** 1 (10%)	**Pain** ***Moderate pelvic pain, n*** I: 1/11, C: 4/9 ***Severe pelvic pain*** 0 in both groups	**Comments** Computer-generated randomization Unclear allocation concealment

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Fedele et al 1992 Italy [80]	**Study design** RCT **Setting/recruitment** Single centre/consecutive enrolment **Population** n=49 Mean age: 31.9±3.6 years (23–38) Stage I: 41% Mean duration of infertility: 3.5 years **Inclusion criteria** Infertile women, laparoscopic diagnosis of endometriosis, stage I or II (rAFS) made previous 3 months **Follow up time** Up to 50 months	**Intervention** Superovulation with buserelin acetate, human menopausal gonadotropins (hMG), and human chorionic gonadotropin (hCG) In 1st cycle: 400 µg buserelin acetate IN, every 8 hours. hMG started ≥14 days of buserelin acetate therapy and after serum estradiol (E2) had been <20 pg/mL for ≥5 consecutive days. 2 ampules of hMG (75 IU FSH and 75 lU LH per ampule) IN each day for 6 days, then no hMG injections was adjusted according to the patient's response. hCG administration was given when E2 levels were ≥250 pg/mL- 2,500 pg/mL, and follicle Ø was ≥17 mm. **Participants** n=24 **Dropout** 0	**Comparison** No treatment for infertility **Participants** n=25 **Dropout** 2(8%)	**Pregnancy, CPR** I: 9/24 (38%), C: 6/25 (24%) ***Cumulative pregnancy rate (CPR)*** 6 months; I: 37%, C: 24%, ns	**Comments** Moderate risk of bias Randomization list. No blinding
Fedele et al 1992 Italy [81]	**Study design** RCT **Setting** Single centre, consecutive enrolment	**Intervention** Buserelin, IN, 400 µg three times daily 15 patients (43%) received drugs to stimulate ovulation	**Comparison** Expectant management 14 patients (39%) received drugs to stimulate ovulation	**Overall pregnancy rate** 12 months; I: 30%, C: 37% 24 months; I: 61%, C: 61%, ns	**Comments** Randomised by computer-generated assignment. Allocation by central telephone.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Population n=71 (95% of eligible) Stage II: 41% >3 years of infertility: 75% **Inclusion criteria** Age ≤38 years, laparoscopically diagnosed, rAFS stage I and II, trying to conceive, unexplained infertility >2 years, normal HSG, no previous therapy for endometriosis **Follow up time** Median 17–18 months	**Duration** 6 months **Participants** n=35	**Duration** 6 months **Participants** n=36		No blinding
Fernandez et al 2004 France [82]	**Study design** RCT, double blind **Setting/recruitment** Multicentre (22)/recruited from gynaecological centres **Population** n=78 Mean age: 34 Previous treatment for endometriosis; Medical: 53% Surgery: 49% **Inclusion criteria** Aged ≥18 years, laparoscopic diagnosed endometriosis, rAFS stage III–IV endometriosis, regular menstrual cycles, no hormonal treatment >1 month prior to study entry	**Intervention** Leuprorelin 3.75 mg SC, monthly intervals + estradiol 2 mg/day + 0.5 mg promegestone **Duration** 1 year **Participants** n=39 **Dropout** Unclear	**Comparison** Leuprorelin 3.75 mg SC, monthly intervals + promegestone 0.5 mg daily, orally+placebo. Started 9 weeks after first GnRH injection **Duration** 1 year **Participants** n=39 **Dropout** Unclear	**Pelvic pain intensity score (Biberoglu&Behrman) mean±SD** I: 0.5±0.84, C: 0.28±0.53 Median score; I: 0, C: 0 Total score; decrease I: 89%, C: 77% **BMD** Lumbar spine; I: –1.9±3.1%, C: –6.1±3.7%, p<0.0001 Total hip; I: –1.4±2.3%, C: –4.9±4%, p<0.0001 Femoral neck; I: –2.3±3.3%, C: –5±4% p=0.0064 **Adverse events** Any AE; I: 97%, C: 97% AE/patient; I: 8.3, C: 9.6 Vaginal bleeding/spotting; I: 88%, C: 85%	**Comments** Permuted blocks (size 4) of treatment External company in charge of treatment packaging and treatment masking generated the allocated sequence list that was kept centrally for blinding ITT analysis

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Follow up time Post treatment			Headache and hot flushes were most reported	
Ferreira et al 2010 Brazil [83]	**Study design** RCT, open labelled **Setting/recruitment** Pain and endoscopy out-patient clinic, single centre /consecutive enrolment **Population** n=44 Mean age: 30 years (range:18–44) **Inclusion criteria** Laparoscopically diagnosed endometriosis 3–24 months, chronic pelvic pain, no oral hormone contraceptives ≤3 months, no depot progestogens or GnRHa ≤6 months **Follow up time** Post treatment (6 months)	**Intervention** Leuprolide acetate (LA) 3.75 mg IM monthly **Duration** 6 months **Participants** n=22 **Dropout** 4 (18%)	**Comparison** LNG-IUS **Duration** 6 months **Participants** n=22 **Dropout** 0	**Pain score reduction (VAS), Mean ±SD** LNG-IUS: 1.2±1.75 LA: 0.7±1.37, ns	**Comments** No ITT analysis Randomized by a computer program at a 1:1 ratio. Unblinded assessor(s). Unclear allocation and concealment.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Finkelstein et al 1994 [84] Finkelstein et al 1998 [85] Finkelstein et al 1999 USA [86]	**Study design** RCT **Setting** Single centre **Population** n=50 Age rage 20–44 years **Inclusion criteria** Symptomatic, laparoscopically proven endometriosis, OC discontinued for ≥2 months, GnRH treatment for ≥9 months prior to study **Follow up time** Post treatment (6 months) and 1-year FU	**Intervention** GnRH analogue nafaralin acetat (NA), 200 μg IN twice daily + Human parathyroid Hormone (PTH), 40 μg (500U) SC daily **Duration** 6 months **Participants** n=28 **Dropout** 8 (29%) (3 due to PTH injection)	**Comparison** GnRH analogue nafaralin acetat (NA), 200 μg IN twice daily **Duration** 6 months **Participants** n=22 **Dropout** 2 (10%)	**Side effects, n (%)** ***Post treatment*** Vasomotor flushing; I: 19 (95), C: 19 (95) Headache; I: 9 (45), C: 13 (65) Emotional instability; I: 8 (40). C: 7 (35) Nausea; I: 7 (35), C: 0 Arthralgia; I: 6 (30), C: 1 (5) Myalgia; I: 1 (5), C: 1 (5) Nasal irritation; I: 3 (15), C: 3 (15) Wight gain; I: 3 (15), C: 2 (10) Hair loss; I: 2 (10), C: 1 (5) Acne; I: 2 (10), C: 3 (15) **BMD, mean ± SD** Post: Lumbar spine Anterior position I :3.4±1.2%, C: –2.8±0.5% Post: Lateral position I: 0, C: 3.5±0.8%	**Comments** Unblinded Unclear allocation and concealment.
Franke 2000 Netherlands [87]	**Study design** RCT, double blind **Setting** Multicentre **Population** n=41 Mean age: 30 years **Inclusion criteria** Endometriosis confirmed by laparoscopy in previous 3 months **Follow up time** Post treatment	**Intervention** Goserelin acetate SC,3.6 mg, every 4 week + 2 mg 17 β-E2 and 1 mg norethisterone Acetate, orally **Duration** 24 weeks **Participants** n=18 **Dropout** 0	**Comparison** Goserelin acetate SC, 3.6 mg, every 4 weeks + placebo **Duration** 24 weeks **Participants** n=23 **Dropout** 1 (4%)	**BMD (g/cm^2)** ***Median ±SD*** I: 1.234±0.12, C: 1.155±0.13 ***Change*** I: 0.2% increase C: 5% decrease, p<0.001 **AFS score,** ***Median (range)*** I: 9 (4–40), C: 6 (0–63), ns ***% decrease*** I: 69%, C: 79% **Side effects, subjective,** Kupperman index score, reduction % I: 0%, C: 113%, p=0.003	**Comments** Randomly assigned in blocks of 4. Unclear allocation. Therapy was started during menstruation.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Giannini et al 2015 Italy [88]	**Study design** Randomized, double-blind, placebo-controlled **Setting** Single centre **Population** n=30 Age: 20–40 years **Inclusion criteria** Age <40 years, stage I–II endometriosis (ASRM), mono or bilateral ovarian endometriomas (2–4 cm), pelvic pain during menstrual cycles or sexual intercourse. Intraoperative and pathological diagnosis and staging of endometriosis were confirmed in all patients. **Follow up time** 60 days after surgery	**Intervention** Surgery + Wobenzym Vital (papain, bromelain, trypsin, chymotrypsin and quercetin) **Duration** 40–60 days before surgery and 60 days after **Participants** n=15 **Dropout** 0	**Comparison** Surgery + placebo **Duration** 40–60 days before surgery and 60 days after **Participants** n=15 **Dropout** 0	**Pain (VAS),** No significant difference	**Comments** Participants were selected for laparoscopic surgical treatment and were required to have been free from estrogen-progestin combinations, progestin-only pills or GnRH analogues for at least 6 months before enrolment and not to use medications influencing inflammation, such as nonsteroidal anti-inflammatory drugs, during the study.
Gomes et al 2007 Brazil [89]	**Study design** RCT **Setting** Single centre **Population** n=22 Age range: 18–44 years **Inclusion criteria** Laparoscopically diagnosed endometriosis ≤3 months,	**Intervention** Lupron Depot (LD), 3.75 mg IM every 4 weeks **Duration** 6 months **Participants** n=11 **Dropout** 3 (27%)	**Comparison** LNG-IUS IU **Duration** 6 months **Participants** n=11 **Dropout** 1 (9%)	**Pain score VAS 0-10, mean±SD** LNG-UIS: 2.1±2.7 LD: 0.4±1.1 **ASRM stage** ***Lower STAGE, n (%)*** LNG-UIS: 6 (60%) LD: 3 (37.5%) ***Score, mean ±SD*** LNG-UIS: 21.3±20.5 LD: 30.8±22.8	**Comments** Randomization via a computer-generated system of sealed envelopes

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	chronic cyclic pelvic pain, • VAS ≥3, • Regular menstrual cycle for ≥3 months, no hormonal therapy for ≥3 months, no progestins or GnRHas ≤9 months **Follow up time** Post treatment: 6 months				
Gong et al 2015 China [90]	**Study design** RCT, open labelled **Setting** Single centre **Population** n=70 (out of 79) Mean age: 32 years **Inclusion criteria** Age 20–50, Stage II–III (rAFS), had conservative surgery by laparoscopy or laparotomy, no hormone treatment prior to 3 months **Follow up time** Post treatment (12 weeks)	**Intervention 1** Surgery + 3 cycles of 28-day goserelin, 3.6 mg, SC, initiated 3–5 days postoperatively **Duration** 3 months **Participants** n=17 **Dropout** 0 **Intervention 2** Surgery +3 cycles of 28-day goserelin, 3.6 mg, SC, initiated days 1–5 of menstruation **Duration** 3 months **Participants** n=17 **Dropout** 0	**Comparison 1** Surgery + 3 cycle of 28-day goserelin, 3.6 mg, SC, initiated 3–5 days postoperatively + estradiol valerate; 0.5 mg daily and dydrogesterone 5 mg **Duration** 3 months **Participants** n=15 **Dropout** 3 (20%) **Comparison 2** Surgery + 3 cycles of 28-day goserelin, 3.6 mg, SC, initiated days 1–5 of menstruation + estradiol valerate; 0.5 mg daily and dydrogesterone 5 mg **Duration** 3 months **Participants** n=15 **Dropout** 3 (20%)	**Pain (dysmenorrhea, dyspareunia, pelvic tenderness), VAS, mean ±SD** I1: 0.6±1.3, C: 1.3±2.3 I2: 0.6±0.9, C2:0.7±1.2 ns **Kupperman index (KMI), mean ±SD** I1: 10.6±8.5, C1: 14.1±6.7 I2: 9.8±5.9, C2: 12.5±6.9 ns **BMD, mean ±SD** LI: 4 I1: 1±0.1, C1: 1±0LI I2: 1±0.1, C2: 1±0.1 Left femur neck I1: 0.8±0.1, C1: 0.8±0.1 I2: 0.8±0.1, C2: 0.8±0.1 ns	**Comments** Web-based computer-generated randomization schedule. Unclear allocation

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Granese et al 2015 Italy [91]	**Study design** RCT **Setting** Multicentre, university hospitals **Population** n=78 Mean age: 31 years Stage III/IV (rAFS): 77% **Inclusion criteria** Age 18–45, no immediate desire for offspring, surgical and histological confirmation of endometriosis, VAS score >40 before surgery, no hormone therapy the 3 months prior surgery. **Follow up time** Post treatment (9 months)	**Intervention** Multiphasic OCs; dienogest + estradiol valerate (E2V) 2 mg of E2V for 22 days + 2 mg of dienogest for 5 days and 3 mg for 17 days; the first two and the last four pills containing only E2V or placebo were removed **Duration** 9 months **Participants** n=39 **Dropout** 3 (8%)	**Comparison** Leuprorelin acetate (LA) 3.75 mg, one dose every 30 days **Duration** 6 months **Participants** n=39 **Dropout** 5 (13%)	**Pelvic pain, VAS, scale 0-100, median** OC: 15.2, LA: 13.8/18.9 p=0.417 **Recurrence, n** Unilateral cyst; OC: 2, LA: 1, ns Bilateral cyst: OC: 0, LA: 1, p=0.486 **QoL, EHP, mean ±SD** OC: 8.6±2, LA: 9.1±1.8, ns **Side effects** Headache; OC: 7 (19%), LA:1 (3%) Decreased libido; OC: 12 (33%), LA: 4 (12%) Spotting; OC: 2 (6%), LA: 0 Vaginal dryness; OC: 8 (22%), LA: 1 (3%) Vasomotor symptoms; OC: 0, GnRH: 1 (3%) Discomfort from amenorrhea; OC: 10 (28%), LA: 0 Weight gain; OC: 2(6%), LA:1 (3%)	**Comments** Random sequence using SPSS version 17.0 Blinding unclear. Expert surgeons (Level II of the Italian Society of Gynecologic Endoscopy)
Guzick et al 2011 USA [92]	**Study design** RCT double-blind **Setting** Academic medical centres, gynaecologic practices **Population** n=47 Mean age: 29 years **Inclusion criteria** Age >18, premenopausal. Pelvic pain ≥3 months, diagnosis by laparoscopy or	**Intervention** Depot leuprolide (DL), 11.25 mg IM every 12 weeks with hormonal add-back continues norethindrone acetate (NA) 5 mg orally **Duration** 48 weeks **Participants** n=21 **Dropout**	**Comparison** Continues monophasic OC (norethindrone 1 mg + ethinyl estradiol 35 mg) + placebo IM injection **Duration** 48 weeks **Participants** n=26 **Dropout** 3 (11.5%)	**Pain reduction (Biberoglu and Behrman (B&B) and, numerical rating scores (NRS)** No significant difference between groups. In both groups pain decreased compare to baseline **Depression, (BDI)** No significant difference between groups. In both groups decreased BDI score compare to baseline **Index of Sexual Satisfaction (ISS)** No significant difference between groups	**Comments** Unclear randomisation and allocation

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	laparotomy within 3 years entry. Diagnosis require either histology consistent with endometriosis or operative records indicating visual evidence of lesions consistent with endometriosis. Moderate to severe pelvic pain (mean NRS ≥5 for ≥3 months). No use of OC last month, no dose of leuprolide, within 5 months, no hysterectomy or oophorectomy **Follow up time** Post treatment (48 weeks)	4 (19%)		**Adverse events** Serous: 0 for both groups Vaginal bleeding; OC: 22/81, NA: 12/72, p=0.24 Hot flashes; OC: 11/82, NA: 12/73, p=0.65	
Hamid et al 2014 Egypt [93]	**Study design** RCT, open label **Setting** Multicentre, 2 private medical centres **Population** n=140 Mean age: 30 years Stage II/IV: 50% **Inclusion criteria** Endometriosis diagnosed by previous laparoscopy (rAFS criteria), unilateral endometrioma, mean diameter ≤5 cm. No history of oophorectomy or previous hormonal treatment the past 6 months **Follow up time** Post treatment (12 weeks)	**Intervention** Cabergoline tablets, 0.5 mg tablets, twice per week for **Duration** 12 weeks **Participants** n=71 **Dropout** 0	**Comparison** LHRH, triptorelin acetate CR, 3 (decapeptyl,) 3.75 mg SC, once a month **Duration** 12 weeks **Participants** n=69 **Dropout** 0	**Endometrioma** No of patients with a decrease of mean endometrioma size >25%, I: 46 (65%), C: 15 (22%), p<0.05 **Side effects, n (%)** Gastrointestinal; I: 9 (13%), C: 0 Nervous; I: 4 (6%), C: 9 (13%) Psychiatric; I: 3 (4%), C: 5 (7%) Cardiovascular; I: 5 (7%), C: 6 (9%) Musculoskeletal; I: 2 (3%), C: 2 (3%) Genitourinary; I: 2 (3%), C: 2 (3%) Dermatologic; I: 1 (1%), C: 1(1%) Ocular; I: 3 (4%), C: 8 (12%) Metabolic; I: 5 (6%), C: 6 (9%) Respiratory; I: 3 (4%), C: 0	**Comments** Allocation concealment was performed by computer generated numbers The sonographer was blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Han et al 2013 China [94]	**Study design** RCT **Setting** Single centre **Population** n=70 **Inclusion criteria** Age range: 18–50 years, diagnosed by pelviscopy or laparotomy, stages III–IV (rAFS), post-surgery **Follow up time** Post treatment (3 months)	**Intervention** Add back therapy: conservative surgery + goserelin, 3.6 mg, sc every 28 days, three cycles + combined daily estradiol valerate 0.5 mg and dydrogesterone 5 mg **Duration** 3 months **Participants** n=35 **Dropout** 3 (8.6%)	**Comparison** Conservative surgery + goserelin, 3.6 mg, sc every 28 days, three cycles **Duration** 3 months **Participants** n=35 **Dropout** 3 (8.6%)	**Endometrial thickness** I: 3.5±1.4, C: 3.5±1.2	**Comments** Unclear randomisation and allocation Unclear if assessor blinded Patient not blinded No ITT analysis
Harada et al 2009 Japan [95]	**Study design** RCT double blind, phase III **Setting** Multicentre (24 centres) **Population** n=271 Mean age: 34 Dyspareunia: 45% Lower abdominal pain: 76% **Inclusion criteria** Age ≥20, regular menstrual cycles, endometriosis diagnosed by laparotomy/ laparoscopy, or imaging analysis of endometriotic ovarian chocolate cysts; subjective symptoms, presence of objective findings, no use of	**Intervention** Dienogest (DNG), 1 mg/twice daily, orally + placebo spray **Duration** 24 weeks **Participants** n=137 **Dropout** 8 (6%)	**Comparison** Intranasal buserelin acetate (BA) 300 µg every morning, noon, and evening, + placebo tablets **Duration** 24 weeks **Participants** n=134 **Dropout** 8 (6%)	**Symptoms score (VAS 0–10), mean ± SD** ***Total score,*** DNG: 2.5±2.3 BA: 2.4±2.4 Lower abdominal pain DNG: 0.9±1, BA: 0.7±0.9 Defecation pain DNG: 0.4±0.7, BA: 0.6±0.8 Dyspareunia DNG: 0.7±0.9, BA: 0.6±0.9 Lumbago DNG: 1±1, BA: 0.9±0.9 Pain on internal examination DNG: 1±0.9, BA: 0.9±0.8 **QoL, SH-36, change from BL** ***General health, mean ±SD*** DNG: 1.1±13.5, BA: 1.8±12.9, ns ***Bodily pain, mean ±SD*** DNG: 22.2±28.4, BA: 18.5±28.3, ns	**Comments** Randomized by the centre according to the permuted block method. The allocation sequence list was generated by computing random numbers and kept centrally to maintain the blindness of the study until the key was disclosed. The enrolment of patients was conducted by an independent centre.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	GnRH agonists, testosterone derivatives, hormonal therapy or aromatase inhibitors ≤16 weeks; no surgery therapy or examination for endometriosis within a menstrual cycle before start **Follow up time** 4 weeks´ post treatment			**Chocolate cyst volume reduction (%)** DNG: 47.4±53%, BA: 46.1±50.6% **Safety** ***Adverse drug reaction (ADRs)*** DNG: 121 (96%), BA: 117 (93%) Genital bleeding; DNG: 122 (95%), BA: 85 (67%) Hot flushes DNG: 64 (50%), BA: 85 (67%) Headache DNG: 32 (25%). BA: 43 (34%) **BMD (g/cm2) % change from BL** DNG: –1±2.3%, BA: –2.6±2.3%	
Harada et al 2008 Japan [96]	**Study design** RCT, double blind, phase III **Setting** Multicentre (18 centres) **Population** n=100 Mean age: 32 years Endometrioma (n): 91 Adenomyosis (n): 14 **Inclusion criteria** Age ≥18 years, regular menstrual cycles, endometriosis diagnosed by laparoscopy/laparotomy or ovarian endometrioma by ultrasound/MR, moderate or severe dysmenorrhea, no medical or surgical treatment for endometriosis ≤8 weeks before study	**Intervention** Monophasic OCP: ethinylestradiol 0.035 mg plus norethisterone 1 mg for 21 days, plus 7 days of placebo **Duration** 4 months **Participants** n=51 **Dropout** 2 (4%) **Continuous rate** 88%	**Comparison** Placebo **Duration** 4 months **Participants** n=49 **Dropout** 2 (4%) **Continuous rate** 86%	**Symptoms, score** ***Dysmenorrhea score,*** VAS, 0–100 I: 27.6±21.6, C: 46.2±24.2, p<0.0001 VRS I: 2.4±1.4, C: 3.7±1.3, p<0.001 ***Non-menstrual pelvic pain score*** VAS, 0–100 I: 19.1±22.9, C: 21.0±26.0 p=0.2560 VRS I: 1.3±1.5, C: 1.2±1.4, ns **Pelvic induration, n (%)** I: 21/49 (43%), C: 14/47 (30%) **Volume of endometrioma (median, ml)** I: 7.6, C: 9.9, p=0.0378 **Average diameter of endometrioma (mean±SD, mm)** I: 25.3±16.2, C: 27.3±17.9, p=0.040	**Comments**

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Follow up time Post treatment			**Side effects** Serious AE; I: 0, C: 0 Irregular bleeding; I: 60%, C: 26.5% Nausea; I: 24%, C: 0%	
Harrison et al 2000 Ireland [97]	**Study design** RCT, double blind **Setting** Single centre, Infertility Unit, Hospital **Population** n=100 Mean age: 32 years Severe/moderate pain: 28% always dysmenorrhea: 43% **Inclusion criteria** Age 20–39, history of infertility of ≥2 years, endometriosis diagnosed by laparoscopy **Follow up time** 6 months	**Intervention** Medroxyprogesterone acetate (MPA), 50 mg/day **Duration** 3 months **Participants** n=50 **Dropout** 3 (6%)	**Comparison** Placebo **Duration** 3 months **Participants** n=50 **Dropout** 7 (14%)	**Pain clinical symptoms** ***Pelvic pain, n (%)*** Week 48 Mild; MPA: 3 (6%), C: 6(12.5%), ns Moderate; MPA: 3 (6%), C: 4 (8%), ns Severe; MPA: 1 (2%), C:0, ns **Symptoms, no change from BL, %.** Week 12 Dysmenorrhea MPA: 17%, C: 69% Breakthrough bleeding: MPA: 69%, C: 94% **AFS Stage** Stage 0: MPA: 13, C: 19 Stage 1: MPA21, C: 20 Stage 2: MPA: 2, C: 0 Stage 3: MPA: 9, C: 5 Stage 4: MPA: 2, C: 0 Decrease: MPA: 21/47, C: 21/42, ns **Investigators' evaluation of patients' well-being** Moderate effective: MPA: 11/48, C: 8/48 Very effective: MPA: 17/48, C: 8/48 Ineffective: MPA: 5 (10%), C: 23 (48%), p<0.05 **Side effects** Medical events; MPA: 40%, C: 80% True drug related events; MPA: 10%, C: 2% Pain, acne and vasodilatation: 66% in MPA and14% in C	**Comments** Randomized by the hospital pharmacy from a block design list supplied by Upjohn (Dublin, Ireland) The Mann-Whitney nonparametric test (symptom data.) Demographic data: unpaired students t-test.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Hashim et al 2012 Egypt [98]	**Study design** RCT **Setting/recruitment** University teaching hospital and a private practice setting **Population** n=136 Mean age: 31 years **Inclusion criteria** Age ≤36, primary infertility due to minimal to mild endometriosis who did not achieve pregnancy after six to 12 months following laparoscopic treatment, no previous pelvic surgery, no associated causes of infertility, the partners had normal semen analysis parameters (modified criteria of WHO) **Follow up time** Unclear	**Intervention** Superovulation; 5 mg letrozole/day (220 cycles) for 5 days combined with intrauterine insemination up to 4 cycles. **Participants** n=69 **Dropout** 6 (9%)	**Comparison** Superovulation; 100 mg cyclesclomiphene citrate/day (213 cycles) for 5 days combined with intrauterine insemination up to 4 cycles **Participants** n=67 **Dropout** 5 (7.5%)	**Clinical pregnancy/cycle** I: 35/220 (16%), C: 31/213 (14.5%, ns **Clinical pregnancy/women** I: 35/69 (50.7%), C: 31/67 (46.3%) **Cumulative pregnancy, cycle 4** I: 64.7%, C: 57.2%, ns **Miscarriage/pregnancy** I: 4 (11.4%), C: 4 (12.9%), ns **Live birth rates** I: 31/69 (44.9%), C: 27/67 (40.3%), ns	**Comments** Computer generated random numeric table Sealed opaque envelopes Assessors ere blinded ITT analysis
He et al 2016 China [99]	**Study design** RCT, double-blinded **Setting/recruitment** University hospital and IVF centre **Population** n=120 Mean age: 31.14±4.19 years Stage II/IV: 23%	**Intervention** Atosiban a single bolus; 6.75 mg, 0.9 mL per vial, given before transfer of frozen-thawed embryo **Participants** n=60 **Dropout** 0	**Comparison** Frozen-thawed embryo **Participants** n=60 **Dropout** 0	**Clinical pregnancy rate** I: 35 (58.3%), C: 23 (38.3%), p=0.044 **Implantation rate** I: 50 (41%), C: 30 (23.4%) **Miscarriage rate** I: 3 (8.6%), C: 2 (8.7%)	**Comments** Clinical Trial Registration No: hiCTR-IOQ- 14005715. A computer-generated system of sealed envelopes was used to randomly allocate the patients

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Inclusion criteria Aged 20–45 years; FSH<10 IU/L; endometriosis diagnosed by laparoscopy; normal serum CA-125 level one or more day-5 good-quality embryo(s) available for transfer; ≤3 ET cycle failures. **Follow up time** Unclear				
Henzl et al 1988 USA, Sweden The nafarelin study group [100]	**Study design** RCT, double blind **Setting/recruitment** Multicentre/ unclear enrolment **Population** n=156 Stage: 45% had III and IV **Inclusion criteria** Age: 18–45 years, laparoscopically diagnosed endometriosis ≤3 months, no hormonal treatment for endometriosis ≥6 months **Follow up time** Post treatment: 6 months	**Intervention** Nafarelin intranasal 400 μg twice daily + placebo **Duration** 6 months **Participants** n=79 **Dropout** 9 (11%)	**Comparison** Nafarelin intranasal 200 μg twice daily + placebo **Duration** 6 months **Participants** n=77 **Dropout** 4 (5%)	**Symptoms of pain (scale 0–3), %** ***(dysmenorrhea, dyspareunia, pelvic pain)*** I: 77%, C: 73% **Change in disease stage (AFS), n (%)** ***Stage I*** Complete remission; I: 9 (50%), C: 2 (13%) No change; I: 9 (50%), C: 14 (87%) Progression; I: 0, C: 0 ***Stage II*** Complete remission; I: 4 (20%), C: 3 (13%) No change; I: 5 (25%), C: 9 (37%) Progression; I: 1 (5%), C: 0 ***Stage III*** Complete remission; I: 1 (5%), C: 0 No change; I: 7 (32%), C: 11 (48%) Progression; I: 1 (5%), C: 1 (4%) ***Stage IV*** Complete remission; I: 0, C: 1 (10%) No change; I: 6 (60%), C: 4 (40%) Progression; I: 0, C: 0 **Adverse effects** Hot flushes: 90% Decreased libido, nasal irritation, vaginal dryness	**Comments** The group receiving Danazol was excluded since no longer in use in Sweden. Unclear randomisation and allocation

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Hornstein et al 1990 US [101]	**Study design** RCT, double blind **Setting** Single centre **Population** n=12 Mean age: 30 **Inclusion criteria** Endometriosis stage II-III (rAFS) diagnosed on videotaped laparoscopy within previous 6 weeks **Follow up time** Post treatment (6 months)	**Intervention** Gestrinone 1.25 mg twice weekly **Duration** 6 months **Participants** n=6 **Dropout** 1 (17%)	**Comparison** Gestrinone 2.5 mg twice weekly **Duration** 6 months **Participants** n=6 **Dropout** 1 (17%)	**Pain** **Pelvic pain, subjective improvement, n/N** I: 4/5, C: 5/5, ns **rAFS endometriosis scores, mean ±SD** Before; I: 20.0±5.2, C: 19.1±4.8 6 months; I: 9.5±3.9 (58% decline) C: 7.1±2.1 (63% decline), ns **Side effects** I: 2/6, C: 6/6 General mild complications **Live birth** C: 1 (25%)	**Comments** Randomized using permuted blocks controlled by a research pharmacist Unclear which scale that has been used to measure pain
Hornstein et al 1995 USA [102] Orwall et al 1994 USA [103]	**Study design** RCT, double blind **Setting/recruitment** Multicentre **Population** n=179 Mean age: 31 Stage: I to IV Pelvic pain and endometriosis **Inclusion criteria** Age 18–46 years, laparoscopically diagnosed endometriosis ≤24 months, 24–6 days menstrual cycle, symptomatic endometriosis, no hormone treatment ≤3 months, prior treatment with nafarelin	**Intervention** Nafarelin 200 μg intranasal twice daily for 3 months, thereafter placebo intranasal for 3 months **Duration** 6 months **Participants** n=91 **Dropout** 0	**Comparison** Nafarelin 200 μg intranasal twice daily **Duration** 6 months **Participants** n=88 **Dropout** 0	**Pain score (mean ±SD),** ***Dysmenorrhoea,*** BL; I: 1.93±0.08, C: l.93±0.08 Post; I: 0.24±0.07, C: 0.33±0.08, ns 3 months; I:1.5±0.1, C: 1.11±0.1, ns 6 months; I: 1.48±0.11, C: 1.52±0.11, ns 12 months; I: 1.76±0.09, C: 1.61±0.1, ns ***Dyspareunia,*** BL; I: 1.82±0.11, C: 1.63±0.10 Post; I: 0.6±0.11, C: 0.74±0.12, ns 3 months; I: 0.63±0.1, C: 0.67±0.12, ns 6 months; I: 0.8±0.11, C: 1.88±0.13, ns 12 months; I: 1.12±0.13, C:1.27±0.13, ns ***Pelvic pain, score*** BL; I: 1.81±0.09, C: 1.62±0.08 Post; I: 0.75±0.09, C: 0.59±0.09, ns 3 months; I: 1.090±0.09, C: 0.76±0.1, ns 6 months; I: 1.19±0.09, C: 1.06±0.1, ns 12 months; I: 1.51±0.11, C: 1.3±0.1, ns	**Comments** ITT analysis Unclear which scale that had been used to evaluate pain

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Follow up time Posttreatment and 3–12 months after end of treatment			***Pelvic tenderness*** BL; I: 1.55±0.07, C: 1.38±0.08 Post; I: 0.49±0.09, C: 0.44±0.08, ns 3 months; I: 0.83±0.10, C: 0.70±0.10, ns 6 months; I: 0.84±0.10, C:1.88±1.11, ns 12 months; I: 1.17±0.1, C: 1.08±0.10, ns ***Pelvic induration*** BL; I: 1.43±0.08, C; l.40±0.08 Post; I: 0.51±0.10, C: 0.54±0.11, ns 3 months; I: 0.70±0.11, C: 0.64±0.11, ns 6 months; I: 0.77±0.10, C: 0.88±0.12, ns 12 months; I: 1.06±0.11, C: 1.02±0.12, ns **Discontinuation due to continuing symptoms or recurrence of symptoms, n (%)** I: 24 (26%), C: 23 (26%) **BMD, decline %** ***Spine bone mineral density,*** 6 months: I: 2.4±0.3%, C: 4±0.3%, p=0.033 12 months; I: 1.5±0.4%, C: 2±0.6% 15 months; I: 1.5±0.4%, C: 1.5±0.4% ***Femoral bone density*** 6 months; I: 1.1±0.7%, C: 3±0.5%, p=0.033 12 months; I: 1.8±0.6%, C: 3.2±0.8% 15 months; I: 2.8±1.2%, C: 2.7±11, ns	
Hornstein et al 1997 USA [104]	**Study design** RCT, double blind **Setting** Multicentre (13) **Population** n=109	**Intervention** Nafarelin, 200 µg twice daily After surgery, patients began treatment with nafarelin or placebo on cycle day 1 or 2 of the next menstrual cycle	**Comparison** Placebo **Duration** 6 months **Participants** n=53	**Total pain (Biberoglu and Behrman), change from BL, mean ±SD** Post Treatment; I: –3.15±2.66, C: –0.97±2.28, p<0.001 6 months FU; I: -1.45±2.73, C: –1.05±2.59, p=0.488	**Comments** Unclear randomisation and allocation

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Mean age: 31 years Moderate/Severe pain: 62% After reductive laparoscopic surgery, laser or electro-surgery **Inclusion criteria** Age 18–47, laparoscopically proven endometriosis, normal menstrual cycles, pelvic pain, dysmenorrhea, or dyspareunia, operative laparoscopy for endometriosis preceding enrolment, no treatment with danazol, androgenic hormones, or GnRH-a ≤3 months, oral contraceptives ≤2 months, or glucocorticoids ≤6 months **Follow up time** Up to 18 months	**Duration** 6 months **Participants** n=56 **Dropout** 7 (12.5%)	**Dropout** 9 (17 %)	**Pre-termination** I: 39 (70%) C: 43 (81%), p=0.163 ***Reason infectivity or recurrence of pain*** I: 47 %, C: 25%, sign ***Requiring alternative medicine*** I: 15 (31 %), C: 25 (57%), p<0.001	
Hornstein et al 1998 USA [105] Surrey et al 2002 [106] USA	**Study design** RCT, double blind **Setting** Multicentre **Population** n=201 Mean age: 29 years Moderate/severe stage: 19% **Inclusion criteria** Age 18–43 years, surgically diagnosed endometriosis ≤12 months, symptomatic, persistent or recurrent pain.	**Intervention 1** Lupron Depot 3.75 mg, IM every 4 weeks + daily oral norethindrone acetate (NETA) 5 mg + placebo **Participants** n=55 **Dropout** Post treatment: 10 (24%) 1st year: 24 (43%) **Intervention 2** Lupron Depot 3.75 mg, IM every 4 weeks + orethindrone 5 mg + daily	**Comparison** Lupron Depot 3.75 mg, IM every 4 weeks + oral placebo **Duration** 52 weeks **Participants** n=51 **Dropout** Post treatment: 12 (30%) 1st year: 20 (39%)	**Symptoms, (Biberoglu & Behrman grading scale) mean change ±SD** Dysmenorrhea, C: –1.9±0.9, I1: –1.9±0.8, I2: –1.8±0.8, I3: –1.7±0.7 Non-menstrual pelvic pain pelvic examination C: –0.9±0.8, I1: –0.8±1, I2: –0.8±0.8, I4: –0.6±0.8 Pelvic tenderness C: –0.8±0.8, I1: –0.8±0.8, I2: –0.8±0.7, I3: –0.7±0.6 **BMD, lumbar spine** C: 0.988±0.097, I1: 1.044±0.137, I2: 1.051±0.112, I3: 1.06±0.132	**Comments** ITT analysis All patients received calcium 1000 mg daily. To maintain blinding: subjective complaints recorded by study coordinator, physical examinations performed by study physician. The second year follow up is not included due to high drop put (70%)

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Patients may have had surgical treatment of their disease at the time of diagnosis; but, pain must have returned to baseline levels for study participation. **Follow up time** Post treatment (1 year) and 1 year FU	oral conjugated equine estrogens 0.625 mg **Participants** n=47 **Dropout** Post treatment: 8 (20%) 1st year:13 (28%) **Intervention 3** Lupron Depot 3.75 mg, IM every 4 weeks + daily oral norethindrone 5 mg + conjugated equine estrogens 1.25 mg **Participants** n=48 **Dropout** Post treatment: 14 (37%) 1st year:22 (46%) **Duration** 52 weeks		**Adverse events, %** Hot flushes; C: 88%, I1: 47%, I2: 58%, I3: 40% **Reason for premature termination** Adverse events C: 18%, I1: 18%, I2: 17%, I3: 13% Bone loss (>8%) C: 2%, I1: 0, I2: 1, I3: 0 Noncompliance C: 14%, I1: 13%, I2: 2%, I3: 17% Lack of improvement C: 2%, I1: 5%, I3: 6%, I3: 17%	
Hurst et al 2000 USA [107]	**Study design** RCT, double blind **Setting** Single centre **Population** n=13 Mean age: 30 years **Inclusion criteria**	**Intervention** Leuprolide acetate 3.75 mg IM for + the last 3 months oral estradiol 1 mg daily **Duration** 6 months **Participants** n=7 **Dropout** 0	**Comparison** Leuprolide acetate 3.75 mg IM + the last 3 months Placebo was added **Duration** 6 moths **Participants** n=6	**Endometriosis related symptoms** (pelvic pain, dysmenorrhea, dyspareunia, induration and pelvic tenderness) no statistical significant difference between the two groups **Adverse events** Hot flushes and headache lower for the intervention group, not statistical significant	**Comments** Randomisation by the hospital's investigational drug service, and all medications were prescribed through this department. GnRH agonist therapy was initiated on cycle day 1 to 3.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Laparoscopic diagnosis and treatment, persistent or recurrent chronic pelvic pain, no previous GnRH analogue treatment **Follow up time** Post treatment (6 months)		**Dropout** 0		
Johnson et al 2004 New Zealand [108] Johnson et al 2007 New Zealand [109]	**Study design** RCT, open labelled **Setting/recruitment** Single centre secondary and tertiary level infertility service setting **Population** n=62 **Inclusion criteria** Age 18–39 years, infertility due to endometriosis ≥ 12 months, early follicular FSH level of ≤10 IU/l; mid-luteal progesterone level of ≥25 mmol/l in a spontaneous Cycle, normal semen **Follow up** 6 months, 2 years	**Intervention** Lipiodol flushing performed by a HSG technique with fluoroscopic X-ray screening 1 ml Lipiodol Ultra Fluide contains 0.48 g iodine. Flushing was carried out by one of two authors in the follicular phase of the cycle between the end of menses and day 12 of the cycle **Participants** n=25 **Dropout** 6 months: 1 (4%) 2 years: 2 (8%)	**Comparison** No treatment **Participants** n=37 **Dropout** 6 months: 0 2 years: 5 (4%)	**Clinical pregnancy, n (%)** 6 months; I: 12 (48%), C: 4 (11%), RR 4.44 (95% CI, 1.61 to 12.21), p=0.001 24 months; I: 14 (56%), C: 16 (43%) RR 1.3 (95% CI, 0.8 to 2.2) **Live birth** 6 months; I: 10 (40%), C: 4 (11%), RR 3.7 (95% CI, 1.30 to 10.50), p=0.007 24 months; I: 12 (48%), C: 12 (32%) RR 1.5 (95% CI, 0.8 to 2.8) **Miscarriage <20 weeks** 6 months; I: 2 (8%), C: 0, NS	**Comments** We only analysed the population with endometrios Computer-generated randomization, allocation concealment by opaque sequentially numbered envelopes ITT analysis
Kauppila et al 1985 Finland [110]	**Study design** RCT, double blind, crossover **Setting** Single centre **Population** n=20	**Intervention** Naproxen sodium for two periods and placebo for the next two successive periods **Duration** 4 months	**Comparison** Placebo for two periods and naproxen sodium for the next two successive periods **Duration** 4 months	**Menstrual pain** 83% of the 40 naproxen sodium treatments and in 41% of the 39 placebo treatments (p=0.008).	**Comments** Moderate risk of bias Unclear randomisation and allocation. Unclear drop out

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Mean age: 33.5 years Menstrual cramps at age of ≥18: 75% Severe endometriosis: 7/20 **Inclusion criteria** Proved endometriosis characterized by moderate to very severe menstrual distress entered the present study mild- severe endometriosis **Follow up time** Post treatment (4 months)	**Participants** n=11 **Dropout** Unclear	**Participants** n=9 **Dropout** Unclear		
Keresztúri et al 2015 Hungary [111]	**Study design** Prospective clinical cohort study **Setting** Single centre, University-level tertiary care **Population** n=238 Mean age: 33 years Stage II/IV: 57% **Inclusion criteria** Laparoscopic treatment, women <40 years, couple not conceiving after at least 1 year of unprotected intercourse; confirmation of an ovulatory cycle, symptoms suggestive of endometriosis, clinical signs, incremental sonographic finding (endometrioma(s)), and a	**Intervention** Controlled ovarian hyperstimulation and intrauterine insemination (COH-IUI). COH according to the monofollicular protocol, initiated in first menstrual cycle after the operation. **Participants** n=119 **Dropout** 3 (2.5 %)	**Comparison** No treatment **Participants** n=119 **Dropout** 2 (1.7%)	**Clinical pregnancy rate** Per protocol; 62 (53%), C: 45 (39%), p=0.026 Stage I-II; I: 31 (65%), C: 25 (50%), ns Stage III-IV; I: 31 (46%), C: 20 (30%), ns **Live birth rate** Per protocol; I: 58 (48%), C: 41 (34%), p=0.024 Stage I-II; I: 30 (63%), C:22 (44%), ns Stage III-IV; I: 28 (41%), C: 19 (28%), ns	**Comments** Non-random allocation was based on age, BMI, and stage of endometriosis in order to obtain two satisfactorily comparable matched study groups. Both study groups underwent the same surgery protocol for endometriosis.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	normal spermier, no other gynecological pathologies or coexisting causes of infertility besides endometriosis were excluded. **Follow up time** 12 months				
Kiesel et al 1996 Germany [112]	**Study design** RCT, double blind **Setting** Multicentre **Population** n=123 **Inclusion criteria** Fertile premenopausal patients with r-AFS >5, no recent use of sex hormones, danazol or GnRH agonists **Follow up time** Post treatment (6 months)	**Intervention 1** Goserelin, 3.6 mg every 4 weeks + placebo for 3 months followed by medrogestone, 10 mg/day for 3 months ("*deferred HRT")* ***Duration*** 6 months ***Participants*** n=40 ***Dropout*** 11 (28%) **Intervention 2** Goserelin 3.6 mg every 4 weeks+ medrogestone, 10 mg/day; "*Goserelin immediate HRT*" ***Participants*** n=40 ***Dropout*** 9 (22%)	**Comparison** Goserelin, 3.6 mg every 4 weeks + placebo **Duration** 6 months **Participants** n=43 **Dropout** 10 (23%)	**BMD, % change** Lumbar spine: statistical significant between control group and intervention group 1 Femoral neck, ward's triangle region: no statistical significant difference between groups. For all three groups, significant decrease compared to baseline. **Change in r-AFS, score, mean** C: –10.42, I1: –14.41, I2: –19.30 ***Responder (change ≥50%)*** C: 54.5 %, I1: 62.2%, I2: 64.1% **Adverse events** Hot flushes	**Comments** Two patient discontinued treatment due to side effects related to treatment (severe depression and continues bleeding)

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Kiilholma et al 1995 Finland [113]	**Study design** RCT, double blind, placebo controlled **Setting** Multicentre, 3 tertiary referral centres, university teaching hospitals and 2 central hospitals **Population** n=88 (95% of eligible) Mean age: 33 years **Inclusion criteria** Laparoscopically confirmed endometriosis (≤3 months), symptomatic patients, total pelvic symptoms score ≥3 with or without infertility **Follow up time** Post treatment, and 6 months post treatment	**Intervention** Goserelin acetate, 3.6 mg, 28-day SC depot formulation + 2 mg 17 β-E2 and 1 mg norethisterone acetate once daily (HRT) **Duration** 6 months **Participants** n=43 **Dropout** 8 (19%)	**Comparison** Goserelin acetate, 3.6 mg, 28-day SC depot formulation + or placebo once daily **Duration** 6 months **Participants** n=45 **Dropout** 5 (9%)	**Subjective improvement** ***Pelvic symptoms score*** BL; I: 4.7, C: 4.7 Post; I: 0.9, C: 0.5, ns, 6 months FU*:* in both groups sign difference compared to BL but not between the two groups **Objective improvement** ***r-AFS, total score*** BL; I: 22.3, C: 19.9 Post; I: 10.7, C: 9.2 Ns between groups, but within groups ***Total additive diameter, mm*** BL; I: 31.8, C: 33.6 Post; I: 12.1, C: 8 Ns between groups, but within groups **Adverse events** Hot flushes; statistical significant difference between groups in favour for intervention group	**Comments** Therapy was started during menstruation, preferably on the 1st day. Unclear randomisation
Kim et al 1996 Korea [114]	**Study design** RCT **Setting** Single centre **Population** n=80 Mean age: 32 Stage I/II: 49% **Inclusion criteria** Infertile patients, scheduled for ovulation induction with IUI	**Intervention** Ultralong protocol: One dose 3.75 mg D-Trp-6-lutcinizing hormone-releasing hormone agonist IM, mid-luteal phase of the menstrual cycle. After 4 weeks; daily s.c. 0.1 mg Decapeptyl for ≥2 weeks prior to ovarian stimulation **Duration** 6 weeks	**Comparison** Long protocol Daily s.c.0.1 mg Decapeptyl, initiated from the mid-luteal phase of the menstrual cycle **Participants** n=41 **Dropout** 0	**Clinical pregnancies, n (%)** I: 19 (49%), C: 11 (27%), p<0.05 ***According to stage:*** ***Stage I/II*** I: 9 (47%), C: 7 (35%) ***Stage III/IV*** I: 10 (50%), C: 4 (19%), p<0.05 **Delivered (% per pregnancy)** I: 6 (32%), C: 4 (36%), ns **Multiple pregnancies** I: 3 (16%), C: 1 (9%), ns	**Comments** Unclear allocation. Not blinded ***For both groups:*** Administration of human menopausal gonadotrophin and human follicle stimulating hormone commenced after complete suppression of ovarian function

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	endometriosis diagnosed and staged by laparoscopy, no medication for ≥6 months. **Follow up** Unclear	**Participants** n=39 **Dropout** 0			
Kitawaki et al 2008 Japan [115]	**Study design** RCT **Setting** Single centre **Population** n=55 Mean age: 35.5±7.7 Stage III/IV: 37.8% **Inclusion criteria** Diagnose of endometriosis after conservative surgery with either laparoscopy or laparotomy and experiencing recurrent endometriosis-related pelvic pains, no first-line surgery or endocrine therapy ≥6 months before enrolment, DIE was defined as presence of histologically confirmed peritoneal endometriosis penetrating >5 mm **Follow up time** Post treatment	**Intervention** Buserelin acetate, 1.8 mg, or leuprorelin acetate 1.88 mg, SC once a monthly 1 month after last GnRH treatment; mid-dose of cyclic OC; ethinyl estradiol 0.05 mg and norgestrel 0.5 mg, or mestranol 0.05 mg and norethisterone 1 mg **Duration** GnRH analogue: 6 months OC: 12 months **Participants** n=35 **Dropout** 1	**Comparison** Buserelin acetate, 1.8 mg, or leuprorelin acetate 1.88 mg, SC montly, 1 month after last GnRH treatment; low-dose of cyclic OC: ethinyl estradiol 0.035 mg and norethisterone 1 mg or ethinyl estradiol EE 0.03 mg and desogestrel 0.15 mg **Duration** GnRH analogue: 6 months OC: 12 months **Participants** n=20 **Dropout** 1	**Pain (VAS)** Treatment with a GnRH-a for reduced dysmenorrhea (p<0.01), non-menstrual pelvic pain (p<0.01), dyspareunia (p<0.01). **Dysmenorrhea;** Worsened in both groups compared with end of GnRH-a-therapy (p<0.05). no significant difference between groups. ***Non-menstrual pelvic pain and dyspareunia;*** Both groups maintained the suppressive effect of the GnRH-a therapy without worsening of the symptoms, no sign difference between groups **Endometrioma, diameter** Reduced significantly by GnRH-a therapy (p<0.01) and by both maintenance therapies (p<0.05). **Safety** Milder AE in low dose compared to mid dose	**Comments** The arm with danazol treatment is not included in the analysis Randomization unclear but likely OK “assigned randomly by chart numbers” GnRH treatment starting from day l–5 of the menstrual cycle
Komsky-Elbaz et al 2013 USA [116]	**Study design** RCT **Setting/recruitment** Single centre	**Intervention** IVF **Participants** n=35	**Comparison** ICSI, only MII oocytes were injected	**Pregnancy rate per ET** IVF: 26.1% ICSI: 21.8%, ns	**Comments** Unblinded Unclear allocation

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Population n=35 Stage III/IV (r-AFS) Sibling oocytes insemination **Inclusion criteria** Age ≤40 years, laparoscopic diagnosis of endometrios, couples where the male is normozoospermic and the woman has ≥6 cumulus–oocyte complexes (COC) retrieved, day 3 FSHlevel <12 mUI/ml **Follow up time** Unclear	Mean no of oocytes/cycle: 7±4.2 **Dropout** 0	**Participants** n=35 Mean no of oocytes/cycle: 7.3±4.1 **Dropout** 0	**Clinical pregnancy rate per ET** IVF: 21.7% ICSI: 21.9%, ns **Ongoing pregnancy ≥12 weeks** IVF: 13% ICSI: 15.6%, ns	For both groups: Routine controlled ovarian hyperstimulation (COH) for IVF using long GnRH agonist Protocol
Koninckx et al 2008 Belgium [117]	**Study design** RCT double-blind, placebo controlled, pilot study **Setting** Single centre **Population** n=21 Age 18–50 years **Inclusion criteria** Pelvic pain and scheduled for surgical excision of a rectovaginal endometriotic nodule ≥1 cm in diameter, treatment with hormonal medication ≥3 months prior to study. If not sterilized, patient had to use a double-barrier method of contraception up to 6	**Intervention** Three infusions of infliximab (anti TNF- α) (5 mg/kg) + surgery 4–6 weeks after the last infliximab dose **Duration** 12 weeks treatment followed by surgery **Participants** n=14 **Dropout** 0	**Comparison** Placebo + surgery **Participants** n=7 **Dropout** 0	**Pain (Biberoglu & Behrman)** No statistical significant difference between groups **Volume of the endometriotic nodule Mean ±SD** I: 15±2.38 mm C: 13.2±3.4 mm **Side effects** No AE in placebo I: 4	**Comments** Randomization was performed by consecutive sealed envelopes opened by the pharmacist prior to the preparation of medication. Randomization code was broken only after the database had been locked. All investigators, research nurses and patients were blinded throughout the study.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	months after receiving the last infusion with infliximab. **Follow up time** 6 months				
Köhler et al 2009 Germany [118]	**Study design** RCT, open labelled **Setting** Multicentre **Population** n=64 Mean age: 29 years Mean r-AFS score: 10.6 **Inclusion criteria** Histologically confirmed endometriosis stage I–III (r-AFS), women between menarche and menopause. No ablative surgery, washout periods for previous hormonal therapies were 2 weeks for oral therapy, 6 weeks for depot treatments, and 2 weeks for intranasal (GnRH agonist) therapy. **Follow up time** Post treatment (24 weeks)	**Intervention** Dienogest 4 mg once a day orally **Duration** 24 weeks **Participants** n=35 **Dropout** 5 (4%)	**Comparison** Dienogest 2 mg once a day orally **Duration** 24 weeks **Participants** n=29 **Dropout** 5 (17%)	**r-AFS score, mean ±SEM** I: 3.9±0.74, C: 3.6±0.95, ns **Clinical symptoms, decrease %** Dyspareunia I: 5.7%, C: 6.9% Diffuse pelvic pain I: 14.3%, C: 27.6% Dysmenorrhea I: 11.4%, C: 13.8% Premenstrual pain I: 2.9%, C: 3.4% **Adverse events** Nausea: I: 2 (6.7%), C: 0 Bloated feeling; I: 2 (6.7%), C: 1 (4.2%) Meteorism; I: 5 (16.7%), C: 12.5%) Headache; I: 7 (23%), C: 17%) Depressive mood; I: 1 (3%), C: 2 (8%) Other; I: 10 (33%), C: 4 (17%)	**Comments** The group with 1 mg dienogest was haltered prematurely and is not included in the analyse Rate of compliance 96% Unclear allocation
Lee et al 2017 Korea [119]	**Study design** Prospective CCT **Setting** Single centre **Population**	**Intervention** Conservative laparoscopic surgery + GnRH agonist with add–back GnRH: leuprorelin acetate 3.75 mg, SC, every 4 weeks (6 cycles in total)	**Comparison** Conservative laparoscopic surgery + oral dienogest; (Visanne) 2 mg/day **Duration** 6 months	**Pelvic pain, (VAS, 1–10)** No significant difference between the groups, both had significant reduced pain compared to baseline	**Comments** All surgery performed by one doctor

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	n=64 Mean age: 30 years r-ASMR stage III: 67% **Inclusion criteria** All reproductive-aged women (18–45 years), conservative laparoscopic surgery for pain and ovarian endometrioma (r-ASRM stage III or IV), endometriosis confirmed by histology; women who did not want to conceive immediately **Follow up time** 3 and 6 months (post treatment)	add–back: 1.0 mg/day of estradiol and 0.5 mg/day of norethisterone acetate **Duration** 6 months **Participants** n=28 **Dropout** 5 (18%)	**Participants** n=36 **Dropout** 10 (27%)	**QOL (World Health Organization Quality of Life Questionnaire (WHOQOL-BREF))** No significant difference between the groups **BMD g/cm^2** ***Lumbar spine (L1–4);*** BL; I: 0.979, C: 0.954 6 months; I: 0.954 (–2.5%), C: 0.932 (–2.3%), ns ***Femur*** I: 0.3%, C: –0.7%, ns **Adverse events n (%)** Hot flush; I: 3 (11.5%), C: 4 (11.1%) Genital dryness I: 3 (11.5%), C: 1 (2.8%) Depression; I: 1 (3.8%), C: 4 (11.1%) Sleep disorder; I: 2 (7.7%), C: 4 (11.1%) Acne; I: 1 (3.8%), C: 3 (8.3%) Headache; I: 1 (3.8%), C: 2 (5.6%) Weight gain; I: 0, C: 1 (2.8%) Decreased libido I: 0, C: 0 ***Uterine bleeding*** Menstruation-like bleeding*; I: 1 (0.8%), C: 14 (53.8%), p<0.05 Spotting; I: 8 (22.2%), C: 20 (55.6%), p<0.05 Irregular bleeding; I: 0, C: 3 (8.3%)	
Li et al 2014 China [120]	**Study design** RCT **Setting** Single centre **Population**	**Intervention** Triptorelin 3.75 mg, IM postoperative during days 1–3 of the menstrual cycle and thereafter every 28–30 **Duration**	**Comparison** Leuprorelin depot, 3.75 mg, IM postoperative during days 1–3 of the menstrual cycle and thereafter every 28–30 **Duration**	**Adverse effects, %** Hot flushes & sweating; I: 37%, C: 37% Anxiety; I: 30%, C: 39%* Depression; I: 32%, C: 24%* Vaginal dryness; I: 44%, C: 32%* Acne; I: 39%, C: 20%* Bone pain; I: 41%, C: 44%	**Comments** Randomized into two groups with use of a random table Patients were kept blind to the choice of

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	n=302 Mean age: 29 years **Inclusion criteria** Age 18-49, diagnosis of ovarian endometrioma following laparoscopic surgery (excision of ovarian endometrioma) (histopathologic confirmation), stage III–IV endometriosis, r-AFS ≥15. Patients advised to use nonhormonal forms of contraception after the recruitment and throughout the treatment period. No hormone treatment previous 6 months **Follow up time** Posttreatment (3 months)	3 months **Participants** n=151 **Dropout** 13 (9%)	3 months **Participants** n=151 **Dropout** 9 (6%)	Headache; I: 18%, C: 12%* Insomnia; I: 23%, C: 20% Irregular bleeding; I: 48%, C: 47% Loss of libido; I: 223%, C: 22% *=p<0.05	different GnRH-a formulations
Loverro et al 2008 Italy [121]	**Study design** RCT, single blind **Setting** Single centre **Population** n=60 Mean age 29 years Endometrioma: 65% **Inclusion criteria** Diagnosed laparoscopically, stage III–IV, with chronic pelvic pain, adnexal mass or infertility; complete laparoscopic excision; r-AFS score >15 points, no previous hormonal treatment. **Follow up time**	**Intervention** Conservative surgery + triptorelin depot 3.75 mg, IM, on the 20th day of the menstrual cycle, thereafter every 28 days **Duration** 3 months **Participants** n=30 **Dropout** 1 (3%)	**Comparison** Conservative surgery + placebo (saline injections) **Duration** 3 months **Participants** n=30 **Dropout** 5 (16%)	**Pelvic pain (Biberoglu & Behrman)** ***Persistence or recurrence,*** I: 13/29, C: 12/25, ns ***Endometrioma recurrence*** I: 4/19, C: 2/16, ns ***Spontaneous pregnancies*** I: 5/14, C: 6/13, ns	**Comments** Computer-generated randomization table

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	5 years				
Makarainen et al 1996 Finland [122]	**Study design** RCT, double blind **Setting** Single centre **Population** n=38 **Inclusion criteria** Laparoscopically confirmed endometriosis, symptomatic pelvic endometriosis, r-AFS ≥2 **Follow up** Post treatment and 6 months	**Intervention** Goserelin acetate 3.6 mg, SC +MPA,100 mg daily **Duration** 6 months **Participants** n=19 **Dropout** Posttreatment: 3 (16%) 6 months: 6 (31%)	**Comparison** Goserelin acetate 3.6 mg, SC + placebo one tablet daily **Duration** 6 months **Participants** n=19 **Dropout** Posttreatment: 1 (5%) 6 months: 3 (16%)	**Endometric implants, disappeared (additive diameter 0)** I: 3, C: 2 **Pelvic symptom score** (dysmenorrhea, dyspareunia, pelvic pain); similar decrease in both groups that remined significant 6 months after end of treatment **Adverse events** Hot flushes and sweating significant less in MPA group 3 and 6 months Other AE occurred in similar frequency in both groups	**Comments** Medical treatment was started within 2 months of diagnostic laparoscopy. No ITT
Matorras et al 2002 Spain [123]	**Study design** RCT **Setting** Single centre, university hospital **Population** n=172 Mean age: 47.7±5.1 years Stages III/IV: 82.1% Adenomyosis: 13% **Inclusion criteria** Bilateral salpingo-oophorectomy (BSO) irrespective of associated surgical procedures, no hormonal treatments during the 6-month period before surgery,	**Intervention** BSO + HRT; sequential administration of estrogens and progesterone (Belchetz's criteria). Two 1.5-mg estradiol 22-cm^2 patches were applied/week (=50 µg release /day). Micronized progesterone administered orally during 14 days, 200 mg/24 hours, 16-day interval free of treatment. HRT was started 4 weeks after BSO **Participants** n=115 **Dropout** 0	**Comparison** BSO+ no treatment **Participants** n=57 **Dropout** 0	**Recurrence rate, n** I: 4/115, C: 0/57, ns Per year; I: 0, C: 0.9	**Comments** Computer randomly generated numbers, ratio 2/1, sealed envelopes

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	no medical treatment for endometriosis. **Follow up time** Mean follow up time was 45 months				
Mendes da Silva 2017 Brazil [124]	**Study design** RCT, double blind **Setting/recruitment** University Hospital, single centre **Population** n=44 (18% of screened) Mean age: 34 years **Inclusion criteria** Ages 20–50 years, laparoscopic diagnosis of endometriosis. Exclusion criteria: pregnancy, allergy to resveratrol, or contraindications to COC, use of agonists of gonadotropin release hormone or danazol in the last month, or had used depot medroxy-progesterone acetate or Mirena. **Follow up time** Post treatment (42 days)	**Intervention** Resveratrol (40 mg/d) + monophasic contraceptive pill (COC); levonorgestrel 0.15 mg/ethinyl estradiol 0.03 mg, continously **Duration** 42 days **Participants** n=22 **Dropout** 2 (9%)	**Comparison** Monophasic contraceptive pill (COC): levonorgestrel 0.15 mg/ethinyl estradiol 0.03 mg, continously + placebo **Duration** 42 days **Participants** n=22 **Dropout** 1 (4.5%)	**Pain score (VAS) Median (range)** I: 3.2 (0, 8), C: 3.9 (0, 8.9), p=0.7 Difference between medians (95% CI) 0.75 (–1.6 to 2.3) **Used pain medication (n)** I: 7 (32%), C: 8(36%) **Side Effects, n** Diplopia I: 1, C: 0 Headache; I: 6, C: 7 Reduced libido; I: 1, C: 0 Nausea; I:1, C: 2 Breast tenderness; I:1, C: 0 Hot flushes; I:1, C: 0 Increased uterine bleeding; I: 1, C: 0 Candidiasis; I:1, C: 0 Dyspareunia; I: 0, C: 1	**Comments** Randomized using a computer-generated randomization list (1:1) sealed envelope ITT analysis ClinicalTrials.gov (no. NCT02475564).
Miller et al 2000 USA [125]	**Study design** RCT, double blind **Setting** Single academic site **Population** n=120	**Intervention** Leuprolide acetate 3.75 mg single IM for 4 weeks **Duration** 4 weeks **Participants**	**Comparison** Placebo **Duration** 4 weeks **Participants** n=60	**Pain score (VAS 0–100) mean±SD** I: 18.91±0.47, C: 9.50±0.44, (p<0.0001) **Endometriosis symptom severity (ESS) scores** I: 7.22±0.30, C: 4.32±0.27 **QoL, SF36, score, mean±SD**	**Comments** ***Statistic metho***d: Paired t tests Unclear allocation

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Inclusion criteria Age 18–40, laparoscopically diagnosed endometriosis ≤24 months, intact uterus and at least one ovary in good health, no treatment within ≤3 months, no treatment with medroxyprogesterone acetate within ≤6 months, not used GnRH-analogue **Follow up** Post treatment: 4 weeks	n=60 **Dropout** 0	**Dropout** 0	Physical component, t score I: –0.64±0.07, C: –0.18±0.06 Mental component, t score I: –0.58±0.05, C: –0.12±0.04 **Adverse event** No adverse events occurred	
Moghissi et al 1987 USA [126]	**Study design** Prospective controlled study **Setting** Single centre **Population** n=144 **Inclusion criteria** Infertile patients, laparoscopically confirmed stage I/II endometriosis (AFS). Patients with ovulatory disorders, cervical factor or male factor were included only if these problems were correctable and ultimately non-contributory. Exclusion; other pelvic disorders, those whose husband had severe oligospermia and were unwilling to have donor anificial insemination	**Intervention 1** Medroxyprogesterone acetate (MPA) 10 mg three times daily orally **Duration** 90 days **Participants** n=36 **Dropout** NR	**Comparison** No treatment **Participants** n=56 **Dropout** NR	**Pregnancy rate** Cumulative pregnancy rate, 30 months; I: 71%, C: 55%, ns	**Comments** Patients were assigned to treatment groups based upon factors which included presence or absence of pain, their desires and fears regarding usage of medication Danazol treated group was excluded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Follow up time Minimum of 30 months				
Muzii et al 2000 Italy [127]	**Study design** RCT **Setting** Single centre **Population** n=70 Mean age: 28 years (range 20–35) Mean r-AFS: 44.7 **Inclusion criteria** Ultrasonographic diagnostic of ovarian endometriomas within 8 weeks, moderate-to-severe dysmenorrhea/ chronic pelvic pain (≥4 VAS), no previous surgical treatment for endometriosis, no oral contraceptives the previous 6 months. No DIE, **Follow up** 12–48 months	**Intervention** Laparoscopic excision of endometriomas by stripping technique After surgery; cyclic monophasic combined OP: ethinyl estradiol, 0.030 mg, and gestodene, 0.075 mg, daily for 21 days followed by a 7-day interval **Duration** 6 months **Participants** n=35 **Dropout** 2 (6%)	**Comparison** Laparoscopic excision of endometriomas by stripping technique + placebo **Duration** 6 months **Participants** n=35 **Dropout** 0	**Endometrioma recurrence, n (%)** I: 2 (6.1%) at 18 and 35 months C: 1 (2.9%) at 12 months **Persistence** Mean time to recurrence (months) I: 18.2, C: 12.7 **Pain recurrence (≥4 VAS, scale 0–10), N (%)** I: 3/33 (9.1%), C: 6/35 (17.1%) **Life table analysis** 12-month: I: 0.062, C: 0.101; p=0.041 24 months: I: 0.094, C: 0.136, ns 36 months: I: 0.121, C: 0.174, ns	**Comments** Randomization via computer generated sequence, blinding unclear Patient not blinded, unclear if assessor was blinded
Muzii et al 2011 Italy [128]	**Study design** RCT **Setting** Multicentre, tertiary care university hospitals. **Population** n=57 Mean age: 30 years	**Intervention** Laparoscopic excision + continuous monophasic combined estroprogestins (ethinyl estradiol, 0.020 mg, and desogestrel, 0.150 mg/) **Duration** 6 months	**Comparison** Laparoscopic excision + cyclic monophasic combined estroprogestins 21 days, followed by a 7-day interval **Duration** 6 months **Participants**	**Endometrioma recurrence, n** 12 months, I: 0, C: 1 (3.6%), ns **Pain recurrence (VAS), n (%)** I: 5 (17%), C: 9 (32%), ns **Pain core** No sign between groups **Mean time to recurrence (symptoms or endometrioma)** I: 16 months, C: 12 months, ns	**Comments** Unclear if assessor blinded ITT analysis

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Inclusion criteria Age: 18-40 years, diagnosis at study entry, ovarian endometrioma >3 cm, moderate to severe dysmenorrhea or chronic pelvic pain (≥4 VAS), no previous medical or surgical therapy for endometrimosis (except for the use of estroprogestins, but not the last 6 months). **Follow up time** >6 months (mean 22)	**Participants** n=29 **Dropout** 0	n=28 **Dropout** 0	**Patient satisfaction, very satisfied or satisfied** 6 months; 100% in both groups 12 months; I: 93%, C: 82%, ns 24 months; I: 83%, C: 68% **Discontinuation** Due to AE: I: 12 (41%), C: 4 (14%), p=0.03 Break through bleeding; I: 10/12, C: 2/4 Headache; I: 2/12, C: 2/4	
Osuga et al 2017 Japan [129]	**Study design** RCT, Phase III, double-blind, placebo-controlled study **Setting/recruitment** Multicenter **Population** n=67 Adenomysosis Mean age: 37 years **Inclusion criteria** Aged ≥20 years, regular menstrual cycles of ≤38 days, adenomyosis diagnosed by MRI and transvaginal sonography, pain symptoms scoring ≥3 on the verbal pain rating scale **Follow up time** Every 4 weeks	**Intervention** Dienogest (DNG) 2 mg/d, orally **Duration** 16 weeks **Participants** n=35 **Dropout** 1 (3%)	**Comparison** Placebo **Duration** 16 weeks **Participants** n=33 **Dropout** 0	**Symptoms** ***Pain score, 0–3 verbal rating scales*** BL; I: 4.6±1.1, C: 4.8±1.0, p=0.298 Change at 16 weeks I: –3.8±1.9, C: –1.4±1.8, p<0.001 ***Pain severity score, 0–3 verbal rating scales*** BL; I: 2.4±0.5, C: 2.5±0.5, p=0.397 Change at 16 weeks I: –1.9±1.0, C: –0.6±0.8 p<0.001 ***Pain, VAS (mm)*** BL; I: 66.3±19.1, C: 69.0±20.6, p=0.518 Change at 16 weeks I: –58.4±23.6, C: –20.6±23.6, p<0.001 **QoL, MOS 36-Item Short-Form Health, mean±SD** Physical functioning I: 2.4±7.9, C: 5±14.0, p=0.085 Role physical I: 12.5±36, C: 6.8±41.1, p=0.038 Bodily pain	**Comments** Randomization by permuted-block (1:1) Allocation concealment centrally by an independent organization and maintained blindness for patients, investigators, and sponsor

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				I: 38.1±29.7, C: 11.7±31.6, p<.001 General health I: 2.3±9.9, C –0.7±14.1, p=0.351 Vitality I: 6.5±16.7, C: 2.0±13.3, p=0.234 Social functioning, I: 8.5±17.1, C: 4.9±22.3, p=0.094 Role emotional I: 4.9±33, C: 7.1±28.6, p=0.275 Mental health I :4±14.5, C: –1.5±17, p=0.0214 **Adverse events** AEs; I: 34/34, C: 76% (25/33) ADRs; I: 34/34, C: 46% (15/33) No serious AEs in either group. Irregular uterine bleeding I: 97% (33/34), C: 39% (13/33) Hot flush; I: 6% (2/34), C: 0,	
Ozdegirmenci et al 2010 Turkey [130]	**Study design** RCT **Setting** Single centre (Women's health teaching and research hospital) **Population** n=86 Mean age: 45 years **Inclusion criteria** Clinical suspicion of adenomyosis, confirmed by TVUS, complaining of menorrhagia and/or dysmenorrhea. absence of bleeding ≥3 months No use of oral progestagen during previous 3 months. **Follow up time**	**Intervention** Levonorgestrel intrauterine system (LNG-IUS) **Duration** 1 year **Participants** n=43 **Drop-out** 0	**Comparison** Hysterectomy **Participants** n=43 **Dropout** 11 (26%)	**Health-related QOL, WHOQOL-BREF TR** All five domain scores: not statistically different between groups; Physical; Z=0.61 4; p=0.539, Psychological; Z=0.773; p=0.440 Social; Z=0.381; p=0.703 Environmental; t=1.368; p=0.176, Environmental-TR; t=1.579; p=0.119 **Amenorrheic** 6 months; I: 10 (3.8%) 1 year; I: 22 (51.4%) **Adverse events** ***LNG-IUS*** Headache: 11.9%, Breast tenderness 7.1% Acne: 4.8% Transient depressive episode: 2.4%	**Comments** Randomization was based on computer-generated codes. Assessors were blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	1 year			Postoperative wound infection: 3%	
Pabuccu et al 2004 Turkey [131]	**Study design** Prospective controlled study **Population** n=171 The patients went through 171 ICSI cycles with ejaculated sperm. These patients were then divided into four groups. Mean age: 30 years Mean year of infertility: 6 years **Setting** University hospital. **Inclusion criteria** Patients with ovarian endometriosis and tubal factor infertility. **Follow up time** Unclear	**Intervention 1** Aspiration of endometriomas at the beginning of controlled ovarian stimulation (COH) in patients with ovarian endometriomas and no history of previous surgery **Participants** n=41 Mean age: 30.2±4.9 **Dropout** *NR*	**Comparison 1** Non-aspirated endometriomas **Participants** n=40 Mean age:30.1±4.5 **Dropout** *NR*	**Clinical pregnancy rate** Aspirated: 24% Nonaspirated: 20% Resected: 25% Tubal: 30%	**Comments** The group with tubal factor infertility is not included
Parazzini et al 1994 Italy [132]	**Study design** RCT, double blind **Setting** Multicentre **Population** n=75 Stage IV: 50% **Inclusion criteria** Age <38 years, unexplained primary/secondary infertility ≥1 year, with or without chronic pelvic pain, diagnosis of	**Intervention** Nasal nafarelin,100 µg/day **Duration** 3 months **Participants** n=36 **Dropout** 0	**Comparison** Placebo **Duration** 3 months **Participants** n=29 **Dropout** 0	**Dysmenorrhea and pelvic pain (VAS 0–10), mean reduction±SD** I: 7.0±4.1, C: 6.9±4.6 **Pregnancy n (%)** I: 7 (19%), C: 7 (18%) **Adverse events** Not reported	**Comments** Randomisation by computer-generated randomisation list. Unclear allocation concealment. Women and investigators were blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	endometriosis stage III or IV (r-AFS), revised, laparotomy as first surgical treatment for debulking or radical surgery of endometriotic lesions, no previous clinical or laparoscopic diagnosis of endometriosis **Follow up time** 12 months				
Parazzini et al 2000 Italy [133]	**Study design** RCT, open label **Setting** Multicentre **Population** n=97 Mean age: 30/31 years Stage II/IV: 45% ***Previous surgery for endometriosis*** Laparoscopy: 81% Laparotomy: 19% **Inclusion criteria** Laparoscopically confirmed endometriosis and pelvic pain lasting 3–12 months after laparotomy, no previous GnRHa or danazol therapy, no estroprogestin pills 6 months before study. **Follow up time** Post treatment (12 months)	**Intervention** Estroprogestin pills (E/P), gestroden 0.75 mg and ethynlestradiol 30 µg **Duration** 12 months **Participants** n=47 **Dropout** 2 (4%)	**Comparison** Tryptorelin, 3.75 mg slow release every 4 weeks for 4 months followed by E/P pill for 8 months **Duration** 12 months **Participants** n=55 **Dropout** 1 (2%)	**Symptoms (Andersch & Milsom's scale, 0–3),** Dysmenorrhea; n (%); I: 14 (30%), C: 16 (30%) Score (median); I: 2, C: 0 Non-menstrual pain n (%); I: 15 (32%), C: 17 (31%) Score (median); I: 0, C: 0 **Use of treatments for pain relief, n (%)** I: 15 (31%), C: 16 (29%)	**Comments** Allocation was done by telephonecal to randomization centre ITT analysis No form of medical treatment for pain during study

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Petta et al 2005 Brazil [134]	**Study design** RCT **Setting** Multicentre (3 centres) **Population** n=83 Mean age: 30 years Stage III/IV: 71% VAS score >7–10: 58.5% Use of medication before study: 17% **Inclusion criteria** Age 18–40 years, laparoscopically + histologically confirmed endometriosis 3–24 months prior study, cyclic chronic pelvic pain with or without dysmenorrhea, VAS pain score ≥3, regular menstrual cycle for ≥3 months, no hormone treatment for ≥3 months, no use of progestins or GnRH-agonist ≥9 months prior to **Follow up time** Post treatment (6 months)	**Intervention** Lupron 3.75 mg every 28 days IM **Duration** 6 months **Participants** n=43 **Dropout** 6 (14%)	**Comparison** LNG-IUS 20 μg/day for 5 years **Duration** 6 months **Participants** n=39 **Dropout** 5 (13%)	**Symptoms, VAS** ***Pain score, mean ± SEM*** LNG-UIS: –6±0.3 GnRH: –6±0.2, ns ***Pain score >3, n (%)*** LNG-UIS: 5 (15%) GnRH: 6 (16%), ns **No bleeding (%)** LNG-UIS: 70%, GnRH a: 98% **Side effects** Abdominal distension; p=0.458 Peripheral oedema; p=0.098 Serious adverse events; 0 in both groups **QoL Psychological general wellbeing index (PGWBI),** Increase, mean ± SD LNG-UIS: 8.3±15 GnRH a: 6.8±18.2, p=0.474	**Comments** Computer-generated system of sealed envelopes Patient not blinded Unclear if assessor was blinded No ITT
Regidor et al 2001 Germany [135]	**Study design** RCT, open label **Setting** Single centre **Population**	**Intervention** Lynestrenol (LYN), 5 mg orally twice per day **Duration** 6 months	**Comparison** Leuprorelin acetate (LA), 3.75 mg sc per month **Duration** 6 months	**Symptoms, Biberoglu & Behrman** ***Dysmenorrhea, improved, n (%)*** LYN: 11 (50%) LA: 22 (85%), p<0.007 ***Chronic pelvic pain, improved, n (%)*** LYN: 13 (59.1%) LA: 18 (69.2%), ns	**Comments** Unclear randomisation and allocations

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	n=48 Mean age: 32 years **Inclusion criteria** Age ≥18, premenopausal, Postoperative r-AFS score (score after removal of endometriotic lesions or adhesions) between I and IV, regular menstruation cycle, no treatment with hormonal drugs ≥3 months **Follow up** Post treatment (6 months)	**Participants** n=22 **Dropout** 0	**Participants** n=26 **Dropout** 0	***Dyspareunia, improved, n (%)*** LYN: 5 (22.7%) LA: 13 (50%), p<0.04 **r-AFS score** LYN: 25.5±27.99 LA: 11.5±14.99 **Side effects, complaints, n (%)** LYN: 18 (82 %), LA: 23 (89 %) Hot flushes LYN: 13 (59 %), LA: 21 (81 %) Sweating LYN: 9 (41 %), LA: 14 (54 %)	
Remorgida et al 1990 Italy [136]	**Study design** Prospective cohort study **Setting** Single centre **Population** n=60 (drop out n=5) Mean age: 33 years Previous medical treatment for endometriosis: 80% Mean infertility: 7 years **Inclusion criteria** Stage II and III endometriosis, no other cause of infertility, free from any medication for at least 6 months **Follow up time** Unclear	**Intervention 1** Long buserelin acetate protocol; analogue luteinizing hormone (LH)-releasing hormone ethylamide, buserelin acetate IN, 200 µg x 5/d, started in luteal phase of the latest menstrual cycle + GnRH analogue (same as control) **Duration** At least 6 months **Participants** n=20 **Dropout** 0 **Intervention 2**	**Comparison** GnRH analogue 3 ampules follicle-stimulating hormone (FSH) 75 IU per ampule, day 3, 4, and 5. Thereafter, a combination of FSH and human menopausal gonadotropin 75 IU LH + 75 IU FSH per ampule, was used; the dosage was decided each day on the basis of the patient's response. **Participants** n=20 **Dropout** 0	**Clinical pregnancy** I1: 10 (56%), I2: 6 (32%), C: 6 (33%), ns **Live birth** I1: 7, I2: 4, C: 5	**Comments** Gamete intrafallopian transfer (GIFT). Patients were assigned to three different stimulation regimens on the basis of their r-AFS score to obtain an even distribution of endometriosis stages among the three groups Unblinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
		Short buserelin acetate protocol: analogue luteinizing hormone (LH)-releasing hormone ethylamide, buserelin acetate IN, 200 µg x 5/d, started in luteal phase of the latest menstrual cycle + GnRH analogue (same as control) **Duration** 3 months **Participants** n=20 **Dropout** 0			
Rickes et al 2002 Germany [137]	**Study design** RCT, open labelled **Setting** Single centre, University clinic for reproductive medicine and gynecologic endocrinology **Population** n=110 Age range: 23–40 years **Inclusion criteria** Age <40 years, stage II to IV endometriosis (ASRM) diagnosed by video-laparoscopy	**Intervention** Surgery+ goserelin 3.6 mg, SC, start day 3 after surgery. before ART, 5 or 6 cycles IUI in patient without fallopian tube otherwise IVF or ICSI **Duration** 6 months **Participants** n=55 IUI, n=27 IVF/ICSI, n=28 **Dropout** 0	**Comparison** Surgery before ART **Participants** n=55 IUI, n=36 IVF/ICSI, n=19 **Dropout** 0	**No of pregnancies, n (%)** I+IUI: 24 (89%) C+IUI: 22 (61%), p<0.05 I+IVF/ICSI: 21 (75%) C+IVF/ICSI: 9 (47%) **Pregnancy related to stage** ***STAGE II*** I+IUI: 86%, C+IUI: 58%, ns I+IVF/ICSI: 100%, C+IVF/ICSI: 70%, ns ***STAGE III-IV*** I+IUI: 50%, C+IUI: 56%, ns I+IVF/ICSI: 82%, C+IVF/ICSI; 40%, p<0.05	**Comments** Randomized by computer in blocks of six

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Follow up Unclear				
Roux et al. 1995 France [138]	**Study design** RCT, double blinded **Setting** Singe centre **Population** n=40 (out of 42 included) Mean age: 34.0±6.5 years **Inclusion criteria** Endometriosis diagnosed by clinical and hystero-salpingography signs and/or laparoscopy. No amenorrhoeic patients, no drugs known to affect bone metabolism **Follow up time** Post treatment	**Intervention 1** Triptoreline, IM, 3.75 mg every 4 weeks + calcium (1 g daily), + nasal salmon calcitonin (sCT), 100 IU daily **Duration** 6 months **Participants** n=13 **Dropout** 0 **Intervention 2** Triptoreline, IM, 3.75 mg every 4 weeks + calcium (1 g daily), + nasal salmon calcitonin (sCT), 200 IU daily **Duration** 6 months **Participants** n=13 **Dropout** 0	**Comparison** Triptoreline, IM, 3.75 mg every 4 weeks + calcium (1 g daily) + placebo **Duration** 6 months **Participants** n=14 **Dropout** 0	**BMD, g/cm2, mean±SD** Lumbar spine; I1: 1.01±0.15, I2: 0.99±0.14, C: 1.03±0.09 Femoral neck; I1: 0.82±0.15, I2: 0.77±0.13, C: 0.83±0.12 Trochanteric area; I1: 0.69±0.10, I2: 0.67±0.08, C: 0.72±0.08 Ward's triangle; I1: 0.70±0.15, I2: 0.64±0.13, C: 0.70±0.12 Intertrochanteric area; I1: 1.04±0.16, I2: 1.02±0.16, C: 1.08±0.13 Radius distal; I1: 0.42±0.06, I2: 0.40±0.06, C: 0.42±0.03 Radius proximal; I1: 0.64±0.04, I2: 0.64±0.03, C: 0.65±0.04 **Side effects** No difference between the groups	**Comments** Randomization and allocation unclear. ITT analysis
Schwertner et al 2013 Brazil [139]	**Study design** RCT, phase II, double blind **Setting**	**Intervention** Taken at bed time: 10 mg melatonin tablets **Duration**	**Comparison** Taken at bed time: placebo tablets **Duration**	**Pain (VAS), adjusted mean difference (95% CI)** Worst pain during the last 24 hours (daily): 1.80 (0.59–1.97), p<0.0001 Dysmenorrhea;	**Comments** Randomization; block size of 4 Envelopes sealed and numbered sequentially

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Single centre, gynaecological clinic **Population** n=40 Mean age: 37 years Stage III/IV: 70% Daily use of opioids: 12.5% Daily use of NSAID: 47.5% **Inclusion criteria** Age 18–45, endometriosis diagnosis by laparoscopic surgery, chronic pelvic pain and/or dyspareunia as a moderate-to severe pain intensity lasting for more than 6 months, score ≥4, requiring regular analgesic **Follow up time** Post treatment (8 weeks)	8 weeks **Participants** n=20 **Dropout** 3 (15%)	8 weeks **Participants** n=20 **Dropout** 1 (5%)	2.6 (0.38–1.71), p<0.0001 Pain during intercourse; 1.40 (0.42–1.49), p<0.0001 Pain during evacuation: 2.18 (1.25–2.30), p<0.0001 Pain during urination: 1.13 (0.41–1.75), p<0.001 **How well did you sleep last night (VASQS},** adjusted MD (95% CI) 1.1(0.11–1.39), p>0.02 **Analgesic use** I: 22.9%; C: 42.2% RR: 1.80 (95% CI, 1.61–2.08)	and contained allocated treatment. Randomization and allocation was administrated by an independent part Blinded assessors To measure adherence; researcher counted number of tablets consumed/ week; patients recorded in a diary if failed take tablets: patients were encouraged take the tablets.
Schlaff et al 2006 US Canada [140]	**Study design** RCT, evaluator-blinded, phase III **Setting** Multicentre **Population** n=274 Mean age: 31 years ***B & B endometriosis*** Composite score at baseline: 5–15 range **Inclusion criteria**	**Intervention** Leuprolide acetate (LA), 1.25 mg IM, every 3 months, (total 2 injections) **Duration** 6 months **Participants** n=138 **Dropout** 36 (26%)	**Comparison** Depot medroxyprogesterone acetate (DMPA), SC, 104 mg/0.65 ml every 3 months **Duration** 6 months **Participants** n=136 **Dropout** 38 (35%)	**Pain and symptoms (Biberoglu & Behrman)** ***6 months:*** DMPA statistically equivalent (p<0.02) to LA for the reduction of 4 of the 5 signs and symptoms (dysmenorrhea, dyspareunia, pelvic pain, and pelvic tenderness). ***12 months:*** DMPA statistically equivalent to LA for all five signs and symptoms >60% of patients in both group continued to show improvement compared with BL in each of the five categories.	**Comments** randomized 1: 1, independent person maintained the randomization code, received the study syranges, and administered the study medication ITT analysis treatments were initiated within the first 5 days of a normal menstrual cycle,

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Premenopausal women, 18–49 years, surgically diagnosed ≤42 months, persistent symptoms of pain. A patient's pain must have returned to its previous level within 30 days after diagnostic laparoscopy or within 3 months after laparoscopy/laparotomy with surgical treatment, persisted for ≥3 months. **Follow up time** 12 months after treatment			**Endometriosis-associated induration** 6 months: DMPA: 74.2%, LA: 86.7% **BMD, median % change** Hip, 6 months; DMPA: –0.3, LA: –1.65, p<0.01 12 months, DMPA: 0, LA: –1.3%, ns Lumbar spine, 6 months; DMPA: –1.1, LA: –3.95, p<0.01 12 months; DMPA: 0.2%, LA: –1.7% **QoL EHP-30** Significant improvements in both groups, measured by and SF-36 scales **Adverse event (most frequently reported (≥5% of patients))** ***Injection-site reaction*** DMPA: 9 (7%), LA: 0% *Headache* DMPA: 10 (8%), LA 14 (10%) ***Insomnia*** DMPA:3 (2.3%), LA: 7 (5%) ***Libido decreases*** DMPA: 3 (2.3%), LA: 7 (5%) ***Intermenstrual bleeding*** DMPA: 7 (5%), LA: 1 (0.7%) ***Hot flushes*** DMPA: 3 (2 %), LA: 15 (11%)	
Seracchioli et al 2010 Italy [141,142]	**Study design** RCT **Setting** Tertiary care University Hospital **Population**	**Intervention** Monophasic combined OC; ethinyl E2, 0.020 mg, and gestodene, 0.075 mg daily **Duration** 24 months	**Comparison** No medical treatment **Duration** 24 months **Participants** n=79/104	**Recurrence of pain (VAS0-10)** ***Dysmenorrhea*** Entire study period: significantly lower in continuous users than cyclic and nonusers (p<0.0005). 6 and 12 months: no significant difference between cyclic and nonusers	**Comments** Computer-generated randomization sequence using numbered, opaque, sealed envelopes

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	n=239/311 Laparoscopic excision of ovarian endometriomas **Inclusion criteria** Age 20–40 years, ovarian endometrioma Ø ≥4 cm, no previous surgery for endometriosis or treatment ≤6 months before study entry **Follow up time** 6–24 months	**Participants** Cyclic OC, 21 days followed by a 7-day interval, n=81/103 Continuous OC, n=79/104 **Dropout** Cyclic: 6 (7.4%)/11 (11%) Continuous :6 (7.6%)/9 (8.7%)	**Dropout** 10 (12 Tertiary care university hospital 6%)/17 (16%)	18 and 24 months: continues users a significant reduction compared to C (p=0.01, p=0.009, resp.). ***Dyspareunia*** No significant difference between groups, except for 18 months, continues user sign lower ***Chronic pain*** No significant difference between groups **Endometrioma recurrence** 24 months; C: 20/69 (29%), Cyclic: 11/75 (14.7%) Continues: 6/73 (8.2%)	Patients not blinded, unclear if assessors were blinded The two studies have partly the same population. During the years between 2008–2010 they have continued recruit women to the study and they have reported different outcomes
Sesti et al 2007 Italy [143]	**Study design** RCT, double blind **Setting/recruitment** Single centre, consecutive sample **Population** n=234 (93% of eligible) Mean age: 31 years Stage III/IV: 100% **Inclusion criteria** Age ≤40 at time of surgery, reproductive, ultrasonographic evidence of endometrioma, moderate/severe symptoms (≥4 VAS), laparoscopic diagnosis of endometrioma (r-AFS), first laparoscopic surgery for endometriosis, and conservative treatment with retention of uterus and ovaries;	**Conservative surgery and Intervention1** Continuous monophasic OC: ethynilestradiol, 30 µg + gestoden, 0.75 mg **Duration** 6 months **Participants** n=40 **Dropout** 2 (5%) **Intervention 2** GnRH analogue; tryptorelin or leuprorelin, 3.75 mg every 28 days **Duration** 6 months	**Comparison** Conservative surgery + placebo **Duration** 6 months **Participants** n=115 **Dropout** 5 (4.3%)	**Pain symptom score (VAS 0–10)** **Mean ± SD** ***Dysmenorrhoea*** 12-month: C: 6.4±1.3, GnRH: 5.9±0.9, OC: 5.5±1.2, diet: 6.4±1.0, p<0.001 ***Non-menstrual pelvic pain*** 12-month: C: 6.2±0.9, GnRH: 5.0±1.1, OC: 5.0±0.8, diet: 4.7±1.1, p< 0.001 ***Deep dyspareunia*** 12-month; C: 4.8±1.2, GnRH: 4.3±1.2, OC: 4.5±1.3, diet: 5.0±1.1, p<0.001 **QoL, SH-36 mean score** Improved in both groups, no significant difference **Side effects** GnRH: all patients amenorrhoeic, and a majority experienced menopausal symptoms. OC: spotting, bloating, weight gain, and headache, but these side effects were generally well tolerated.	**Comments** Computer-generated randomization sequence ITT analysis Unclear if participants in the arm with dietary treatment was blinded since given either orally or by injections Partly same patients as in [144]

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	complete excision of all evident ovarian and peritoneal disease; ultrasonographic and clinical follow-up after surgery, no estrogen-suppressing drugs 6 months prior first surgery, no previous surgical treatment for endometriosis; surgical findings of concomitant DIE **Follow up time** 18 months after surgery	**Participants** n=42 **Dropout** 3 (7%) **Intervention 3** Dietary therapy; salts, vitamins, minerals, lactic ferments, fish oil **Duration** 6 months **Participants** n=37 **Dropout** 2 (5.4%)			
Sesti et al 2009 Italy [144]	**Study design** RCT, double blind **Setting/recruitment** Single centre, consecutive sample **Population** n=259 (95% of eligible) Mean age: 30 years Stage III/IV: 45% **Inclusion criteria** Age ≤40 at time of surgery, reproductive, ultrasonographic evidence of endometrioma, moderate/severe symptoms (≥4 VAS), laparoscopic diagnosis of	**Intervention1** Laparoscopic cystectomy + continuous monophasic OC (ethynilestradiol, 30 µg + gestoden, 0.75 mg) **Participants** n=64 **Dropout** 4 (6.3%) **Intervention 2** Laparoscopic cystectomy + GnRH (tryptorelin or leuprorelin, 3.75 mg every 28 days)	**Comparison** Laparoscopic cystectomy +placebo **Duration** 6 months **Participants** n=65 **Dropout** 5 (7.7%)	**Recurrence of endometrioma, n (%)** C: 10 (16.6), OC: 9 (15.0), GnRH: 6 (10.3), Diet: 11 (17.8) **Diameter of endometrioma (mm), mean ±SD** C: 27.5±7.3, OC: 30.3±6.5 GnRH: 28.7±9.4, Diet: 27.0±6.4	**Comments** Computer-generated randomization sequence ITT analysis Unclear if participants in the arm with dietary treatment was blinded since given either orally or by injections Partly the same patients that was included in [143]. Therefore, in the analysis these two

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	endometrioma (r-AFS), first laparoscopic surgery for endometriosis, and conservative treatment with retention of uterus and ovaries; complete excision of all evident ovarian and peritoneal disease; ultrasonographic and clinical follow-up after surgery, no estrogen-suppressing drugs 6 months prior first surgery, no previous surgical treatment for endometriosis; surgical findings of concomitant DIE **Follow up time** 18 months after surgery	**Participants** n=65 **Dropout** 7 (10.8%) **Intervention 3** Laparoscopic cystectomy + Dietary therapy; salts, vitamins, minerals, lactic ferments, fish oil **Participants** n=65 **Dropout** 3 (4.6%) **Duration for all groups** 6 months			articles are referred as one study
Shaaban et al 2015 Egypt [145]	**Study design** RCT, open label **Setting** Single centre **Population** n=62 (44% of eligible) Mean age: 39 years adenomyotic uteri **Inclusion criteria** Age 20–45 years, adenomyosis confirmed by 2D TVUS and colour Doppler ultrasound, contraception for at least 6 months, complaining of pain	**Intervention** LNG-IUS **Duration** 6 months **Participants** n=31 **Dropout** 2 (6.5%)	**Comparison** Combined oral contraceptive (COC), 30 µg of ethinyl estradiol and 75 µg of gestodene, cyclic use **Duration** 6 months **Participants** n=31 **Dropout** 3 (9.7%)	**Pelvic pain, VAS score** (mean ± S.D) Baseline: I: 6.23±0.67, C: 6.55±0.68 Post: I: 1.68±1.25 C: 3.90±0.54 Intergroup comparisons p<0.001 **Patients' satisfaction** (number of patients) Post: I: 25/31 C: 18/31	**Comments** Randomization via computer-generated random table. Allocation concealment was done using serially numbered closed opaque envelopes

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	and bleeding that was associated with adenomyosis **Follow up time** Post treatment (6 months)				
Shokeir et al 2015 Egypt [146]	**Study design** RCT, double blind **Setting** Single centre, University hospital **Population** n=62 Mean age: 33 years Stage III/IV: 19% **Inclusion criteria** Age ≥18, laparoscopically confirmed endometriosis, patent fallopian tubes, ≥6 months CPP, pain score on VAS, no hormonal therapy in the previous 3 months, a no desire to conceive within 1 year **Follow up time** 1, 2 and 3 months FU	**Intervention** Office hysteroscopic-guided pertubal diluted bupivacaine infusion (0.25%) **Participants** n=32 **Dropout** 2	**Comparison** Placebo **Participants** n=30 **Dropout** 0 (6%)	**Pain mean (95% CI)** ***VAS score (0–100),*** BL: I: 7.7 (7.9–8.2), C: 7.9 (8.2–6.8) 1 month: I: 6.1 (5.5–6.3), C: 7.4 (7.5–6.7), p<0.05 2 months; I: 5.6 (5.8–6.0), C: 7.5 (7.9–6.8), p<0.01 3 months; I: 5.4 (4.9–5.0), C: 7.7 (7.5–6.6), p<0.001 ***VRS 1–100*** BL; I: 90.2 (90.5–91.9), C: 91.8 (91.3–92.3) 1 month; I: 35.4 (29.3–41.6), C: 91.2 (90.5–91.9) 2 months; I: 34.2 (28.6–39.8), C: 89.9 (92.1–93.1) 3 months; I: 38.6 (32.4–44.8), C: 90.2 (92.0–88.9) **Overall satisfaction** Satisfaction; I: 22 (73%), C: 2 (7%) Uncertain: I: 4 (13%), C: 2 (7%) Dissatisfied; I: 4 (13%), C: 26 (87%)	**Comments** Computer-generated randomization sequence, 1:1 ratio, numbered, sealed envelopes. Patients were asked to stop any nalgesic medications before enrolment
Sillem et al 1999 Germany [147]	**Study design** RCT, double blind **Setting** Single centre **Population** n=23 Mean age: 30 years	**Intervention** Goserelin 3.6 mg sc every four weeks, 1st injection given on cycle day 3–5 plus 5 mg medrogestone orally twice daily **Duration** 6 months	**Comparison** Goserelin 3.6 mg sc every four weeks, 1st injection given on cycle day 3–5 plus placebo **Duration** 6 months	**BMD,** Lumbar BMD; mean relative loss; I: 4%, C: 4 % Absolute values, g/cm^2 BL; I: 1.19±0.11 C: 1.28±0.18 Post; I: 1.14±0.1, C: 1.23±0.16 Femoral neck/ward's triangle: no change in either group	**Comments** Unclear randomization and allocation procedure Pill counts were conducted at each visit to assure compliance.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Inclusion criteria Laparoscopically proven symptomatic endometriosis **Follow up time** 12 months (6 months after end of treatment)	**Participants** n=11 **Dropout** 0	**Participants** n=12 **Dropout** 0		
Soysal et al 2004 [148]	**Study design** RCT, double blind **Setting** Single centre **Population** n=80 Mean age: 32 years **Inclusion criteria** Endometriosis laparoscopy and biopsy-proven endometriosis, severe endometriosis (r-ASRM score >40), underwent conservative surgery for endometriosis, no treatment for endometriosis previous 3 months **Follow up time** Post, 12, 18 and 24 months	**Intervention** Laparoscopy/laparotomy surgery + anastrozole 1 mg/day + goserelin, SC depot injections, 3.6 mg every 4 weeks **Duration** 6 months **Participants** n=40 **Dropout** 0	**Comparison** Laparoscopy/laparotomy surgery + placebo + goserelin, SC depot injections, 3.6 mg every 4 weeks **Duration** 6 months **Participants** n=40 **Dropout** 0	**Recurrence rate** Kapan Meier survival curve:>24 versus 17 months; p=0.0089, in favour for intervention. 24 months; RR (95%, CI): 4.3 (1.3±9.8) No of patients with recurrence I: 3 (7.5%), C: 14 (35%) **Symptoms, change from BL, mean ± SD** ***VRS (Biberoglu and Behrman)*** Dysmenorrhoea; Post; I: 1.7±0.8, C: 1.5±0.8, ns 24 months; I: 1.3±0.7, C: 0.8±0.9, p<0.05 Dyspareunia Post; I: 2.1±0.7, C: 2.1±0.8, ns 24 months; I: 1.9±0.8, C: 1.2±1, p<0.001 Pelvis pain Post; I: 1.8±1, C:2±0.7, ns 24 months; I: 1.8±0.9, C: 1.1±0.6, p<0.001 **BMD, lumbar, mean±SD** Post; I: 93.8±33.2, C: 60.2±28.2, p=0.003 24 months; I: 27.1±46.3, C: 25.2±28.9, ns	**Comments** Computer generated randomization sequence using numbered, opaque, sealed envelopes. ITT analysis (last observation carried forward procedure)

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				Depression, anxiety and loss of sexual interest, Greene scale Post; I: 30.3±1.9, C: 29.5±1.9, ns **Vasomotor function, Blatt-Kupperman scale** Post; I: 54.1±4.7, C: 53.9±6, ns	
Stratton et al 2008 USA [149]	**Study design** RCT, double blind **Setting** Single centre **Population** n=93 Mean age: 32 years r-ASRM stage III/IV: 31% History of laparotomy: 15% **Inclusion criteria** Age 18–45 years, 3-month history of pelvic pain, biopsy-proven endometriosis at study laparoscopy, significant postoperative pelvic pain reduction, excellent health with a BMI ≤40 kg/m^2, except for use of antidepressants, medications for migraines and headaches, and allergy medications. No use of hormonal contraception, selective estrogen receptor modulators, progestins, estrogens, steroids, or ovulation induction in the past 3 months or other medical or surgical treatment for	**Intervention** Laparoscopic surgery + Raloxifene, 90 mg twice daily **Duration** 6 months **Participants** n=47 **Dropout** 9 (19%)	**Comparison** Laparoscopic surgery + placebo **Duration** 6 months **Participants** n=46 **Dropout** 11 (24%)	**Pain (VAS)** Raloxifen significantly earlier return of pain than the placebo group, p=0.03 ***Dysmenorrhea/non-menstrual pain*** Significantly in both groups, gradual return by 6–12 months, no difference between groups **Recurrence** I: 23/36, C: 17/35 Biopsy proven I: 16/23, C: 13/17 **BMD, g/cm2, mean ±SD** I: –0.007±0.007, C: 0.013±0.004, p=0.01 T score; I: –0.061±0.063, C: 0.116±0.044, p=0.02 **QoL (Duke Health Profile)** Similar in both groups, no change from BL, except for mental health I: –5.3, C: 5.8, p<0.05 **Adverse events, n (%)** Pelvic pain; I: 14 (30), C: 11 (24) Ovarian cyst; I: 8 (17), C: 5 (11) Headache; I: 10 (21), C: 9 (20) Migraines; I: 6 (13), C: 8 (18), Depression; I: 8 (17), C: 4 (9) Number reduced/stopped study drug;	**Comments** The Pharmaceutical Development Service created the allocation sequence, using a table of random numbers and alternating blocks of 8 and 10, which was accessible only to the pharmacy. Treatment assignment was concealed from study staff and participants until the study ended. ITT analysis

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	endometriosis in the past 6 months. **Follow up time** 12 months from study start			I: 15 (31), C: 22 (49) All ns	
Strowitzki et al 2010 Germany, Italy, and Ukraine [150]	**Study design** RCT, double blind **Setting** Multicentre (n=33) **Population** n=198 Mean age: 32 years r-ASRM stage III/IV: 71% **Inclusion criteria** Age 18–45 years, laparoscopically and histologically confirmed endometriosis (stages I–IV (r-ASRM)), within 12 months of study start, EAPP score ≥30 mm on VAS), no amenorrhea ≥3 months, no primary need for surgical treatment of endometriosis, no previous use of hormonal agents within 1–6 months **Follow up time** Post treatment (12 weeks)	**Intervention** Dienogest, 2 mg once daily orally. Treatment started on day 2 of the first menstruation **Duration** 12 weeks **Participants** n=102 **Dropout** 4 (4%)	**Comparison** Placebo **Duration** 12 weeks **Participants** n=96 **Dropout** 6 (6%)	**Endometrios associated pelvic pain (VAS, 0–100)** Significantly superior to placebo ITT; p=0.00165, PP; p=0.00007 **VAS score, reduction** ITT; I: −27.4 mm, C: 15.1 mm, MD: 12.3 (95% CI, 6.4 to 18.1), p<0.0001 **Change in intake of analgesic medication (tablets/28 days)** I: −4.4±6.4, C: 3.7±8.2 RD: 0.74 (95% −1.412 to −2.895), ns **QoL, SF-36, improvement** Bodily pain; I: 21.8±22.8%, C: 10.3±20.5% Role emotional; I: 18.4±33.9%, C: 9.6±46.4% Mental and Physical sum scale: similar improvements in both groups **Profiles of symptoms and sign severity (Biberoglu and Behrman)** No sign difference between groups **Global assessment efficacy, (CGI)** Very much/much improved; I: 52.9%, C: 22.9% Very much/much satisfied; I: 43.1%, C: 20.8%	**Comments** 1:1 blocked randomization list generated by a Central Randomization Service To preserve blinding, the two treatments were indistinguishable in appearance. Each center had both dienogest and placebo tablets pre-coded. Treatment compliance was monitored by tablet counts and patient diaries. ITT analysis and PP analysis Patients were offered analgesic medication in the form of self-administered ibuprofen tablets up to 1200 mg/day

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				Safety variables, events n (%) Serious AE: 0, AE withdrawal; I: 2, C: 1 Headache; I: 11 (10.8%), C: 5 (5.2%) Cystitis; I: 3 (2.9%), C: 0 Nausea; I: 3 (2.9%), C: 1 (1%) Nasopharyngitis; I: 2 (2%), C: 5 (5.2%) Bronchitis; I: 2 (2%), C: 3 (3.1%) Influenza; I: 2 (2%), C: 3 (3.1%) Depression; I: 2 (2%), C: 2 (2.1%) Breast discomfort; I: 2 (2%), C: 1 (1%) Asthenia: I: 2 (2%), C: 0 Vomiting; I: 0, C:3 (3.1%) Gastritis; I: 0, C: 2 (2.1%) Proteinuria; I: 0, C: 2 (2.1%) Vaginal candidiasis; I: 0, C: 2 (2.1%)	
Strowitzki et al 2010 Germany, Poland, Portugal, Spain and Austria [151] Strowitzki et al. 2012 [152]	**Study design** RCT, open label **Setting** Multicentre **Population** n=252 Mean age: 31 years r-AFS stage III/IV: 45% **Inclusion criteria** Age 18–45 years, laparoscopic diagnosis and histologically confirmed endometriosis stage I-IV, experiencing pain, no previous use of hormonal agents (GnRH agonists ≤, progestins/danazol ≤3 months or OC ≤1 month), no	**Intervention** Dienogest (DNG) 2 mg once daily, orally **Duration** 24 weeks **Participants** n=124 **Dropout** 30 (24%)	**Comparison** Leuprolide acetate (LA) 3.75 mg depot IM every 4 weeks **Duration** 24 weeks **Participants** n=128 **Dropout** 32 (25%)	**Pain VAS score, Mean ±SD** ***Score decrease*** DNG: 12.7±20.3, LA: 11.9±16.9, ns ***Absolute reduction*** DNG: 47.5±28.8, LA: 46±24.8, MD: 1.5 (95% CI, –9.26 to 6.25), ns The non-inferiority of DNG relative to LA was therefore demonstrated, based on the pre-specified non-inferiority margin of 15 mm (p<0.0001). ***No improvement in pain score, (%)*** DNG: 96.7%, LA: 85.8% P for non-inferiority,<0.0001 **Pain intensity, B&B score** Severe/very severe, total score (%) DNG: 5%; LA: 4%, ns Free from total pelvic symptoms DNG, 53%, LA, 53%, ns Free from Dysmenorrhea, (%) DNG: 82%, LA: 90%, ns	**Comments** Randomisation done centrally with a randomization list and in block The outcome BMD is not included since only a small fraction of the participates were evaluated

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	primary need for surgical treatment **Follow up time** Post treatment (24 weeks)			Free from dyspareunia DNG: 70%, LA: 70%, ns Free from pelvic tenderness DNG: 57%, LA: 55%, ns **QoL, SH-36, score, mean ± SD** Physical health summary DNG: 45.4±10.9, LA: 45.9±11.7, ns Mental health summary DNG: 51.6±6.7, LA: 51.2±7.1, ns **Adverse events, %** Headache; DNG: 12.5%, LA: 19.5% Weight gain; DNG: 6.7%, LA: 3.9% Depression; DNG: 5%, LA: 8.6% Decreased libido; DNG: 4.2%, LA: 6.3% Acne; DNG: 4.1%, LA: 4.7% Alopecia; DNG: 3.3%, LA: 5.5% Migraine; DNG: 2.5%, LA: 4.7% Sleep disorder; DNG: 1.7%, LA: 7.8% Vaginal dryness; DNG: 1.7%, LA: 7% Hot flushes; DNG: 0, LA: 7%	
Surrey et al 1992 USA [153]	**Study design** RCT, blinded **Setting** Single centre **Population** n=20 Stage III/IV: 80% Earlier endometrios surgery: 16/20 **Inclusion criteria** Symptomatic endometriosis, diagnostic laparoscopy	**Intervention** Leuprolide acetate, 3.75 mg. IM, every 28 days + norethindrone, daily oral dose of 5 mg for the first 4 weeks, then 10 mg daily as tolerated for the remaining 20 weeks of therapy **Duration** 24 weeks **Participants** n=10	**Comparison** Leuprolide acetate, 3.75 mg. IM, every 28 days + placebo **Duration** 24 weeks **Participants** n=10 **Dropout** 0	**Pain score, (scale 0–5)** BL; I: 44±7, C: 59±12 4 weeks; I: 20±8, C: 32±6 12 weeks: symptoms reach nadir in both groups, no difference between groups **AFS score, total and modified** Decrease in both groups. No significant difference between groups but within groups Mean decline; I: 57.8±10.6%, C: 55.7±6.1% **BMD, lumbar spine, week 48 % change, mean ± SEM**;	**Comments** Unclear randomization and allocation Treatment beginning in the midluteal phase within 3 months of laparoscopy

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Patients with < four visible endometriotic implants or with an endometrioma >5 cm in diameter were excluded. **Follow up time** Post treatment (24 weeks)	**Dropout** 1 (10%)		I: –2.7±0.75, C: –5.6±0.7%, p<0.05	
Tahara et al 2000 Japan [154]	**Study design** RCT, open labelled **Setting/recruitment** Single centre (university hospital)/unclear enrolment **Population** n=15 Mean age: 35 years Stage III/IV: 67% **Inclusion criteria** Symptomatic endometriosis, endometriosis confirmed by laparoscopy or laparotomy **Follow up time** Post treatment (24 weeks)	**Intervention** Nafarelin treatment, 200 mg, twice daily for 4 weeks then nafarelin 200 mg daily once daily for 20 weeks **Duration** 4+20 weeks **Participants** n=8 **Dropout** 0	**Comparison** Nafarelin treatment, 200 mg, twice daily **Duration** 24 weeks **Participants** n=7 **Dropout** 0	**Pelvic pain/pain, Biberoglu & Behrman scale, mean ±SD** BL: I: 8.2±1.3, C: 7.8±1.9, ns 8 weeks: I: 4.4±1.2, C: 4.2 ±1.3, ns 16 weeks; I: 3.7±1.1, C: 3.8±0.8, ns 24 weeks; I: 3.8±0.9, C: 3.5±0.9, ns **Vasomotor symptoms (hot flashes or dizziness), n (%)** Post; I: 2 (25%), C: 6 (86%) **BMD loss %, Lumbar spine:** I: 1.38%, C: 5.6%, p<0.05	**Comments** Moderate risk of bias Random number table
Takenaka et al 2015 Japan [155]	**Study design** Prospective study **Setting** 2 centres **Population** n=30 Mean age: 30/31 years Ovarian on both side: 39.3% **Inclusion criteria**	**Intervention** Dienogest, daily, 1 mg + laparoscopic cystectomy **Duration** DNG: 12 weeks thereafter surgery **Participants** n=15 **Dropout**	**Comparison** Leuprorelin, 1.88 mg SC every 4 weeks +laparoscopic cystectomy **Duration** LA: 12 weeks thereafter surgery **Participants** n=15	**VAS score (scale 0–100)** Pre-surgical medication with both dienogest and leuprorelin was associated with substantial reductions in VAS scores (p<0.05; Wilcoxon signed–rank test). **Size of cyst, reduction** Before surgery DNG: 10.2% L: 18.2%	**Comments** Not blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Age 20–39 years, regular menstrual cycles, presence of ovarian endometrial cysts of ≥30 mm in diameter diagnosed by imaging analysis (MR + TVUS), indications for laparoscopic cystectomy **Follow up time** 12 weeks post-surgery (24 weeks from start)	0	**Dropout** 0		
Tanmahasamut et al 2017 Thailand [156]	**Study design** RCT, double-blinded **Setting/recruitment** Single centre **Population** n=40 (77% of eligible) Duration of symptoms; 1.63 years Stage III–IV: 60% Sexual active: 70% **Inclusion criteria** Moderate-to-severe dysmenorrhea or chronic pelvic pain for more than 6 months, undergoing laparoscopic conservative surgery **Follow up time** 1, 3 and 6 months after surgery	**Intervention** Desogestrel, 0.075 mg per tablet, once daily before bedtime **Duration** 24 weeks **Participants** n=20 Mean age: 29.1±4.9 **Dropout** 1 (5%)	**Comparison** Placebo **Duration** 24 weeks **Participants** n=20 Mean age: 32.7±6.7 **Dropout** 1 (5%)	**Pain symptoms, (VAS), change Median (range), 6 months** ***Overall pain*** I: –84 (–100, 19), C: –57 (-100, 0), p=0.005 ***Dysmenorrhea*** I: –84 (–100, 19), C: –61 (–96, 0), p=0.005 ***Pelvic pain*** I: –81 (–100, 23), C: –51 (–100, 35), p=0.007 ***Dyspareunia*** I: –59 (–91, 22), C: –51 (–84, 13), p=0.342 **Compliance (%), mean ± SD** I: 93.4±8.6, C: 90.9±10.5, p=0.594 **Patient satisfaction, per protocol** RR 23.2, 95% CI, 2.6 to 208.6; p<0.001 **Side effects, per protocol, n (%)** Acne; I: 13 (68.4), C: 9 (47.7), p=0.324 Breast pain; I: 10 (52.6), C: 9 (47.4), p=1.0 Headache; I: 8 (42.1), C: 8 (42.1), p=1.0	**Comments** Randomisation via computer-generated list of random numbers. The codes were individually contained in a sealed opaque envelope www.clinicaltrials.gov (NCT01559480) ITT analysis Operation performed using mechanical instruments and electrosurgery. Adhesions were dissected using microscissors. Ovaries were completely mobilized

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				Nausea/vomiting; I: 4 (21.1), C: 3 (15.8), p=1.0 Hair loss; I: 4 (21.1), C: 3 (15.8), p=1.0 Mood change; I: 3 (15.8), C: 1 (5.3), p=0.604 Rash; I: 1 (5.3), C: 2 (10.5), p=1.0 Amenorrhea; I: 7 (36.8), C: 0 Spotting; I: 8 (42.1), C: 2 (10.5) Light bleeding; I: 1 (5.3), C: 0	
Tanmahasamut et al 2012 Thailand [157]	**Study design** RCT, double blind **Setting** Single centre (University Hospital) **Population** n=55 (9% of eligible) Mean age: 33 years ASRM stage IV: 53% **Inclusion criteria** Women with moderate to severe dysmenorrhea, chronic pelvic pain, or both for more than 6 months and who were scheduled for laparoscopic surgery **Follow up time** Up to 12 months after surgery	**Intervention** Laparoscopic surgery + immediate levonorgestrel-releasing intrauterine system (LNG-IUD) insertion **Participants** n=28 **Dropout** 1 (4%)	**Comparison** Laparoscopic surgery + expectant management **Participants** n=27 **Dropout** 3 (11%)	**Symptoms** Dysmenorrhea VAS, median (range) I: 4.5 (0–11.5), C: 23.0 (7–65), p<0.001 Median reduction: I: 81.0 (51.5–87.5) C: 50.0 (0–78.0), p=0.006 Noncyclic pain VAS, median (range) I: 0 (0–0), C: 5 (0–39.75), p<0.017 Median reduction: I: 48.5 (19.5–84.25), C: 22.0 (–1.5 to 46.5), p=0.038 Dyspareunia VAS, media (range) I: 0 (0–5.5), C: 3 (0–100), ns Median reduction: I: 15.0 (4.0–38.5), C: 19.0 (21–66.75), p=0.831 **QoL, SH-36** I significantly better than C in total score, p=0.014; physical subscale, p=0.036, mental subscale: p= 0.229 **Adverse events, n (%)** Any; I: 20/23, C: 18/23 Bloating; I: 10(37), C: 16(70) Acne; I: 16 (60), C: 13 (57) Oily skin; I: 20 (74), C: 16(70) Melasma; I: 6 (22), C: 0 Weight gain; I: 17 (63), C: 13 (57) Breast tenderness; I: 18 (67), C: 9 (39)	**Comments** Computer-generated list of random numbers. Sealed opaque envelope, sequentially numbered and chronologically opened ITT analysis Side effect per protocol analysis A significant difference in sexual activity at baseline

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				Headache; I: 13 (48), C: 17 (74) Nausea; I: 11 (41), C: 9 (39) Leukorrhea; I: 1 (4), C: 3 (13)	
Taylor et al 2017 USA, Canada [158] **Elaris Endometriosis II (Elaris EM-II)**	**Study design** RCT, double-blind, phase 3 trials **Setting/recruitment** Multicentre, 151 sites **Population** n=872 Dropout: 219 (25%) Median age: 31 years Mean months since surgery: 42 None use of analgesic: 9% **Inclusion criteria** Aged 18–49 years, surgical diagnosis of endometriosis in previous 10 years, had moderate or severe endometriosis-associated pain **Follow up time** 3 and 6 months	**Intervention 1** Elagolix, an Oral GnRH Antagonist, 150 mg once daily (low dose) **Duration** 6 months **Participants** n=249 **Intervention 2** Elagolix, an Oral GnRH Antagonist, 200 mg twice daily (high dose) **Duration** 6 months **Participants** n=248	**Comparison** Placebo **Duration** 6 months **Participants** n=374	**Pain symptoms, clinically meaningful reduction (%)** ***Dysmenorrhea*** 3 months; C: 19.6%, low dose: 46.4%, high dose: 75.8% RR high vs C: 3.9 (2.9, 4.9) RR low vs C: 2.4 (1.7, 3.1) 6 months; C: 23.1%, low dose: 42.1%, high dose: 75.3% RR high vs C: 3.3 (2.5, 4) RR low vs C: 1.8 (1.3, 2.3) ***Nonmenstrual Pelvic Pain*** 3 months; C: 36.5%, low dose: 50.4%, high dose: 54.5% RR high vs C: 1.5 (1.2, 1.8) RR low vs C: 1.4 (1.1, 1.7) 6 months; C: 34.9%, low dose: 45.7%, high dose: 62.1% RR high vs C: 1.8 (1.4, 2.1) RR low vs C: 1.3 (1, 1.6) **Endometriosis associated pain (NRS), change in score (0–3), 6 months** ***Dysmenorrhea*** C: −0.44±0.05, low dose: −0.89±0.06, high dose: −1.75±0.06, p<0.001 ***Non-menstrual pelvic pain*** C: –0.31±0.04, low dose: −0.48±0.04, high dose: −0.72±0.04, p<0.01, p<0.001 ***Dyspareunia*** C: −0.29±0.04, low dose: −0.39±0.05, high dose: −0.49±0.05, p high dose p<0.01 ***Use of rescue analgesic agent***	**Comments** Randomly assigned by an interactive voice-response system (2:2:3 ratio) Four intervals: washout of hormonal therapies, screening period <100 days, including two menstrual cycles, 6-month treatment period; and a follow-up period of up to 12 months, unless the woman was enrolled in the corresponding 6-month extension study Clinically meaningful threshold for mean change from baseline, as compared with placebo, was −0.81 for dysmenorrhea and −0.36 for non-menstrual pelvic pain

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				C: −0.27±0.04, low dose: −0.35±0.04, high dose: −0.56±0.05, p high doe <0.001 ***Use of rescue opioid*** 3 months; C: −0.10±0.02, low dose: −0.07±0.03, high dose: −0.22±0.03, p high dose <0.01 **BMD, mean % change f (95% CI), 6 months** ***Lumbar spine*** C: 0.47, low: –0.31, high: –2.61 ***Total hip;*** C: 0.22, low: –0.32, high: –1.51 ***Femoral neck;*** C: 0.02, low: –0.39, high –1.89 **Adverse events (AE), n (%)** Any; C: 277 (74.1), low dose: 201 (80.7), high dose: 205 (82.7) Serious AE; C: 12 (3.2), low dose: 2 (0.8), high dose: 7 (2.8) Severe AE; C: 56 (15.0), low dose: 26 (10.4), high dose: 43 (17.3) Discontinuation; C: 22 (5.9), low dose: 16 (6.4), high dose: 23 (9.3) Death; C: 0, low dose: 0, high dose: 0 AE significant difference from placebo Hot flushes; C: 26 (7.0), low dose: 59 (23.7), high dose: 105 (42.3), p<0.001 Headache; C: 37 (9.9), low dose: 38 (15.3), high dose: 43 (17.3), p high dose <0.05 Insomnia; C: 9 (2.4), low dose: 16 (6.4), high dose: 18 (7.3), p<0.05 Mood swings; C: 10 (2.7), low dose: 10 (4.0), high dose: 11 (4.4)	

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				Night sweats; C: 5 (1.3), low dose: 6 (2.4), high dose: 14 (5.6), p high dose <0.01	
Taylor et al 2017 Five continents [158] **Elaris Endometriosis II (Elaris EM-II)**	**Study design** RCT, double-blind, phase 3 trials **Setting/recruitment** Multicentre, 1587 sites **Population** n=817 Drop out: 185 (23%) Median age: 33 years Mean months since surgery; 47 None use of analgesic: 9.5% **Inclusion criteria** Surgically diagnosed endometriosis, moderate or severe endometriosis-associated pain **Follow up time** 3 and 6 months	**Intervention 1** Elagolix, an Oral GnRH Antagonist, 150 mg once daily (low dose) **Duration** 6 months **Participants** n=226 **Intervention 2** Elagolix, an Oral GnRH Antagonist, 200 mg twice daily (high dose) **Duration** 6 months **Participants** n=229	**Comparison** Placebo **Duration** 6 months **Participants** n=3760	**Pain symptoms, clinically meaningful reduction (%)** ***Dysmenorrhea*** 3 months; C: 22.7%, low dose: 43.4%, high dose: 72.4% RR high vs C: 3.2 (2.5, 4), RR low vs C: 1.9 (1.4, 2.5) 6 months; C: 25.4%, low dose: 46.2 %, high dose: 76.9% RR high vs C: 3.1 (2.4, 3.8) RR low vs C: 1.8 (1.3, 2.3) ***Non-menstrual Pelvic Pain*** 3 months; C: 36.5%, low dose: 49.8%, high dose: 57.8% RR high vs C: 1.6 (1.3, 1.9) RR low vs C: 1.4 (1.1, 1.6) 6 months; C: 40.6%, low dose: 51.6%, high dose: 62.2% RR high vs C: 1.5 (1.2, 1.8) RR low vs C: 1.3 (1, 1.5) **Endometriosis associated pain (NRS), change in score (0–3), 6 months** ***Dysmenorrhea*** C: −0.52±0.05, low dose: −1.06±0.06, high dose: −1.65±0.06, p<0.001 ***Nonmenstrual pelvic pain*** C: −0.48±0.04, low dose: −0.63±0.04, high dose: −0.80±0.04, p<0.01, p<0.001 ***Dyspareunia*** C: −0.30±0.04, low dose: −0.39±0.05, high dose: −0.60±0.05, p high dose <0.001	**Comments** Randomly assigned by an interactive voice-response system (2:2:3 ratio) Four intervals: washout of hormonal therapies, screening period <100 days, including two menstrual cycles, 6-month treatment period; and a follow-up period of up to 12 months, unless the woman was enrolled in the corresponding 6-month extension study clinically meaningful threshold for mean change from baseline, as compared with placebo, was −0.85 for dysmenorrhea, −0.43 for nonmenstrual pelvic pain

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				Use of rescue analgesic agent C: −0.32±0.03, low dose: −0.40±0.04, high dose: −0.52±0.04, p high dose <0.001 Use of rescue opioid 3 months; C: −0.12±0.02, low dose: −0.12±0.02, high dose: −0.21±0.02, p high dose <0.01 **BMD, mean % change, 6 months** ***Lumbar spine*;** C: 0.56, low: –0.72, high: –2.49 ***Total hip*;** C: 0.58, low: –0.47, high –1.58 ***Femoral neck*;** C: 0.31, low: –0.35, high: –1.42 **Adverse events (AE), n (%)** Any; C: 260 (72.2), low dose: 179 (79.2), high dose: 194 (84.7) Serious AE; C: 12 (3.3), low dose: 12 (5.3), high dose: 5 (2.2) Severe AE; C: 32 (8.9), low dose: 23 (10.2), high dose: 21 (9.2) Discontinuation; C: 22 (6.1), low dose: 10 (4.4), high dose: 23 (10.0) Death; C: 0, low dose: 0 (0.4), high dose:0 AE significant difference from placebo Hot flushes; C: 37 (10.3) low dose: 51 (22.6) high dose: 109 (47.6), p low dose <0.01 Headache; C: 51 (14.2), low dose: 42 (18.6), high dose: 52 (22.7), p high dose <0.001	

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				Insomnia; C: 12 (3.3), low dose: 13 (5.8), high dose: 24 (10.5), p high dose <0.01 Mood swings; C: 8 (2.2), low dose: 13 (5.8) high dose: 6 (2.6), p low dose <0.001, Night sweats; C: 1 (0.3), low dose: 3 (1.3), high dose: 5 (2.2), p high dose <0.001	
Teixeira et al 2017 Brazil [159]	**Study design** RCT, double blind **Setting** Single centre **Population** n=50 Mean age: 35 years Hormonal therapy: 81% NSAIDs: 100% **Inclusion criteria** Aged 18–45 years, diagnosis of DIE by MRI or TVS after bowel preparation, score >5 on VAS endometriosis-associated pelvic pain. Presence of chronic pelvic pain refractory to conventional therapy (one year of use at least). **Follow up time** Post treatment (24 weeks)	**Intervention** Three homeopathic potencies of estrogen (12cH, 18cH and 24cH), twice daily orally **Duration** 24 weeks **Participants** n=23 **Dropout** 4 (17%)	**Comparison** Placebo, twice daily orally **Duration** 24 weeks **Participants** n=27 **Dropout** 2 (7%)	**Change in EAPP global score (VAS: range 0 to 50)** ITT; MD: 12.82, 95% CI, 6.74–18.89; p<0.001 PP: MD: 12.03; 95% CI, 5.32–18.74, p<0.001 **Changes in EAPP partial scores (VAS: range 0 to 10)** Dysmenorrhea; MD 3.28; 95% CI,1.04–5.52; p<0.001 Non-cyclic pelvic pain; MD 2.71; 95% CI, 0.36–5.05; p=0.009 Cyclic bowel pain; MD 3.40; 95% CI, 1.12–5.68; p<0.001	**Comments** Randomization sequence created by an independent supervisor using a random number generator. 1:1 ratio ITT analysis, n=44 The result from QoL and depressing is not included since significant difference between groups from start
Telimaa et al 1987 Finland [160]	**Study design** RCT, double blind **Setting**	**Intervention** Medroxyprogesterone acetate (MPA), 100 mg daily	**Comparison** Placebo **Duration**	**Resolution** Complete; MPA: 50%, C: 12% Partial resolution: MPA: 13%, C: 6%, p<0.01	**Comments** Unclear randomization and allocation

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Single centre **Population** n=39 (total n=59) Mean age: 32 years **Inclusion criteria** Mild/moderate endometriosis, endometriosis confirmed by laparoscopy or laparotomy **Follow up time** Post treatment (6 months) and 12 months (6 months from end of treatment)	**Duration** 6 months **Participants** n=20 **Dropout** 4 (20%)	6 months **Participants** n=19 **Dropout** 2 (10.5%)	**Alleviation of symptoms (VAS score)** Pelvic pain, lower back pain, defecation pain and total sum: significantly lower in MPA compared to placebo at 3, 6 months as well as 6 months after end of treatment **Side effects, frequency (%)** Acne; MPA: 39, C: 6 Edema; MPA: 67, C: 6, p<0.05 Muscle cramps; MPA: 17, C: 0 Spotting; MPA: 39, C: 17	The group treated with danazol was excluded from the analysis Treatment started 1st day of menstruation
Thomas et al 1987 UK [161]	**Study design** RCT, double blind **Setting** Single centre **Population** n=40 Age range: 21–35 Median r-AFS score for endometriosis: 2 (range 1–8) **Inclusion criteria** Women after a laparoscopy for infertility at which endometriosis was diagnosed visually and scored using AFS. Only patients in whom the disease did not impede collection of the oocyte by the tubal fimbria were included.	**Intervention** Gestrinone 2.5 mg twice weekly, orally **Duration** 6 months **Participants** n=20 **Dropout** 0	Comparison Oral placebo **Duration** 6 months **Participants** n=20 **Dropout** 3 (15%)	**Elimination of visual endometriosis** 6 months: I: 12 (60%), C: 4 (24%)	**Comments** Unclear randomization and allocation

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Follow up time Post treatment				
Trummer et al 2017 Seven countrys [162]	**Study design** RCT, double blind **Setting** Multicentre (28 centres) **Population** n=110 (70% of screened) Mean age: 32 years Stage II/IV: 50% Sub-fertility, yes: 24.5% **Inclusion criteria** Age 18–45 years, endometriosis, determined by diagnostic laparoscopy/ laparotomy (24 months and six weeks prior to study), pelvic pain score ≥40 mm VAS, no hormonal contraception during study, willingness to use only ibuprofen to treat pain associated with endometriosis **Follow up time** Post treatment (12 weeks)	**Intervention** CCR1 antagonist BAY 86-5047, tablets taken three times daily. A screening phase of 4–8 weeks prior to treatment and a 12-week treatment phase, in which BAY 86-5047 was titrated up to a dose of 1800 mg/day over the first 10 days **Duration** 12 weeks **Participants** n=56 **Dropout** 13 (23%)	**Comparison** Placebo, tablets taken three times daily **Duration** 12 weeks **Participants** n=54 **Dropout** 6 (11%)	**The individual absolute change in EAPP, (VAS) + cumulative change in consumption of analgesics between** p=0.75 **VAS score** BL: I: 64.8 mm, C: 67.2 12 weeks; I: 49.2, C: 47.8, p= 0.45 **Intake of analgesics (%)** BL; I: 33.9%; C: 44.4% 12 weeks; I: 11.5%, C: 15.4%, p=00.82 **Change in B&B scores** p=1.0 **Global assessment of efficacy by the patient and investigator** Much improved; I: 33.3%, C: 28.5% **Adverse events (aes)** Severe events; I: 7	**Comments** Blocked randomization list generated by the sponsor's central randomization service. The treatment was taken continuously with no medication-free days. Diary to record their intake of treatment and analgesics (ibuprofen), pain severity using the VAS and the occurrence of adverse events (AEs).
Tummon et al 1997 Canada UK [163]	**Study design** RCT **Setting/recruitment** Multicentre **Population** n=103 (311 cycles)	**Intervention** Superovulation with FSH and intrauterine insemination (IUI) Ovarian stimulation on menstrual day 3; daily IM injection of FSH. Women <28 years old started 75 IU	**Comparison** No treatment **Participants** n=50 (184 cycles) **Dropout** 0	**Live birth** I: 14 (11%) of 127 cycles, C: 4 (2%) of 184 cycles OR 5.6 (95%CI, 1.8 to 17.4) in favour for treatment **Cumulative live birth** I: 30%, C: 10%, p=0.002	**Comments** Despite randomization a difference between groups were observed in the proportion having had previous laparoscopic reductive surgery of minimal or

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Mean infertility: 42.5 months Mean age: 31 years **Inclusion criteria** Age 20–39 years, regular menstrual cycles, presumptive evidence of ovulation, normal serum PRL, normal TSH, bilateral tubal patency, minimal or mild endometriosis diagnosed by laparoscopy in the 12 months before enrolment, >40 X 10^6 per ejaculate on screening semen analysis Exclusion: hormonal endometriosis therapy ≤6 months, ovulation induction ≤3 months, previous ovulation induction with exogenous gonadotropins, female body weight <52 kg or >88 kg **Follow up time** Unclear	of FSH lower, women >37 years started 75 IU of FSH higher. Dosage adjusted to individual response. When ≥1 follicle was >1.8 cm in diameter, a final trigger of 5,000 IU of hCG, IM. IUI was performed 17–23 hours later **Participants** n=53 (127 cycles) **Dropout** 0		**Adverse events** None	mild endometriosis: women having had surgical reduction with superovulation and IUI (25/53, 47%) was lower (p=0.04) than in women with no treatment (34/50, 68%).
Walch et al 2008 Austria [164]	**Study design** RCT, open labelled **Setting** Single centre, university hospital **Population** n=41 Mean age: 32.2±6.3 years Stage III/IV: 37%	**Intervention** Implanon (Implantable Rod) **Duration** 1 year **Participants** n= 21 **Dropout** 7 (33%)	**Comparison** Depot medroxyprogesterone acetate (DMPA) **Duration** 1 year **Participants** n=20	**Pain (VAS score),** Mean decrease %, 6 months; I: 68%, C: 53%, ns Mean score change, 6 months; –3.47 (95% CI, 20.61, –13.67), p=0.69 **Use of analgesics** 12 months; I: 7/17, C: 5/13 **Side effects, n (%)** Moderate/severe ASE;	**Comments** Computer-generated randomization stratified by computer according to pretherapeutic pain score and body weight

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Inclusion criteria Age 19–50, symptomatic Stage I–IV endometriosis (r-AFS), proven histologically by laparoscopy or laparotomy, patients with dysmenorrhea, non-menstrual pelvic pain and dyspareunia, no oral contraceptive pill within 1-month, hormonal treatments during the last 3 months before study entry **Follow up time** 6 months and 1 year		**Dropout** 4 (20%)	I: 5 (24%), C: 8 (40%) Decrease in libido; I: 5 (24%), C: 6 (30%) Acne; I: 0, C: 1 (5%) Loss of hair; I: 1 (5%), C: 2 (10%) Breast tenderness; I: 5 (24%), C: 3 (15%) Headache; I: 3 (14%), C: 4 (20%) Depressive symptoms; I: 0, C: 2(10%) Hot flushes; I: 1 (5%), C: 2 (10%) Mean weight gain ± SD; I: 1.7±3.7, C: 1.9±5.9 **Patient's satisfaction, %** Very satisfied; I: 24, C: 26% Satisfied; I: 33%, C: 32% Uncertain; I: 29%, C: 10% Very/dissatisfied; I: 14%, C: 32%	
Warnock et al 2000 USA [165]	**Study design** RCT, double blind **Setting** Single centre **Population** n=33 Mean age: 29 years **Inclusion criteria** Laparoscopically diagnosed endometriosis, received 6 months of GnRH agonist therapy. Patients with prior history of GnRH agonist therapy, and those with	**Intervention** GnRH, 3.75 mg IM every 28 days + 25 mg sertraline daily for 3 days, thereafter 50 mg daily. Dose was adjusted if needed. Medication increased by 25 mg at each visit for patients scoring ≥6 on the HRSD up to a maximum of 200 mg per day. **Duration** 6 months with GnRH thereafter 3 months with setraline	**Comparison** GnRH, 3.75 mg IM every 28 days **Duration** 6 months **Participants** n=15 **Dropout** 0	**Depression, Hamilton Rating Scale for Depression** BL; I: 4.2±2.7, C: 5.7±2.4 Post; I: 5.3±4.2, C: 10.3±6.3, p=0.009 **HRDS >10** BL; I: 0/8, C: 0/15 Post; I: 1/17, C: 8/15 p=0.03	**Comments** Poor description of material and method as well as the results.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	depressive mood symptoms (HRDS >10), were excluded from the study. **Follow up time** Post treatment: 3 months	**Participants** n=18 **Dropout** 1			
Vercellini et al 1999 Italy [166]	**Study design** RCT, open label **Setting** Multicentre **Population** n=269 Mean age: 30 years Stage III/IV: 87% **Inclusion criteria** Premenopausal women with chronic pelvic pain who underwent conservative surgery for endometriosis, r-AFS score≥4 **Follow up time** 1 and 2 years	**Intervention** Conservative surgery + depot goserelin 3.6 mg SC monthly **Duration** 6 months **Participants** n=133 (seeking pregnancy n=69) **Dropout** 1 year: 26 (20%) 2 years: 52 (39%)	**Comparison** Conservative surgery + expectant management **Duration** 6 months **Participants** n=134 (seeking pregnancy n=76) **Dropout** 1 year: 31 (23%) 2 years: 60 (45%)	**Pain recurrences, moderate/severe, n (%) (Biberiglu & Behrman scale)** 1 year; I: 14 (13.1%), C: 22 (21.4%), p=0.143 2 years; I: 19 (23.5%), C: 27 (36.5%), p=0.082 **Total pain score=0, n** I: 95 (75%), C: 77 (62%) **Pregnancy rate** I: 8 (11.6%), C: 14 (18.4%)	**Comments** Computer-generated randomisation, centralised treatment allocation by telephone, Treatment with GnRH analogue within one week of conservative surgery
Vercellini et al 2002 Italy [167]	**Study design** RCT, open-label **Setting** Single centre, endometriosis outpatient clinic **Population** n=90 (66% of eligible) Age >30 years: 55.5% Stage III/IV: 57%	**Intervention** Cyproterone acetate, 12.5 mg/day, orally **Duration** 6 months **Participants** n=45 **Dropout**	**Comparison** Continuous low-dose monophasic OC; ethinyl estradiol, 0.02 mg and desogestrel 0.15 mg **Duration** 6 months **Participants** n=45	**Symptoms** ***Non-menstrual pain*** ***VAS score, Median (IQR)*** Post: I: 14 (0–40), C: 20 (0–30) Median decrease; I: 32 (17–44), C: 30 (17–47), ns Verbal rating; I: 0 (0–0), C: 0 (0–1) ***Dysmenhorrea*** ***VAS score, Median (IQR)*** Post: I: 0 (0–0), C: 0 (0–1)	**Comments** Computer-generated randomization sequence (1:1) using serially numbered, opaque, sealed envelopes Women assigned to cyproterone acetate were instructed to use

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Inclusion criteria Age 18–40 years, not desiring pregnancy, had undergone conservative surgery (laparoscopy/laparotomy) for stage I-IV symptomatic disease within 12 months. Only women with confirmed surgical eradication and who had recurrent pelvic pain for more than 6 months, no other therapies than non-steroidal anti-inflammatories **Follow up time** Post treatment (6 months)	6 (13%)	**Dropout** 9 (20%)	Median decrease: I: 68 (58-79), C: 60 (50-75), ns Verbal rating; I: 2 (1–2), C: 1(1–2) ***Deep dyspareunia*** ***VAS score, Median (IQR)*** Post: I: 13 (10–30), C: 15 (0–20) Median decrease: I: 20 (10–45), C: 30 (20–40), ns Verbal rating; I: 1 (0–1), C: 1 (0–1) **QoL (SF-36), mean ± SD** General health; I: 65.8±15.6, C: 60.6±13.1, ns Pain; I: 81.3±19.4, C: 69.8±20.9, ns **Satisfied with treatment, n (%)** Very satisfied I: 6 (13%), C: 5 (11 %) Satisfied: I: 27 (60%), C: 25 (56%) **Depression (HADS), mean ± SD** I: 9.5±7.4, C: 10.4±4.9 **Sexual function (Revised Sabbatsberg Sexual Rating Scale), Mean ± SD** I: 47.4±20.5, C: 49.5±14.9, ns **Adverse events n (%)** Spotting; I: 12 (28%), 18 (44%) Breakthrough bleeding, I: 3 (7%), C: 4 (10%) Bloating/swelling; I: 14 (32%), C: 15 (37%) Weight gain: I: 8 (19%), C: 10 (24%) Decreased libido; I: 7 (16%), C: 2(5%) Depression; I: 5 (11%), C: 2 (5%) Hot flushes; I: 3 (7%), C: 0	mechanical forms of contraception. ITT analysis

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				Irritability; I:3 (7%), 1 (2%) Vaginal dryness; I: 2 (5%), C: 0 Headache; I: 2 (5%), C: 7 (17%) Nausea; I: 0, C: 4 (10%)	
Vercellini et al 2003 Italy [168]	**Study design** RCT, open labelled **Setting** Single centre (tertiary care and referral centre for women with endometriosis) **Population** n=40 (55% of eligible) Stage III/IV: 78% **Inclusion criteria** Parous women ≤40 years, symptomatic stage I-IV endometriosis (r-AFS), undergoing first-line operative laparoscopy for symptomatic endometriosis, did not want children, dysmenorrhea ≥6 months. Exclusion; previous hormonal treatment 3 months before study entry (6 months for GnRH agonists) **Follow up** 12 months	**Intervention** Laparoscopic surgery + immediate levonorgestrel-releasing intrauterine system (LNG-IUD) insertion **Participants** n=20 **Dropout** 2 (10%)	**Comparison** Laparoscopic surgery + expectant management **Participants** n=20 **Dropout** 1 (5%)	**Pain symptoms score** **VAS 0–100, median (IQR)** ***Dysmenorrhea*** I: 22 (12–39) C: 41 (21–58) Absolute risk reduction: 35% (95% CI, 9–61) ***Deep dyspareunia*** I: 16 (12–33), C: 34 (20–44) Median reduction; I: 31 (20–45), C: 15 (10–40), ns ***Non-menstrual pain*** I: 31 (20–48), C: 36 (21–45) Median reduction: Dysmenorrhea moderate-severe recurrence I: 2/20, C: 9/20 **Overall degree of satisfaction with treatment** Satisfied/very satisfied; I: 75%, C: 50%	**Comments** Computer-generated randomization sequence using serially numbered, opaque, sealed envelopes
Vercellini et al 2005 Italy [169]	**Study design** RCT, open labelled **Setting** Single academic centre	**Intervention** Monophasic estrogen-progestogen combination; ethinyl E2, 0.01 mg	**Comparison** Norethindrone acetate, 2.5 mg/day. **Duration**	**Pain symptoms** ***Dysmenorrhea*** VAS score, Mean ± SD Post: I: 8.7±20.7, C: 3±11.3 Mean decrease:	**Comments** Computer-generated randomization (1:1) sequence using serially numbered,

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Population n=90 Age ≥30 years: 61% Stage III/IV: 59% **Inclusion criteria** Age 1–35 years, recurrent moderate or severe pelvic pain after unsuccessful conservative surgery for symptomatic rectovaginal endometriosis, no ovarian endometrioma of diameter ≥3 cm at vaginal ultrasonography; or no therapies for endometriosis other than nonsteroidal anti-inflammatory drugs in the 3 months before study entry **Follow up time** Post treatment (12 months)	(continuous) + cyproterone acetate, 3 mg/day **Duration** 12 months **Participants** n=45 **Dropout** 7 (16%)	12 months **Participants** n=45 **Dropout** 5 (11%)	I: 63.7±23.3, C: 72.8±22.5, ns VRS; I: 0.3±0.7, C: 0.1±0.4 ***Deep dyspareunia*** VAS score, Mean ± SD Post: I: 10.8±22.9, C: 13.8±23.0 Mean decrease: I: 35.6±28.3, C: 37.6±22.2, ns VRS; I: 0.4±0.8, C: 0.5±0.8 ***Non-menstrual pain*** VAS score, Mean ± SD Post: I: 25±27.9, C: 14.5±20.9 Mean decrease: I: 27.5±31.2, C: 43.0±21.7, ns VRS; I: 0.8±0.9, C: 0.4±0.6 ***Dyschezia*** VAS score, Mean ± SD Post: I: 10.0±17.1, C: 7.5±14.1 Mean decrease: I: 42.9±22.0, C: 45.7±21.8, ns VRS; I: 0.3±0.5, C: 0.3±0.5 **Degree of satisfaction n (%)** Post: very satisfied: I: 6 (13%), C: 11(24%) Satisfied: I: 22 (49%), C: 22 (49%) **Amenorrhea n (%)** Post: I: 17 (45%), C: 29 (72%) **Break through bleeding (n)** I: 7, C: 2 **Side effects, n (%)** Overall, I: 16 (39%), C: 21 (50%) Weight gain; I: 7 (17%), C: 12 (29%) Headache; I: 3 (7%), C: 2 (5%) Nausea; I: 3 (7%), C: 0	opaque, sealed envelopes ITT analysis

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				Depression; I: 2 (5%), C: 3 (7%) Decreased libido; I: 2 (5%), C: 4 (9%) Acne; I: 1 (2%), C: 2 (5%) Bloating/swelling; I: 1 (2%), C: 4 (9%) Brest tenderness; I: 1 (2%), C: 0	
Wickström et al 2012 Sweden [170] Wickström et al 2013 Sweden [171]	**Study design** RCT, double-blind randomized controlled trial (phase II) **Setting** Recruitment through advertisements and from the gynaecological outpatient unit at the participating three clinics **Population** n=42 **Inclusion criteria** Presence of peritoneal or ovarian endometriosis verified by laparoscopy and dysmenorrhea with a pain score of .50 mm on the VAS. Main exclusion criteria were reduced patency in the fallopian tubes and intention to achieve pregnancy during the forthcoming year. **Follow up time** 6, 9 and 12 months	**Intervention** Perturbation with lignocaine 1 mg/ml in Ringer solution **Duration** Three consecutive menstrual cycles **Participants** n=24 **Dropout** 4 (17%) 8 (33%)	**Comparison** Placebo (perturbation with Ringer solution) **Duration** Three consecutive menstrual cycles **Participants** n=18 **Dropout** 4 (22%) 8 (44%)	**Pain (VAS)** ***Improved ≥50%*** 6 months; I: 2, C: 0 9 months; I: 4, C: 0 **QoL, EHP-30, median** ***Pain*** 6 months; I: –13.6, C: –11.4 12 months; I: –8, C: –11.4 Control/powerlessness 6 months; I: –8.3, C: –6.3 12 months; I: –12.5, C: –20.8 ***Emotional well-being*** **6 months**; I: –4.2, C: –12.5 12 months; I: –20.8, C: –12.5 ***Social support*** 6 months; I: –18.8, C: –6.3, p=0.034 12 months; I: –12.5, C: –6.3 ***Self-image*** 6 months; I: –8.3, C: 0 12 months; I: –8.3, C: 0 ***Sexual intercourse*** 6 months; I: –10, C: 5 12 months; I: –7.5, C: –7.5	**Comments** ITT analysis Patients were randomized sequentially as they were eligible Solutions for perturbation were produced and released in a double-blinded manner The number of participating patients was calculated for pain (VAS) endpoint and was not adjusted for the possible effects on quality of life.
Wong et al 2010 China [172]	**Study design** RCT **Setting** Single centre	**Intervention** Levonorgestrel-releasing intrauterine system (LNG-IUS)	**Comparison** Medroxyprogesterone acetate (MPA), 150 mg IM 3 monthly depot	**Symptom** Pain score: No significant difference between groups at any time point except 3 years when significant lower in intervention group	**Comments** Randomisation using Randomization.com, permuted block 10.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Population n=30 Mean age: 39 years **Inclusion criteria** Age ≥30, history of conservative surgery within the past five years for III and IV endometriosis, no evidence of lesion recurrence, no desire for pregnancy in the coming three years **Follow up time** 3 years	**Duration** 3 years **Participants** n=15 **Dropout** 3 years: 2 (13%)	**Duration** 3 years **Participants** n=15 **Dropout** 3 years: 5 (33%)	Dyspareunia: No significant within or between groups Bowel/urinary: No significant within or between groups **Recurrence** Pelvic endometric lesion: None in both groups Cyst: Common in intervention group **Compliance** I: 2, C: 8, p<0.025 **Change in BMD, Mean ± SD** Hip g/cm^2; I: 0.023±0.05, C: –0.03±0.04, p<0.02 % change; I: 2.56±5.66, C: –4.27±5.73, p=0.01 Lumbar spine, g/cm^2: I: 0.071±0.04, C: –0.017±0.04, p<0.001 % change; I: 7.02±3.56, C: –1.66±3.85, p<0.001	ITT analysis
Zheng 2013 China [173]	**Study design** Prospective controlled study **Setting** Single centre, Hysteroscopic centre **Population** n=46 Mean age: 37±5 years **Inclusion criteria** Women with adenomyosis, menorrhagia and dysmenorrhea, desired to retain	**Intervention** Transcervical resection of the endometrium + levonorgestrel-containing intrauterine system (LNG-IUS) **Participants** n=23 **Dropout** 3 (13%)	**Comparison** Levonorgestrel-containing intrauterine system (LNG-IUS) **Participants** n=23 **Dropout** 4 (17%)	**Dysmenhorrea (VAS, 0–10)** No statistical significant between groups, but within groups as compared to baseline **Amenorrheic** 6 months; I: 95%, C: 8.6% 12 months; I: 100%, C: 16% **Adverse events** Insomnia; C: 1 Depression; C: 1 Irregular bleeding; C: 1	**Comments** Blinding unclear

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	uterus, not seeking fertility treatment or desire to extend family, in good health with no significant cardiac or liver disease, had not used any hormone therapy in the preceding 6 months, not yet menopausal, had hysteroscopic examination to exclude endometrial polyps and sub-mucous fibroid, had endometrial biopsy excluding hyperplasia or neoplastic condition within 3 months of the study, and had a diagnosis of adenomyosis confirmed by MRI or transvaginal scan. **Follow up time** 3, 6, 12 months following insertion				
Zhu et al 2014 China [174]	**Study design** RCT, open labelled **Setting** Single centre **Population** n=104 Mean age: 28.5 years Stage I: 60% **Inclusion criteria** Aged 20–40 years, infertile women with minimal or mild endometriosis confirmed by laparoscopy (r-AFS), no	**Intervention** Laparoscopy + OC: 30 µg ethinyl estradiol and 150 µg desogestrel/tablet,daily **Duration** 63 days **Participants** n=52 **Dropout** 2 (4%)	**Comparison** Laparoscopy + no medical treatment **Duration** NA **Participants** n=52 **Dropout** 0	**Pelvic pain (VAS score, scale 0–100), median (IQ range)** I: 15 (0–46) C: 29 (0–56), p<0.05 **Pregnancy rate** I: 20 (38.5%) C: 24 (46%) **Live birth** I: 14 (70%) C: 19 (79) **Miscarriage** I: 4 (20%), C: 3 (12.5%) **Side effects, n (%),**	**Comments** Computer-generated list of random numbers. Sealed envelopes ITT analysis The arm/group receiving herbs and CO was excluded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	previous medical or surgical treatments for endometriosis, **Follow up time** 22.17±3.39 months, range, 14–27 months			***Intervention group only*** Irregular bleeding: 14 (27%) Breast tenderness: 13 (25%) Weight gain: 9 (17%) Gastrointestinal discomfort: 4 (7.7%)	
Zupi et al 2004 Italy [175]	**Study design** RCT **Setting** Single centre, university hospital **Population** n=150 Mean age: 36 years **Inclusion criteria** Aged 20–43 years, regular menstrual cycles, a history of symptomatic severe endometriosis diagnosed surgically (r-AFS), relapse of endometriosis-related pain after previous endometriosis surgery. Stage III and IV **Follow up time** Post treatment and 6 months	**Intervention 1** Leuprolide acetate 11.25 mg every 3 months + transdermal E_2 25 µg and daily oral norethindrone 5 mg **Duration** 12 months **Participants** n=50 **Dropout** 4 (8%)	**Comparison 1** Leuprolide acetate 11.25 mg every 3 months **Participants** n=50 **Dropout** 6 (12%) **Comparison 2** Estroprogestin; oral ethinyl E_2 30 µg + gestodene daily 0.75 mg **Participants** n=50 **Dropout** 7 (14%) **Duration** 12 months	**Symptoms (VAS),** ***Pelvic pain, mean±SD*** 6 months; I: 1.5±0.4, C1: 1.3±0.5, C2: 1.9±0.8 Post; I: 0.3±0.1, C1: 0.2±0.1, C2: 0.8±0.5 12 months FU; I: 3.7 ±2.7, C1: 3.2±2.6, C2: 5.9±2.5 ***Dysmenorrhea, mean±S D*** 6 months; I: 0±0, C: 0±0, C2: 1.9±1.1; Post; I: 0±0, C: 0±0, C2: 0.9±0.5 12 months FU; I: 3.1±1, C: 3.4±1.2, C2: 4.9±2 ***Dyspareunia, mean±SD*** 6 months; I: 2.4±1.6, C: 2.6±1.3. C2: 2.7±1.5 Post; I: 1.2±0.6, C: 1.4±0.5, C2: 1.3±0.6 12 months FU; I: 2.7±1.5, C: 2.2±1.1, C2: 3.9±1.4 **QoL (SF-36), mean±SD** ***General health*** Post: I: 59.2±13.7, C: 54.9±12.7, C2: 51.2±14.2 6 months FU; C: 51.6±13.7, C2: 51.3±13I: ***Pain*** Post; I: 63.6±17, C: 62.1±14, C2: 58.3±14.2 6 months FU;	**Comments** computer-generated randomization number sequence. Assessor blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				I: 57.2±11.4, C1: 58.4±18.1, C2: 50.4±18.5 **BMD lumbar spine (g/cm^2), mean±SD** 6 months; I: 1±0.11, C: 1±0.112, C2: 1.04±0.125 Post; I: 0.995±0.102, C: 0.981±0.099, C2:1.035±0.121 12 months FU; I: 1.01±0.09, C: 0.995±0.11, C2: 1.052±0.132 **Adverse events, (%)** Hot flushes; I: 26%, C: 77%, C2: 0% Emotional change; I: 11%, C: 36%, C2: 7% Abnormal bleeding; I: 7%, C1: 2%, C2: 16% Other; I: 4%, C: 9%, C2: 12%	

ADI = Addative diameter of implants; **BDI** = Beck Depression Inventory; **BL** = Baseline; **BMD** = Bone mineral density; **CGI** = Clinical Global Impressions; **EHP-30** = Endometriosis health proifile-30; **EAPP** = Endometriosis-associated pelvic pain; **ET** = Embroy transfer; **FSI** = Female sexual function index; **IQR** = Inter quartile range; **LA** = Leuprolide acetate depot; **STAI** = State-trait anxiety inventory; **EEC stage** = Endoscopic endometriosis classification; **HADS** = Hospital anxiety and depression scale; **LHRH** = Luteinizing hormone releasing hormone; **LNG-IUS** = Levonorgestrel-releasing intrauterine system; **MPA** = Medroxyprogesterone acetate; **NRS** = Numeric rating scale; **NS** = Non-significant results; **HRT** = Hormone replacement therapy; **IM** = Intra muscular; **IS** = Injected subcutaneously; **OC** = Oral contraceptive; **OCP** = Oral contraceptive pill; **r-AFS** = Revised American Fertility Society; **US** = Ultrasound; **VRS** = Verbal rating scale; **TPSS** = Total Pelvic Symptom Score; **2D-TVUS** = Two-dimensional transvaginal ultrasound; **FSH** = Follicle-stimulating hormone; **LH** = Luteinizing hormone; **IUI** = Intrauterine insemination; **ICSI** = Intracytoplasmic sperm injection; **IVF** = In vitro fertilization

Laparoscopy, alphabetic order

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Abbott 2004 UK [176]	**Study design** RCT, blinded, crossover study **Setting** Single centre **Population** n=39 (23 % of eligible) Mean age: 32 years Previous medical treatment: 51% Previous surgical treatment: 17% **Inclusion criteria** Clinical symptoms and signs suggestive of endometriosis e.g. dysmenorrhea, non-menstrual pelvic pain, dyspareunia or dyschezia, and pelvic abnormality on examination, in association with histologic evidence of endometriosis at the time of surgery **Follow up time** 6 and 12 months	**Intervention** Immediate surgery (IS); excision by laparoscopy at 1st surgery **Participants** n=20 **Dropout** 0	**Comparison** Delayed surgery group; Staging laparoscopy performed at 1st time of surgery. At surgery 2, 6 months later, surgical excision of endometriosis **Participants** n=19 **Dropout** 0	**Change in pain (ISG), n (%)** ***Surgery 1*** Improvement I: 16 (80), C: 6 (32) No change/worse pain I: 4 (20), C: 13 (68) ***Surgery 2*** Improvement I: 8 (53), C: 15 (83) No change/worse pain I: 7 (47), C: 3 (17) **Pain symptoms, VAS score; MD (95% CI)** ***Dysmenorrhea*** 6 months: 10.8 (–7.4 to 29.1), p=0.24 12 months: –1.1 (–20.8 to 18.6), p=0.91 ***Non-menstrual pelvic pain*** 6 months: –8.5 (–29.5 to 12.4), p=0.41 12 months: 3.4 (–11.8 to 18.7), p=0.65 ***Dyspareunia*** 6 months: –6.4 (–29.9 to 17.2), p=0.58 12 months: –6.5 (–24.7 to 11.5), p=0.47 ***Dyschesia*** 6 months: 2.5 (–21.5 to 26.6), p=0.83 12 months: –3.1 (–20.6 to 14.5), p=0.72	*Low risk of bias* **Comments** Computer-generated randomization blocks of 10, concealment achieved by third-party allocation Assessor blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				QoL (EQ-5D), mean (SD) 12 months Index summary; I: 0.82, C: 0.85 VAS summary; I: 88.6 (10.4), C: 82.7 (16.2) **Sexual activity, score mean (SD)** Discomfort; 6 months; I: 2.4 (1.9), C 3.1 (1.9), ns 12 months; I: 1.8 (1.7), C: 1.8 (1.5), ns	
Alborzi et al 2004 Iran [177]	**Study design** RCT, “double blind” **Setting** 2 centres **Population** n=100 Mean age: 28 years Stage III/IV: 62% Infertility: 62% **Inclusion criteria** Laparoscopy for endometriomas >3 cm, no previous surgical treatment of endometriosis or estrogen-suppressing drugs in the last 6 months **Follow up time** 1 year, 2 years	**Intervention** Cystectomy **Participants** n=52 **Dropout** 0	**Comparison** Fenestration and coagulation **Participants** n=48 **Dropout** 0	**Recurrence of cyst per person** 1 year: I: 3 (5.8%), C: 9 (18.8 %), p=0.09 2 years: I: 9 (17.3%), C: 15 (31.3%), p=0.16 **Recurrence of symptoms of endometrioma** 1 year: I: 2 (5.3%), C: 6 (20%), p=0.13 2 years: I: 6 (15.8%), C: 17 (56.7%), p=0.001 **Clinical pregnancy rate** 1 year: I: 59.4 %, C: 20% (estimated from the figure in the article)	**Comments** Computerized randomization, before surgery Patients were aware of the two methods of surgery, but they and the surgeon did not know which one was better. All surgery was performed by the same person

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Benassi et al 2003 Italy [178]	**Study design** RCT, double blind **Setting** Single centre, university hospital **Population** n=44 Age range: 23–36 AFS score range: 18–66 (moderate to severe endometriosis) **Inclusion criteria** Clinical and sonographic evidence of ovarian endometriosis volume of ≥30 ml second- and third-degree dysmenorrhea scores14, no included previous surgery and medical treatment for endometriosis in previous 6 months. **Follow up time** 6, 12 and 18 months	**Intervention** Laparoscopic excision with Mesna 20% solution (approx. 80 ml) **Participants** n=22 **Dropout** 0	**Comparison** Laparoscopic excision with saline 5% solution, (approx. 80 ml) **Participants** n=22 **Dropout** 0	**No of patients with cysts, n (%)** 6 months; I: 1 (5%), C: 3 (14%), ns 12 months; I: 1 (5%), C: 4 (18%), ns 18 months; I: 1 (5%), C: 5 (23%), ns **Dysmenorrhea, scale unclear, n (%)** 6 months; I: 2 (9%), C: 4 (18%), ns 12 months; I: 2 (9%), C: 5 (23%), ns 18 months; I: 3 (14%), C: 7 (32%), ns **Pregnancy, n** 6 months; I: 0, C: 0, ns 12 months; I: 1, C: 0, ns 18 months; I: 2, C:1, ns	**Comments** Low risk of bias Randomized using a computer-generated sequence The same surgeon operated on all patients.
Brown et al 2007 UK, USA [179]	**Study design** RCT, double blind **Setting/recruitment** Multicentre **Population** n=187 Mean age: 32.4±5.8 years Infertility: 117 (63%) **Inclusion criteria** Aged ≥18 years, in good health, laparoscopic diagnosis of	**Intervention** Laparoscopic surgery and Adept **Participants** n=124 **Dropout** *Unclear but for the whole population that had Adept 6.6%*	**Comparison** Laparoscopic surgery and Ringer's solution (LRS) **Participants** n=119 **Dropout** *Unclear but for the whole population who got LRS 6.3%*	**Pelvic pain symptoms (VAS)** No sign difference between groups **Adverse events** Related; I: 55%, C: 38% SEA; I: 44%, C: 36% Headache; I: 34%, 32% Nausea; I: 16%, C: 17% Post procedural discharge; I: 14%, C: 13% Dysmenorrhea; I: 13%, 11% Constipation; I: 11%, C: 10%	**Comments** Low risk of bias Randomized by computer-generated randomization on a 1:1 basis Only the population with endometriosis is included (189/449) Safety: ITT analysis Efficacy results: PP

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	endometriosis, no use of concomitant systemic corticosteroids, antineoplastic agents, and/or radiation. Intraoperative exclusion criteria: patients requiring an additional non-obstetric/gynecologic surgical procedure; unplanned surgery necessitating opening the bowel, any laparotomy procedure; use of another adhesion reduction agent **Follow up time** 1 and 2 months				The study solutions were presented in identical 1 litre infusion bags, and each bag had an outer wrap that contained the study code and patient number on an identification label.
Bulletti et al 2001 Italy [180]	**Study design** Prospective cohort study **Setting** Single centre **Population** n=28 Mean age: 30.4±4.6 years **Inclusion criteria** Laparoscopy for uncontrolled dysmenorrhea, diagnosis of endometriosis stage II–IV, retrograde bleeding **Follow up time** 3 and 24 months	**Intervention** Laparoscopy and endometrial ablation (EA) with roller ball of 50 Watt **Participants** n=14 **Dropout** 0	**Comparison** Laparoscopy **Participants** n=14 **Dropout** 0	**Recurrence, 2nd laparoscopy, n (%)** I: 0, C: 9 (64%) **Dysmenorrhea (verbal score, 0–5) median** 3 months; I: 1, C: 3 24 months; I: 3, C: 4 **Pain symptoms, n (%)** Disappearance; I: 9 (64%), C: 0 Significant reduction; I: 3 (21%), C:0	**Comments**

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Carmona et al 2011 Spain [181]	**Study design** RCT **Setting/recruitment** Single centre **Population** n=90 Mean age: 32 years Dysmenorrhea: 42% Infertility: 22% **Inclusion criteria** Age 18–40 years, uni- or bilateral symptomatic endometriomas ≥3 cm, no counter indication for use of GnRH-agonists, no previous pelvic surgery, no evidence of DIE, no previous use of estrogen suppressive drugs, including OC, GnRH-agonists, progestins, or danazol in preceding 6 months. **Follow up time** 12–60 months	**Intervention** Ovarian cystectomy **Participants** n=45 **Dropout** 9 (20%)	**Comparison** Laser vaporization+ 2 months with IM triptorelin, 3.75 mg **Participants** n=45 **Dropout** 7 (16%)	**Recurrence endometrioma** ***Per patient*** 12 months: I: 4 (11%), C: 12 (31%), p=0.04 60 months: I: 8 (22%), C: 14 (37%), p=0.2 ***Per endometrioma*** 12 months; I: 4 (9%), C: 4 (8%), ns 60 months; I: 8 (18%), C: 14 (28%), ns ***Time of recurrence (months), mean±SD*** I: 18.1±10.1, C: 7.5±4.3, p<0.003 **Pregnancy rate in patients desiring pregnancy, %** 12 months: I: 19.2%, C: 20.8%, ns 60 months: I: 38.1%, C: 44.4%, ns	**Comments** Computer-generated randomization list generated using the method of simple randomization Sealed opaque envelopes Interventions performed by the same team of surgeons with wide experience in both techniques
Ceccaroni et al 2012 Italy [182]	**Study design** Prospective controlled study **Setting/recruitment** Single centre/consecutive enrolment **Population** n=126 Age range: 24–46 years Previous pelvic surgery: 45% Previous pregnancies: 11%	**Intervention** Laparoscopic complete excision using non-nerve sparring (classic) **Participants** n=65 **Dropout** 0	**Comparison** Nerve-sparing laparoscopic complete excision (the Negrar model) **Participants** n=61 **Dropout** 0	**QoL** (modified from Bergmark's serie + including sexual functions (DSMIV criteria) + psychological status (Short WHOQoL of OMS) Comparable between the groups **Relapse rate** I: 8%, C: 5%, p=0.6 **Sexual function, n (%)**	**Comments** Unclear if assessor was blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Inclusion criteria Unclear **Follow up time** >12 months			Perception of sexual sensation without orgasm; I: 0, C: 7 (11%), p<0.001 Unchanged sexual pleasure; I: 29 (48%), C: 7 (11%), p<0.001 Reduced sexual pleasure and orgasm frequency; I: 11 (18%), C: 3 (5%), p<0.01 **Denervated patients' data** Days of self-cauterization, mean (SD); I: 39.8 (19.5), C: 121.1 (67.9), p<0.01 Severe neurological pelvic dysfunction, n (%); I: 1 (2%), C: 56 (86%), p<0.001 Candidates for neuromodulation due to urinary incontinence for >2 years; I: 1 (2%), C: 10 (15%), p<0.05	
Che et al 2014 China [183]	**Study design** Prospective controlled study **Setting** Single centre **Population** n=108 (139 invited) **Inclusion criteria** Age >25 years, fertile women, diagnosed with DIE by symptoms, clinical examination, and imaging techniques. Patients with a contraindication to laparoscopy	**Intervention** Conventional surgery (open & laparoscopy) **Participants** n=63 **Dropout** 0	**Comparison** Nerve sparing surgery (open and laparoscopy) **Participants** n=45 **Dropout** 0	**Pain symptoms (VAS), mean (range)** 6 months; I: 1.7 (0–4), C: 2.2 (0–9) 12 months, I: 1.8 (0–3), C: 2.1 (0–6) 24 months; I: 2.2 (0–5), C: 2.5 (0–6) **Urinary symptoms (IPSS score,) mean (range)** 6 months; I: 7.8 (0–30), C: 6.1 (0–24) 12 months; I: 5.9 (0–26), C: 5.4 (0–22) 24 months; I: 5.6 (0–25), C: 5.5 (0–23)	**Comments** Low/moderate risk of bias Patients were assigned to each group based on patients' requirements

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	because of severe medical illness were excluded. **Follow up time** 6–24 months			**Sexual function (FSFI score), max score 36, mean ± SD** BL; I: 18.9±4.5, C: 19.3±4.8 6 months; I: 25.3±5.1, C: 26.2±5.2 12 months; I: 24.9±4.9, C: 25.8±5 24 months; I: 23.6±4.7, C: 24.9±4.6	
Daniels et al 2009 UK [184]	**Study design** RCT, patient-blinded **Setting/recruitment** Multicentre (18 hospitals)/Patients presenting to gynaecology outpatient clinics **Population** n=487; endometriosis n=146 Mean age: 31 years **Inclusion criteria** Laparoscopy diagnoses endometriosis, minimal endometriosis, chronic pelvic pain ≥6 months, located within/ below anterior iliac crests, no previous LUNA, hysterectomy or therapeutic procedures for, or diagnosis of, moderate to severe endometriosis **Follow up time** 1 and 3 months, 1,2,3 and 5 years	**Intervention** Laparoscopic uterosacral nerve ablation (LUNA) **Participants** n=66 **Dropout** Unclear (21 % for the whole group)	**Comparison** Laparoscopy without pelvic denervation (no LUNA) **Participants** n=80 **Dropout** Unclear (21% for the whole group)	**Pain symptoms, (VAS), MD (95% CI)** ***Worst pain level*** 12 months; MD: −0.02 (−0.61 to 0.65), ns Over all time points; MD: −0.04 (−0.33 to 0.25), ns Over all time points, ***Noncyclical pain*** 12 months; MD: 0.17 (−0.40 to 0.74), ns Over all time points; MD: −0.11(−0.50 to 0.29), ns ***Dysmenorrhea*** 12 months; MD: −0.10 (−0.7 to 0.50), ns Over all time points MD: −0.09 (−0.49 to 0.30), ns ***Dyspareunia*** 12 months; MD: 0.34(−0.34 to 1.02), ns Over all time points; MD: 0.18 (−0.22 to 0.62), ns **QoL EuroQoL EQ-5D** 12 months, MD (95% CI) 0.03 (−0.03 to 0.09), p=0.3 EQ-VAS, MD (95% CI) −0.78 (−3.9 to 5.4), p=0.3 **At least 1 day off work** I: 27%, C: 22%, p=0.2	**Comments** Randomized via a telephone call to the Birmingham University Clinical Trials Unit, or via Internet-based randomization service Only data from the population endometriosis is included

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Darai et al 2010 [185] Touboul et al 2014 [186] France	**Study design** RCT **Setting/recruitment** Single centre **Population** n=52 (out of 79) Mean age: 33 years Prior surgery for endometriosis: 67% **Inclusion criteria** Age ≥18 years, diagnosed with colorectal endometriosis based on digestive and gynecologic symptoms, clinical examination, imaging techniques including TVS, rectal endoscopic sonography, and MR, no prior colorectal surgery for benign or malignant disease **Follow up time** Median 19 months and 51 months (4 years)	**Intervention** Laparoscopically assisted colorectal resection **Participants** n=26 **Dropout** 0 Long term; 6 (23%)	**Comparison** Open colorectal resection (laparotomy) **Participants** n=26 **Dropout** 0 Long term: 6 (23%)	**Symptoms** ***Dysmenorrhea*** 19 months, median, (range); I: 5 (1.19), C: 5.5 (–7 to 10), ns 51 months, mean; I: 2.3, C: 2.2 ***Dyspareunia;*** 19 months, median, (range): I: 4.3 (–1,9), C: 3.8 (0 to 10), ns 51 months, mean; I: 2.2, C: 2.2 ***Back pain*** 19 months, median; I: 2.8, C: 1.9, 51 months, mean; I: 3.2, C: 3.8 ***Abdominal cramping*** 19 months, median; I: 2.6, C: 2.4 51 months, mean; 2.7, C: 3.9 ***Dysuria*** 51 months, mean; I: 1.9; C: 2.4, ns ***Dyschesia*** 19 months, median; I: 3.4, C: 3.3 51 months, mean; I: 3.1, C: 4.2 **QoL (SF-36) median change (range)** ***Sum physical*** 19 months: I: 14.8 (–49 to 81), C: 19.2 (–29 to 55.2), ns 51 months; I: 20 (–34,81), C: 19.5 (–38, 63), ns ***Sum menthal*** 19 months: I: 25.4 (–26.5 to 70), C: 24.1 (–20.7 to 73), p=0.92 51 months, I: 20.0 (–34 to 81), C: 19.5 (–38 to 63), ns **Fertility** 19 months: Higher pregnancy rate in laparoscopic groups, p=0.006	**Comments** Randomization was performed at the department of gynaecology through using minimization alg01ithrn Non-inferiority trial Not blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				All spontaneous pregnancy occurred in intervention group. **Postoperative complication** 19 months: n >1: similar in both groups Total no of complication; higher in open surgery, p=0.004 **Postoperative recovery** 19 months: Faster in intervention group, p<0.001 **Hospital stay** No difference between groups	
Fanfani et al 2010 Italy [187]	**Study design** Matched case control study **Setting** 2 centres **Population** n=136 Median age: 33 years (range 22–46). Previous surgery: 15% Medical therapy before surgery: 18% Stage IV: 100% **Inclusion criteria** DIE with rectosigmoid involvement, nodules maximum diameter 3 cm with bowel stenosis 60%, presence of endometriosis-related symptoms. Preoperative work-up included bimanual palpation, vaginal and	**Intervention** Laparoscopic complete excision with full thickness discoid resection of rectosigmoid endometriosis **Participants** n=48 **Dropout** 12 (25%)	**Comparison** Recto-sigmoid segmental resection **Participants** n=88 **Dropout** 19 (21.5%)	**Recurrence, %** I: 14%, C: 11.5%, ns **Patients subjective satisfaction** Total; I: 89%, C: 93%, ns **Severe complications** Early post-operative; I: 6 (12.5%), C: 0 **Pregnancy** I: 6/22 (27%), C: no data	**Comments** Same surgical teams for both groups. Operative time was significantly longer in the control group than in the case group

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	abdominal ultrasound scan, double-contrast barium enema (DCBE), in cases of suspicious adenomyosis or doubtful ultrasound scan, abdominopelvic MRI **Follow up time** Median 33 months (case) Median 30 months (control)				
Fererro et al 2012 Italy [188]	**Study design** RCT **Setting** Single centre, university teaching hospital **Population** n=100 (121 eligible) Mean age: 32 years **Inclusion criteria** Age <40 years, bilateral endometriomas with largest diameter ≥3 cm, tried to conceive for ≥1 year before study. Male partners with normal semen parameters, patients with wish to spontaneously conceive after surgery. Exclusion criteria: previous ovarian or endometriosis surgery, polycystic ovary syndrome, premature ovarian failure, other endocrine diseases, bilateral tubal occlusion, uterine malformations, presence of non-endometriotic ovarian cysts, malignant ovarian disease, use of	**Intervention** Stripping of bilateral endometriomas. Hemostasis by use of laparoscopic suturing **Participants** n=50 **Dropout** 0	**Comparison** Stripping of bilateral endometriomas. Hemostasis by bipolar coagulation **Participants** n=50 **Dropout** 0	**Clinical pregnancy rate, n (%)** I: 18 (36 %), C: 15 (30%), ns **Recurrence of endometrioma** I: 1 (3.2%), C: 3 (6%), ns	**Comments** Blocked randomization (Random Allocation software version 1.00) Not blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	hormonal therapies 4 months before study, desire to use hormonal therapies after surgery **Follow up time** 12 months				
Healey et al 2010, 2014 Australia [189] Healey et al 2014 Australia [190]	**Study design** RCT, double blind **Setting/recruitment** Single centre, outpatient setting with pain symptoms suggestive of endometriosis booked for operative laparoscopy **Population** n=178 Mean age: 28 years Stage III–IV (r-AFS): 11% Previous surgery for endometrios: 17% Previous medications for endometrios: 18% **Inclusion criteria** Age ≥18, pain symptoms suggestive of endometriosis laparoscopy diagnostic, no use of continuous hormonal therapy. Excluded if endometriosis involving muscle levels of bowel, bladder, or ureter. **Follow up time** 12 months and 60 months	**Intervention** Ablation **Participants** n=89 At 5 years n=42 **Dropout** Pre: 4 (4.5%) 12 months: 37 (41.6%) Lost to follow up at 5 years 43 (48%)	**Comparison** Excision **Participants** n=89 At 5 years n=40 **Dropout** Pre: 4 (4.5%) 12 months: 32 (35.6%) Lost to follow up at 5 years 45 (50.5%)	**Pain (VAS, 0–10),** ***Reduction in score mean ±SD, 1 year*** Overall pain; I: 2.9±2.9, C: 2.9±3.4 Pelvic pain; I: 2.7±2.7, C: 2.6±3.5 Period pain; I: 2±3.9, C 2.4±3.9 Back pain; I: 1.1±2.8, C: 1.6±3.9 Rectal pain; I: 0.5±2.7, C: 1.4±3.7 Thigh pain; I: 0.4±3, C: 0.9±2.9 Abdominal pain; I:2±3.7, C: 2.4±3.1 Defecation pain; I: 0.7±3.1, C: 1.8±3.5 Volding pain; I: 0.6±2.7, C: 0.4±2.3 Nausea; I: 0.6±3.6, C: 1.7±2.7 Abdominal bloating; I: 1.5±2.8, C: 2.4±3.4 Vomiting; I: 0.9±2.3, C: 1.1±2.4 Dyspareunia; I: 1.8±4.1, C: 3.1±4.1 ***Reduction in score, median, 5 years*** Overall pain; I: 5.5, C: 5.8 Pelvic pain; I: 5.9, C: 6.2 Period pain; I: 5.3, C: 6.5 Back pain; I: 5, C: 4.7 Rectal pain; I: 1, C: 0.5 Thigh pain; I: 0.3, C: 0.8 Abdominal pain; I: 4.8, C: 3.2 Defecation pain; I: 2.5, C: 1.3 Volding pain; I: 0.3, C: 0.5 Nausea; I: 2.5, C: 0.7 Abdominal bloating; I: 5, C: 4.8	**Comments** Computer random number generator Consecutively numbered opaque envelopes, Blinded participants, assessors and medical staff The null hypothesis was: no difference in VAS scores between the two treatment groups at I year FU

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				Vomiting; I: 0, C: 0 Dyspareunia; I: 3.2, C: 6, p=0.03 **Pregnancy rate** 5 years: No difference p=0.27	
Hoo et al 2014 UK [191]	**Study design** RCT, double blind **Setting** Single centre, Endometriosis centre **Population** n=55 Mean age: 33 years Each participant had only one of their ovaries suspended and acted as their own control. At the end of the operation, women were randomized to have one ovary suspended for 36–48 h postoperatively. One of the two ovarian suspension sutures were cut to allow that ovary to fall back into the lesser pelvis. A new transabdominal suture was then re-inserted at the same site to act as a placebo **Inclusion criteria** Premenopausal women >19 years, diagnosed with severe pelvic endometriosis by preoperative TVUS. Women with evidence of severe endometriosis requiring extensive dissection of both pelvic sidewalls and/or rectovaginal space with preservation of the ovaries and	**Intervention** Suspended ovary **Duration** 36–48h **Participants** n=55 **Drop-out** 3 (5.5 %)	**Comparison** Unsuspended ovary **Participants** The women acted as their own control	**Ovarian adhesions, n (%)** Total; I: 20 (38.5%), C: 27 (51.9%) p=0.23 Moderate-severe; I: 5 (10%), 10 (19.2%) ***Pain symptoms, (VAS) OR (before vs after)*** Dysmenorrhea: 0.03 (0.00–0.21), p<0.001 Deep dyspareunia: 0.10 (0.01–0.39) p<0.001 Pelvic pain: 0.06 (0.00–0.35), p<0.001	**Comments** Suitability for randomization was determined at surgery Patients and ultrasound operators were blinded to womens randomization allocation. 17 patients had hormone treatment after surgery

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	the uterus were included in the study. **Follow up** 3 months				
Hong et al 2014 South Korea [192]	**Study design** Prospective controlled clinical trial **Setting** Multicentre; University Hospital or Medical Centre **Population** n=390 Mean age, intervention/comparison: 43±5.3/34.2±7.3 years **Inclusion criteria** Patients with pathologically proven DIE in the cul-de-sac. **Follow up time** 9 months (VAS, SF-36)	**Intervention** Laparoscopic Douglasectomy with hysterectomy **Participants** n=75 **Dropout** 19 (25%)	**Comparison** Laparoscopic Douglasectomy without hysterectomy **Participants** n=315 **Dropout** 28 (8.9%)	**Pain symptoms (VAS), change** I: 2.7±1, C: 1.58±1.1 **QoL (SF-36,) change, mean ± SD** General change; I: 41.9±8.5, C: 39.4±8.6 Body pain; I: 52.7±10.2, C: 54.5±8 **Perioperative complications, n (%)** I: 5 (7%), C: 10 (3%)	**Comments** Significant differences in age and BMI between groups. Longer operation time in hysterectomy group.
Johnson et al 2004 New Zealand [193]	**Study design** RCT, double blind **Setting/recruitment** Single centre **Population** n=123 Among these 67 with endometriosis Mean age: 30 years Previous laparoscopy/laparotomy: 87% Used opiate: 9% Dysmenorrhea: 91%	**Intervention** Laparoscopy + LUNA (laparoscopic uterine nerve ablation) **Participants** n=32 **Dropout** 12 months: 6 (19%)	**Comparison** Laparoscopy (and No LUNA) **Participants** n=35 **Dropout** 12 months: 5 (14%)	**Pelvic pain (VAS), 24 hrs post operation, Median (IQR)** BL; I: 6 (3, 7), C: 6 (5, 9) 24 hrs post op; I: 0.5 (0, 4), C: 1 (0,5) Resolved, n (%) I: 13 (41%), C: 6 (17%) Partially resolved I: 4 (13%), C: 6 (17%) No change 2 (6%), C: 1 (3%) Increase I: 0, C: 2 (6%) **Pain symptoms (VAS),**	**Comments** Participant and assessors were blinded

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Inclusion criteria Aged 18–45 years inclusive; a history of chronic pelvic pain, no change in medication for the three months prior to trial recruitment. Exclusion criteria: previous hysterectomy or pelvic malignancy, previous LUNA, known ovarian cysts, **Follow up time** 24 hours, 3 months and 12 months			**change from BL, median (IQR);** ***Non-menstrual pain*** 3 months: I: –1.3 (–3.1, 1), C: –3.5 (–5, –2) 12 months: I: 2 (–6, –2), C: –3.5 –5.8, –1), ns ≥50% reduction, n (%) 3 months; I: 9/28 (32%), C: 18/34 (53%) 12 months; I: 11/22 (50%), C: 15/30 (50%), ns ***Dysmenorrhoea*** 3 months: I: 0 (–3.5, 0), C: –2 (–5, 0) 12 months; I: 0 (–7, 1), C: –3 (–5.5, 0), ns ≥50% reduction, n (%) 3 months; I: 6/26 (23), C: 11/28 (39) 12 months; I: 7/21 (33), C: 11/24 (46), ns ***Deep dyspareunia*** 3 months: I: 0 (–3, 0), C: –3.5 (–7, –1) 12 months; I: 0 (–5, 0), C: –2 (–6, 0.5), ns ≥50% reduction, n (%) 3 months; I: 5/17 (29), C: 10/18 (56) 12 months; I: 6/10 (60), C: 8/16 (50), ns ***Dyschezia*** 3 months: I: 0 (–4.5, 0.8), C: –3 {–5.5, 0) 12 months; I: 0 (–3, 0.25), C: –1(–5, 0), ns ≥50% reduction, n (%) 3 months; I: 9/19 (47), C: 18/25 (72) 12 months;	

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				I: 7/14 (50), C: 10/23 (43) **Satisfaction, n (%)** 12 months: I: 18/26 (69%) C: 24/39 (80%) **Further surgery for pain by 12 months** I: 1/32, C: 2/35 **Prolapse by 12 months (suggestive symptoms)** I: 3/32, C: 2/35	
Landi et al 2006 Italy [194]	**Study design** Prospective cohort study **Setting/recruitment** Single centre/consecutive enrolment **Population** n=65 Mean age: 32 years Previous surgery for endometriosis: 71% **Inclusion criteria** Women with DIE, no medical therapy with progestins, GnRH agonist or birth control pills for ≥3–4 months prior surgery **Follow up time** Range 8–23 months for control group and 0.2–5 months for the intervention group	**Intervention** Nerve-sparing complete excision with segmental bowel resection **Participants** n=45 **Dropout** 0	**Comparison** Laparoscopic complete excision with segmental bowel resection **Participants** n=20 **Dropout** 1	**Symptoms, n (%)** ***Dysmenorrhea*** Disappeared; I: 6 (29%), C: 13 (30%) Decreased; I: 11 (52%), C: 26 (59%) Same; I: 0, C: 1 (2%) Increased; I: 1 (5%), C: 2 (5%) ***Dysuria*** Disappeared; I: 18 (90%), C: 39 (93%) Decreased; I: 0, C: 0 Same; I: 0, C: 1 (2%) Increased; I: 2 (10%), C: 2 (5%) ***Dischetia*** Disappeared; I: 16 (84%), C: 25 (61%) Decreased; I: 2 (11%), C: 10 (24%) Same; I: 1 (5%), C: 0 Increased; I: 0, C: 6 (15%) ***Dyspareunia*** Disappeared; I: 11 (69%), C: 17 (44%)	**Comments** Unclear if assessor was blinded The follow up time for the intervention group was much shorter

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				Decreased; I: 4 (25%), C: 17 (44%) Same; I: 1 (6%), C: 1 (3%) Increased; I: 0, C: 4 (10%) **Intensity score (VAS 0–10), change median (IQR)** ***Dysmenorrhea;*** I: 6 (4–8.3), C: 4.5 (2–7.3), ns ***Dysuria;*** I: 1 (1–1.8), C: 3 (1–4), p=0.03 ***Dischetia***; I: 6 (1–8), C: 4 (1–7), ns ***Dyspareunia;*** I: 2.5 (1–6.8), C: 5 (3–9), ns **Patient satisfaction, n (%)** Not satisfied; I: 1 (5%), C: 2 (5%) Satisfied; I: 1 (5%), C: 16 (36%) Very satisfied; I: 18 (86%), C: 26 (59%) **Minor and major complications** None **Long term sequalae** Severe constipation; I: 3, C: 15 Impaired vaginal lubrification; I: 3, C: 14	
Mereu et al 2010 Italy [195]	**Study design** Prospective controlled study **Setting/recruitment** Single centre, endometriosis referral centre/consecutive enrolment **Population** n=56 Mean age: 33 years	**Intervention 1** Laparoscopic excision + laparoscopic ureterolysis **Participants** n=35 **Dropout** 0	**Comparison** Laparoscopic excision + ureteroureterostomy **Participants** n=17 **Dropout** 0	**Complications, n (%)** Reinterventions; I: 4 (11%), C: 0 Ureteronecystostomy; I: 7 (20%), C: 2 (12%) Transient deficit-bladder voiding I: 6 (17%), C: 2 (17%) Bowel voiding; I: 6 (17%), C: 1 (6%) Urinary infection; I: 4 (11%), C: 1 (6%) Total; I: 27 (77%), C: 6 (35%)	**Comments**

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Previous treatment for EM; Hormonal: 89% Surgery: 63% **Inclusion criteria** Laparoscopic surgical treatment of DIE with preoperative moderate-severe ureter dilatation (≥1cm) detected by abdominal ultrasound and confirmed by IVP or by intraoperative detection of ureter dilatation **Follow up time** 1, 6, 12, and 24 months				
Meuleman et al 2014 Belgium [196]	**Study design** Prospective controlled follow up study **Setting/recruitment** University Hospital **Population** n=203 Mean age: 32 years (range 20–47) **Inclusion criteria** Women who underwent reproductive surgery and were classified as having as moderate or severe endometriosis (-rAFS III or IV, respectively). 58% had DIE with colorectal extension **Follow up time** Median 20 months	**Intervention** Bowel resection for DIE **Participants** n=76 **Dropout** 6 months 19 (25%)	**Comparison** No bowel resection **Participants** n=127 **Dropout** 6 months 49 (38.6 %)	**Pain symptoms (VAS), mean ± SE** 6 months Pelvic pain; I: 2.3±0.3, C: 2.1±0.3 Dysmenorrhea; I: 4.5±0.3, C: 3.6±0.4 Dyspareunia; I: 2.6±0.3, C: 2.4±0.3 **QoL (EHP-30) change, mean ± SE** 6 months; I: 19.1±1.8, C: 13.7±2.3 **Fertility** ***Cumulative live birth rate*** 1 year; I: 44%, C: 36% 2 years; I: 58%, C: 50% 3 years; I: 73%, C: 67% **Mode of conception, n (%)** Spontaneous; I: 18 (38%), C: 13 (48%) Stimulation + HIUI; I: 6 (13%), C: 1 (4%) IVF; I: 14 (29%), C: 10 (37%) IVF + donor sperm; I: 1 (2%), C: 0	**Comments** The majority (n=143/203; 70%) of patients included in the study had previously been operated for endometriosis elsewhere at least once before surgical treatment.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
				Intracytoplasmatic sperm injection; I: 6 (13%), C: 1 (4%) Cryo; I: 1 (2%), C: 2 (7%) Oocytes reception; I: 2 (4%), C: 0	
Moscarini et al 2014 Italy [197]	**Study design** Prospective controlled study **Setting** Single centre **Population** n=109 Men age: 33 years Previous pregnancy: 23/109 **Inclusion criteria** Age 25–40 years, ovarian endometrioma >3 cm Ø (TVS), regular menstrual cycle, post-operative treatment with GnRH analog for 3 months after surgery, tubal patency assessed by laparoscopic chromopertubation, no previous medical treatment for endometriosis, no presence of adenomyosis, no previous surgery for ovarian endometrioma, no co-existence of DIE **Follow up time** 2 years	**Intervention** Laparoscopic excision with stripping technique **Participants** n=45 **Dropout** 0	**Comparison** Ovarian cystectomy **Participants** n=64 **Dropout** 0	**Ultrasound relapse, n (%)** I: 25 (56%), C: 15 (15%), p=0.001 **Symptomatic recurrence, n (%)** I: 24 (53%), C: 14 (22%), p=0.0007 **Spontaneous pregnancy, n (%)** I: 2 (4%), C: 2 (22%), p=0.007 **% of specimen with adjacent ovarian tissue, n (%)** I: 12 (27%), C: 32 (50%), p=0.01	**Comments** Patients blinded, but unclear if assessor was blinded Patients were treated with the same post-operative medical therapy
Mossa et al 2010 Italy [198]	**Study design** RCT **Setting** Single centre	**Intervention** Direct stripping at the original adhesion site **Participants** n=47	**Comparison** Circular excision around initial adhesion site **Participants** n=43	**Recurrence** Total; I: 32%, C: 23% ***Recurrence + dysmenorrhea*** I: 6%, C: 5%, ns ***Recurrence + dyspareunia*** I: 2%, C: 2%, ns	**Comments** Computer generated randomisation. All laparoscopic procedures were

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Population n=92 Median age 29±8 years (range, 21–37 years) Infertility: 24% Dysmenorrhea: 40% Dyspareunia: 8% Pelvic pain: 19% No symptoms: 8.7% **Inclusion criteria** Mono or bilateral ovarian cysts, >3 cm, highly suggestive of endometrioma at TVUS. Exclusion criteria: previous medical or surgical treatments for endometriosis; gynecological comorbidity at the time of surgery **Follow up time** 4, 12 and 36 months	**Dropout** 2 (2%) for the whole population	**Dropout** 2 (2%) for the whole population	***Recurrence + pelvic pain*** I: 0, C: 2%, ns ***Recurrence in same ovary*** I: 21.3%, C: 16.3% **Accuracy (complete cystic wall removement)** I: 75%, C: 93% **Clinical pregnancy** 36 months; I: 2 (18%), C: 3 (30%)	executed by the same surgeon.
Muzii et al 2016 Italy [199]	**Study design** RCT, blinded **Setting/recruitment** Multicentre/ consecutive recruitment **Population** n=51 (82% of eligible) Mean age: 33±6 years Mean cyst Ø: 4 cm Pain: 61% Infertility: 39% **Inclusion criteria** Age 18–40 years, regularly menstruating, ultrasonographic	**Intervention** Combined excision/ablation technique on the other endometrioma **Dropout** 0	**Comparison** Conventional stripping technique of endometrioma on one side **Dropout** 0	**Cyst recurrence rates, 6 months** I: 1 (2%), C: 2 (5.9%) **Major complications** None	**Comments** Computer-generated randomisation, opaque, sealed envelope Patients/ personnel were blinded Oral contraceptives were allowed if pain recurred ≥1 month after surgery and not responsive too non-steroidal anti-inflammatory

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	diagnosis of endometrioma >3 cm on both ovaries, pain and/ or infertility as indication to surgical treatment, no major present or past chronic illness. A second sonogram was performed, at least 8 weeks apart from the first one, to confirm presence no previous surgical or medical treatment for endometriosis previous 3 months. **Follow up time** 1,3 and 6 months after surgery				drugs (NSAIDs) Patients served as their own control
Pados et al 2009 Greece [200]	**Study design** RCT **Setting/recruitment** Single centre/consecutive recruitment **Population** n=20 Age range: 22–40 years Infertility: 20% **Inclusion criteria** Diagnosis of endometrioma ≥3 cm in diameter. No history of cancer, suspected malignancy, pre-surgical evidence of premature ovarian failure and no use of estrogen-suppressive drugs in the last 6 months. Exclusion criteria; pregnancy and BMI > 0 kg/m^2 **Follow up time** 6, 12 months	**Intervention** Laparoscopic cystectomy **Participants** n=10 **Dropout** 0	**Comparison** Three-stage procedure: laparoscopy with drainage + GnRH agonists for 3 months + second laparoscopy with CO2 laser at a power density of 14 000 W/cm^2, after 12 weeks after end of GnRH agonist treatment **Participants** n=10 **Dropout** 0	**Recurrence endometriomas, n** 12 months: I: 0, C: 2, ns	**Comments** Randomization performed by choosing opaque envelopes. Assessor blinded All surgery was performed by the same person

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Posadzka et al 2016 Poland [201]	**Study design** RCT **Setting** Single centre **Population** n=70 Age range: 19–40 years **Inclusion criteria** Patients scheduled for surgical treatment of ovarian endometriosis. exclusion criteria included: laparotomy, inflammation in the pelvic area or neoplasm in the medical history, use of contraceptive drugs and pregnancy. **Follow up time** 3 and 6 months	**Intervention** Excisional cystectomy with CO_2 laser ablation **Participants** n=24 **Dropout** 3 months: 0 6 months: 1	**Comparison** Excisional cystectomy combined with electroablation **Participants** n=34 **Dropout** 3 months: 1 6 months: 5	**Relapse** 3 months; I: 7 (29%), C: 5 (15%) 6 months; I: +4 (17%), C: +1 (2%) **Pregnancy, n** 3 months; I: 0, C: 1 4 months; I: 0, C: 4 (13.7%)	**Comments** Computerized randomisation
Qiong-Zhen et al 2013 China [202]	**Study design** RCT **Setting** Single centre, University hospital **Population** n=86 Mean age: 34 years **Inclusion criteria** Bilateral endometriotic cysts with a mean diameter of 4–6 cm, confirmed via ultrasound; age 30–38 years; regular menstrual flow; no previous surgical treatment of	**Intervention 1** Laparoscopic cystectomy with injection of saline solution **Participants** n=28 **Dropout** 3 (10.7%) **Intervention 2** Laparoscopic cystectomy with vasopressin injection	**Comparison** Routine laparoscopic cystectomy without injection **Participants** n=29 **Dropout** 2 (6.9%)	**Pregnancy rate, mean (SD)** C: 2 (6.9), I: 3 (10.7), I2: 3 (10.3)	**Comments** Random numbers were according to admission number. All operations were performed by a single experienced surgeon No intraoperative or postoperative complications in the 3 groups

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	endometriosis; no medical treatment of endometriosis in the previous 9 months; no intent to become pregnant for 1 to 2 years after the operation; **Follow up time** 3, 6, 12 months	**Participants** n=29 **Dropout** 3 (10%)			
Scioscia et al 2017 Italy [203]	**Study design** RCT **Setting/recruitment** Single centre, Tertiary referral centre **Population** n=227 Mean age: 35 years Previous surgery: 54% **Inclusion criteria** Age >18 years, preoperative evidence of bowel endometriosis (ultrasound, magnetic resonance imaging, or double-contrast barium enema), primary laparoscopic approach **Follow up time** Unclear	**Intervention** Fast-track protocol: no preoperative bowel preparation, early restoration of diet, no postoperative antibiotics, and early postoperative mobilization **Participants** n=62 **Dropout** 0	**Comparison** Conventional care **Participants** n=162 **Dropout** 0	**Readmission within 30 days, n (%)** I: 11 (17.7), C: 26 (15.8), p=0.69 **Median hospital stay, days (range)** I: 3 (3–12), C: 7 (4–33), p<0.001 **Complications, n (%)** Severe complications required reoperation; I: 6.5%; C: 8.5%, p=0.20	**Comments** Randomization based on the scheduled day of surgery assigned by secretaries who were blind to the study Secretaries were unaware of the study, and surgeons and anesthetists were blinded to the group assigned to them. All surgeons were senior consultants with high experience in performing laparoscopic interventions Clinical Trials Registry (identification number UMIN000014199)
Seracchioli et al 2014 Italy	**Study design** RCT, double blind **Setting/recruitment**	**Intervention 1** Laparoscopy + transient ovarian suspension; 1-stitch	**Comparison** Laparoscopy **Participants**	**Pain symptoms, improvement, mean±SD** ***Dysmenorrhea*** BL: I: 6.3±3.2, C: 5.8±3, ns	**Comments** Computer generated randomization with sealed envelopes

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
[204]	Single centre, tertiary care University Hospital/ consecutive recruitment **Population** n=88 Mean age: 33/34 years Previous surgery for endometriosis: 48% **Inclusion criteria** Age; 20–40 years, ultrasound diagnosis of ovarian and posterior DIE scheduled to undergo laparoscopic surgery. Only patients using cyclic oral contraceptives for the previous 3 months before surgery were included. **Follow up time** 6 months	simple technique; the ovary was temporally suspended to the peritoneum of the lower anterolateral abdominal wall next to the ipsilateral round ligament of the uterus using a 2-0 reabsorb able continuous suture, mean absorption time of 56 days (range, 45–70 days). **Participants** n=44 **Dropout** 4 (9%)	n=44 **Dropout** 4 (9%)	***Pelvic pain*** I: 3.6±2.7, C: 3.5±2.7, ns ***Dyspareunia*** I: 5.5±2.8, C: 4±2.4, p=0.014 ***Dyschezia*** I: 4.2±3.9, C: 3±2.5, ns ***Dysuria*** I: 1.8±3.2, C: 1.3±2.5, ns **Complications,** Early postoperative, n (%) I: 3 (7.5%), C: 6 (15%) **Ovarian adhesions (TVUS), n (%)** Absent; I: 15 (33%). C: 7 (16%) Minimal; I: 13 (29%), C: 4 (9%) Moderate; I: 13 (29%), C: 25 (57%) Severe; I: 4 (9%), C: 9 (21%)	Patients and medical staff were blinded Patients used oral contraceptives before and after study At 6 months FU all patients used OCP
Sutton et al. 2001 UK [205]	**Study design** RCT **Setting** Single centre, referral centre for the treatment of endometriosis **Population** n=51 Mean age: 28 years (range 20–41) Endometrios stage III: 10% **Inclusion criteria** Patients with a history and physical or laparoscopic examination suggestive of endometriosis (Stage	**Intervention** Laser vaporisation + Laparoscopic uterosacral nerve ablation (LUNA) **Participants** n=27 **Dropout** Unclear, total study dropout: 5 (9.8%)	**Comparison** Laser vaporisation **Participants** n=24 **Dropout** Unclear, total study dropout:5 (9.8%)	**Pain symptoms (VAS)** ***Dysmenorrhea*** 3 months; p=0.0030 in favour for non-LUNA 6 months; p=0.0217 in favour for non-LUNA ***Chronic non-menstrual pain*** 3 months; p=0.9750 6 months; p=0.3231 ***Dyspareunia*** 3 months; p=0.3961 6 months; insufficient data	**Comments** The patients randomly allocated to the LUNA group also underwent bilateral ablation of the uterosacral ligaments. Patients and research nurse were blinded.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	I–III). No pregnancy or expected to become pregnant within the study duration; no medical treatment for endometriosis within the last 6 months, no previous surgical treatment for endometriosis **Follow up time** 3 and 6 months				
Var et al 2011 Turkey [206]	**Study design** RCT, cross randomization **Setting** Single centre, tertiary education and research hospital **Recruitment** NR **Population** n=48 Mean age: 27±4 years **Inclusion criteria** Infertile, aged 20–35 years, diagnosis of bilateral endometrioma, similar endometrioma sizes, and endometriomas sized 4–6 cm. Exclusion: previous ovarian surgery or suppressive treatment due to endometriosis **Follow up time** 12 months	**Intervention** Cystectomy (removing capsule + coagulation) **Participants** n=48 **Dropout** 0	**Comparison** Coagulation (fenestration + coagulation of inner cyst wall) **Participants** n=48 **Dropout** 0	**Recurrences** 12 months: I: 0, C: 2 **Adverse events** No complications occurred during or after surgery	**Comments** Coagulation and cystectomy were performed on either side of patients for their endometriomas, randomly. All operations were performed by the same surgeon.

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
Vercellini et al 2009 Italy [207]	**Study design** Prospective controlled study **Setting/recruitment** Singe centre/consecutive enrolment **Population** n=438 **Inclusion criteria** Age <40 years, underwent repetitive or first-line conservative surgery for stage I– IV endometriosis. Exclusion: persistent anovulation, bilateral tubal occlusion, or severe dyspermia of the partner, other diseases that might affect reproduction or who planned to undergo immediate IVF-ET. **Follow up time** 24 months	**Intervention** Second line surgery **Participants** n=27(+62) 62 patients who were operated on twice in study department were included in both groups as separate cases **Dropout** 0	**Comparison** First line surgery **Participants** n=349(+62) **Dropout** 0	**Pregnancy rates** Spontaneous conception I: 20/89 (22%), C: 165/411 (40%), p=0.02 Cumulative pregnancy rate 12 months; I: 14%, C: 32% 24 months; I: 26%, C: 38%	**Comments**
Vercellini et al 2003 Italy [208]	**Study design** RCT **Setting** Two academic departments **Population** n=180 (273 considered) **Inclusion criteria** Age 18–40 years, first-line operative laparoscopy for symptomatic minimal to severe endometriosis, pelvic pain >6 months duration, no treatment for endometriosis other	**Intervention** Laparoscopic surgery plus uterosacral ligament resection **Participants** n=90 **Dropout** 1 year: 12 (13%) 3 years: 31 (34%)	**Comparison** Operative laparoscopy **Participants** n=90 **Dropout** 1 year: 12 (13%) 3 years: 33 (37%)	**Pain symptoms (VAS), median reduction (IQR)** ***Dysmenorrhea*** 1 year; I: 52 (24–70), C: 58 (40–74) 3 years; I: 37 (20–56), C: 43 (26–64) ***Deep dyspareunia;*** 1 year; I: 43 (30–61), C: 33 (20–55) 3 years; I: 24 (16–36), C: 20 (17–38) ***Nonmenstrual pain*** 1 year; I: 32 (14–58), C: 31 (22–42) 3 years; I: 28 (14–40), C: 22 (0–37) ***Recurrence dysmenorrhea,*** 1 year;	**Comments** Treatment allocation was performed with a computer-generated randomization sequence by using serially numbered, opaque, sealed envelopes

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	than non-steroid anti-inflammatory drugs up to 6 months before study entry; presence of vaginal endometriotic lesions **Follow up time** 1 year and 3 years			I: 23/78 (29%), C: 21/78 (27%) 3 years; I: 21/59 (36%), C: 18/57 (32%) **QoL, (SF-36), 1 year, mean ± SD** General health; I: 70.6±17.2, C: 67.2±16.8 Pain; I: 71.5±27.9, C: 77.7±22.6, ns **Depression (HASD), 1 year, mean ± SD** Anxiety; I: 7.4±3.6, C: 7.1±3.4 Depression; I: 4.3±3.2, C: 47±3.6 Total; I: 11.7±4.2, C: 11.1±5.3, ns **Revised Sabbatsberg sexual rating scale, mean ± SD** I: 53.8±18.8, C: 55.4±15.6, ns **Patients satisfaction** Very satisfied/satisfied; I: 55 (61%), C: 59 (65%) **Complications** None	
Wright et al 2005 United Kingdom [209]	**Study design** RCT, double blind **Setting/recruitment** District general hospital, recruited from a specialist pelvic pain clinic on the grounds of a history of dysmenorrhea, pelvic pain, backache, dyspareunia or dyschezia **Population** n=24	**Intervention** Ablation **Participants** n=12 **Dropout** 0	**Comparison** Excision **Participants** n=12 **Dropout** 0	**Pain symptoms (ranked ordinal scale)** ***Symptom score, mean ± SD*** BL: I: 25.2±5.3, C: 24.7±9.5 6 months; I: 18.1±5.5, C: 16.9±5.8, p=0.84 ***Symptom signs, mean ± SD*** BL; I: 9.7±2.4, C: 9±1.4 6 months; I: 8.1±3.7, C: 5.7±1.8, p=0.18 ***Total score, mean ± SD*** BL: I: 34.8±6.7, C: 33.8±10	**Comments** Randomization by opening a consecutively numbered envelope blocks of 10 Poor description of the population

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	Inclusion criteria Laparoscopy diagnosed endometriosis, stage 1–2, history of dysmenorrhea, pelvic pain, backache, dyspareunia, or dyschezia. Infiltrating and nodular disease were excluded **Follow up time** 6 months			6 months; I: 26.2±8.6, C: 22.6±6.7, p=0.57 **Symptoms; ablation vs excision (mann-withey) p value** Dysmenorrhea; 0.4/0.23 Pelvic pain: 0.42 Dyspareunia: 0.31 Dyschezia: 0.91 Constipation: 0.84 Diarrhea: 0.71 Cramps: 0.58 Exercise pain: 0.63 **Signs; ablation vs excision (mann-withey) p value** Back pain: 0.34 Fatigue: 0.73 Tenderness: 0.80 Adnexal pain: 0.083	
Zullo et al 2003, 2004 Italy [210] [211]	**Study design** RCT, double-blind **Setting/recruitment** Single centre, university-affiliated department/Unclear **Population** n=141 (162 eligible) Mean age: 31.5±7.3 years **Inclusion criteria** Ednometriosis diagnoses by clinical and/or ultra-sonograph, sexually active, fertile age, severe dysmenorrhea for >6 months, unresponsive to medical treatment,	**Intervention** Conservative laparoscopic surgery **Participants** n=70 **Dropout** 7 (10%) 24 months: 10 (14%)	**Comparison** Conservative laparoscopic surgery + presacral neurectomy **Participants** n=71 **Dropout** 8 (11%) 24 months: 10 (14%)	**Cure rate, r-AFS stage, n (%)** ***Stage I*** 6 months; I: 11 (61), C: 14 (88) 12 months; 11 (61), C: 14 (88) 24 months; I: 18 (30), C: 16 (27) ***Stage II*** 6 months; I: 13 (62), C: 19 (86) 12 months; I: 12 (57), C: 19 (86) 24 months; I: 21 (35), C:21 (35) ***Stage III*** 6 months; I: 10 (59), C: 15 (88) 12 months; I: 10 (59), C: 15 (88) 24 months; I:15 (25), C:16 (27) ***Stage IV*** 6 months; I: 4 (57), C:7 (88) 12 months; I: 3 (43), C: 6 (75) 24 months; I:6 (10), C: 7 (12)	**Comments** computer-generated randomization list The same experienced operator performed the laparoscopic procedures

First author Year Country Reference	Study design Setting/recruitment Population Inclusion criteria Follow up time	Intervention (I) Duration Participants Dropout	Comparison (C) Duration Participants Dropout	Outcome/Result I = intervention C = comparison	Comments
	BMI <30 kg/m^2. No use of an intrauterine device, no neurologic alterations of lumbar-sacral tract, previous pelvic surgery. **Follow up time** 6, 12 and 24 months			***Deep RVS*** 6 months; I: 2 (33), C: 5 (71) 12 months; I: 1 (17), C: 4 (57) **Cured** 6 months; I: 38 (87%), C: 55 (60%) p<0.05 12 months; I: 36 (86%), C: 54 (57%), p<0.05 24 months; I: 50 (83%), C: 32 (53%) **Pain** Complete relief, % 6 months; I: 11%, C: 13% 12 months; I: 10% C:12% Dysmenorrhea nor requiring medical therapy 6 months; I: 27%, C: 42% 12 months; I: 26%, C: 42% **QoL (SF-36)** 24 months; (p<0.05) increased in control compared with intervention. **Complications, long term** None in interventional group Control group; Constipation: 6 months; 21 (3%) 12 months; 9 (14%) 24 months; 9 (15) Urine urgency: 6 and 12 months; 3 (4.8%) 24 months; 3 (5) 24 months; I: 11/60, C: 0/60	

EHP-30 = Endometric healt profile 30; **FSFI** = Female sexual function index; **IPSS** = International prostate score symptoms; **TVUS/TVS** = Transvaginal ultrasound; **RVS** = Rectovaginal septum; **HASD** = Hospital anxiety and depression scale; **LRS** = Ringers' solution

Cohort studies, Deep infiltrating endometriosis and Surgery

First author Year Country Reference	Study design Setting Recruitment Inclusion criteria Follow up time	Intervention Participants Dropout	Outcome/Result	Comments
Angioli et al 2014 Italy [212]	**Study design** Prospective cohort study **Setting** Single centre, University Teaching **Hospital** **Recruitment** Consecutive enrolment **Inclusion criteria** Moderate to severe complaint of at least one pain symptom associated or not with infertility, presence of rectovaginal endometriosis with vaginal involvement determined by clinical and instrumental investigation, age >45 years, exclusion: full thickness bowel endometriosis infiltration with mucosal involvement **Follow up time** 2 years	**Intervention** Three consecutive surgical steps: vaginal route, laparoscopic approach and final vaginal excision **Participants** n=34 Mean age: 32.7±4.4 Mean BMI: 21.2 ±3.2. **Dropout** 0	**Pain, VAS, mean ±SD** ***Dysmenorrhea*** BL: 8.1±2.2 12 months: 2±2.8 24 months: 2.4±3 p: Pre vs 3–6 to 12–24 months<0.05 ***Chronic pelvic pain*** BL: 5.8±3.8 12 months: 1.3±2.4 24 months: 2±2.7 p: Pre vs 3–6 to 12–24 months<0.05 ***Dyspareunia*** BL: 5.9±2.9 12 months: 3.3±3.2 24 months: 2.9±2.7 p: Pre vs 3–6 to 12–24 months<0.05 ***Recurrence, n*** DIE: 0 ***Fertility*** Infertile women: 7/15 (58%) Deliverers: 6/7 ***Complications n (%)*** Major: 0 Vascular lesions: 2 (5.9%) Ureteral stenosis: 1 (2.9%)	**Comments** No woman received hormonal therapy three months prior to surgery.
Angioni et al 2006 Italy [213]	**Study design** Prospective cohort study **Setting** Single centre **Recruitment** Unclear	**Intervention** Complete laparoscopic Excision of DIE, without rectum involvement, with the opening and partial excision of the posterior Vaginal fornix	**Pain, Biberoglu and Beherman, %** ***Chronic pain*** Total remission: 38% Improved: 22% ***Dysmenorrhoea*** Total remission: 38% Improved: 22% ***Dyspareunia*** Total remission: 45%	**Comments**

First author Year Country Reference	Study design Setting Recruitment Inclusion criteria Follow up time	Intervention Participants Dropout	Outcome/Result	Comments
	Inclusion criteria Deep pelvic endometriosis of the cul-de-sac, retrocervical region and rectovaginal septum without intestine involvement, indication for surgery was pelvic pain, five patients had associated infertility. **Follow up time** 12, 24, 36, 48 and 60 months	**Participants** n=31 (of 173 undergoing laparotomy) Mean age: 27.7 years, range 19–38 Incomplete laparoscopic surgery: 15/31 reated for persistent pelvic pain (estroprogestins GnRH agonist, and NSAIDs) for ≥2 years **Dropout** 0	Improved: 25% Avoiding intercourse at BL: 28/31 Satisfying sexual life after surgery: 20/28 (71%) ***Recurrence, n*** 5 years: 0 ***AFS stage of disease, n*** Stage I–II Before: 8, After: 31 Stage III–IV Before: 23, After: 0	
Ballester et al 2014 France [214]	**Study design** Prospective cohort study **Setting** Single centre **Recruitment** Unclear **Inclusion criteria** Age >18 years, suspected posterior DIE based on symptoms, clinical examination and imaging techniques (TVS/ MRI). Exclusion criteria were: prior surgery for DIE, on antidepressants, pharmacological treatment for overactive bladder or antihypertensive treatment **Follow up time** Median 66 months, range 54–89	**Intervention** ***DIE without colorectal involvement:*** Complete laparoscopic resection including resection of the uterosacral ligaments (89%), Ovarian cystectomy (28%) Colpectomy (17%). ***DIE and colorectal involvement:*** Complete laparoscopic colorectal resection including resection of USL (72%), Ovarian cystectomy (32%), Colpectomy (40%), Hysterectomy (16%) Parametrectomy (12%) **Participants** n=56 (27% of eligible) Median age: 31 (range 20–49) **Dropout, n** 6 For urodynamic test: 16	**QoL, BFLUTS** BL: 11.5±5.5 Long term: 12.4±6.7, p=0.1 **Urinary dysfunction, BFLUTS** BL: 16.1±7.8 (n=34) Long term: 17±6.8, p=0.5 **Urodynamic tests and electromyography** n=34 Uroflowmetry: no difference Pressure/flow measurements: no difference	**Comments**

First author Year Country Reference	Study design Setting Recruitment Inclusion criteria Follow up time	Intervention Participants Dropout	Outcome/Result	Comments
Belghiti et al 2014 France [215]	**Study design** Prospective cohort study **Setting** Single centre, University hospital **Recruitment** Consecutive enrolment **Inclusion criteria** Symptomatic DIE with colorectal involvement, DIE diagnosed clinically by 2 experienced surgeons on the following criteria: visible dark blue nodules on the posterior vaginal fornix at speculum examination or infiltration associated with palpable induration at vaginal and rectal digit examination. **Follow up time** Median 60 months	**Intervention** Laparoscopically assisted and open colorectal resections (complete resection) Procedures included adnexal surgery, uterosacral ligament, torus uterinum, parametrium, or vaginal resection; ureterolysis; and ureteral re-implantation when required. **Participants** n=198 Median age: 34 years (range, 23–53 years) Previous surgery for endometriosis: 116 (56%) Infertility: 86 (44%) **Dropout** 0	**Complications** Digestive tract complications: 15 (7.5%) Rectovaginal fistulas: 9 (4.5%) Anastomotic leakages: 6 (3%).	**Comments** TVS followed by MRI to assess the presence of colorectal lesions, unifocality or multifocality of bowel endometriosis, and location of associated DIE lesions
Camanni et al 2009 Italy [216]	**Study design** Prospective cohort study **Setting** Single centre **Recruitment** Consecutive enrolment **Inclusion criteria** Histologically confirmed endometriosis affecting the ureter. **Follow up time** 6, 12 and 24 months	**Intervention** Laparoscopic conservative management of ureteral endometriosis **Participants** n=80 (out of 808 who underwent surgery for pelvic endometriosis) Severe ureteral stenosis n=13 Endometriotic tissue surrounding circularly and encasing the ureter but not causing severe stenosis (n=32).	**Long-term surgical complications** 3 (3.7%) **Degree of satisfaction** 24 months Very satisfied: 69% Satisfied: 15.5% Not satisfied: 15.5%	**Comments** Time for follow up (FU) varies and only 19 out of 80 patients have 24 months FU. However, endometriosis in the uretral I rare and therefor included

First author Year Country Reference	Study design Setting Recruitment Inclusion criteria Follow up time	Intervention Participants Dropout	Outcome/Result	Comments
		Endometriotic tissue on the ureteral wall but not encasing the organ (n=35). Stage III/IV: 75% **Dropout** 0		
Donnez et al 2010 Belgium [217]	**Study design** Prospective cohort study **Setting** Single centre **Recruitment** Unclear **Inclusion criteria** Palpation of a nodule plus at least one symptom of pain associated or not with infertility; type II or III nodules, no previous surgery for endometriosis; surgical procedure performed by one of the authors. **Follow up time** Median 3.1 years (range 2–6 years)	**Intervention** Deep endometriotic nodule excision by shaving surgery (laparoscopy); separation of the anterior rectum from the posterior vagina, excision or ablation of deep endometriosis after complete dissection of the nodule from the posterior part of the cervix, systematically removing the posterior vaginal fornix and vaginal closure **Participants** n=500 Mean age: 26.1 (18–39 years) Dysmenorrhea: 95% Deep dyspareunia: 86% Rectal dyschezia: 48% Pelvic pain associated with Infertility: 324 (64.8%) **Dropout** 0	**Complication** Rectal perforation: 7 (1.4%) Ureteral injury: 4 (0.8%) Temporary urinary retention: 4 (0.8%) **Pregnancy rate** 388 (78%) wished to conceive Pregnant naturally: 221/288 (57%) IVF: 107/167 (64%) Overall pregnancy rate: 328/388 (84%) **Recurrence of severe pelvic pain, scale Biberoglu and Berhman** Population wishing to conceive; 24/388 (6.2%) Population not wishing to conceive: 15/112 (13%), p=0.05 Overall: 7.8% (39/500 Repeat surgery n=12	**Comments** After delivery, progestogens were administered.

First author Year Country Reference	Study design Setting Recruitment Inclusion criteria Follow up time	Intervention Participants Dropout	Outcome/Result	Comments
Hidaka et al 2012 Japan [218]	**Study design** Prospective cohort study **Setting** Single centre **Recruitment** Consecutive enrolment **Inclusion criteria** Endometriosis-related pain (difficulty in daily living, or dysmenorrhea/dyspareunia/defecation pain requiring analgesics) in whom DEL and diagnosed as stage III/ IV endometriosis **Follow up time** 36 months	**Intervention** Laparoscopic radical surgery **Participants** n=198 non-DEL removal Group: radical surgery including adhesiotomy and cystectomy of the ovarian endometriosis, but not removal of deep endometriotic lesion (DEL) n=47 Mean age: 33 (20–47) Dysmenorrhea (moderate or severe), n (%): 36 (76.6) Previous surgery for endometriosis: 11 (23.4%) Radical DEL removal combined with conservative surgery: n=151 Mean age: 32 (24–48) Dysmenorrhea (moderate or severe), n (%): 118 (78.1) Previous surgery for endometriosis: 36 (23 .8%) **Dropout** Non DEL: 0 DEL: 6	**Pain (scale 0–4)** Non DEL:1.7±0.7, p<0.001 DEL group: 0.6±0.7, p<0.001 **Recurrence rate** Non DEL: 24/47 (51%) DEL group: 117/145 (81%) p=0.0153 in favour for Del group **Recurrent dysmenorrhea, require hormone therapy** Non DEL: 23 (49%) DEL group: 28 (18.5%) **Surgery related complications** *Rectal injury* Non DEL: 0 DEL group: 2 (1.3%) *Ureteral injury* Non DEL: 0 DEL group: 0	**Comments**
Klugsberger et al 2015 Austria [219]	**Study design** Prospective cohort study **Setting** Single centre	**Intervention** Laparoscopic rectal resection **Participants** n=24 Mean age: 35.9±6.21 years	**Pregnancy** 7 (31.8%)	**Comments** All operations were carried out by the same team of four visceral surgeons and four gynecologists.

First author Year Country Reference	Study design Setting Recruitment Inclusion criteria Follow up time	Intervention Participants Dropout	Outcome/Result	Comments
	Recruitment Unclear **Inclusion criteria** Symptomatic DIE histological confirmation, age >18 years, and legal **Follow up time** Median follow-up period of 42.4±14.04 months	**Dropout** 2		The patients were classified postoperatively Enzian classification. Only data when FU was 2 years or more was included.
Possover et al 2017 Denmark [220]	**Study design** Prospective cohort study **Setting** Tertiary referral unit specializing in advanced gynaecologic surgery and neuropelveology **Recruitment** Consecutive **Inclusion criteria** Large resection of the sciatic nerve (30% of the nerve) and followed for at least 5 years **Follow up time** At least 5 years	**Intervention** Laparoscopic, no conversions to open surgery. All procedures were done with bipolar forceps and scissors; sciatic nerve resection was done with cold scissors. In 33 patients, one-third of the nerve was resected; in 6 patients, approximately one-half of the nerve was resected; and in 2 patients, approximately two-thirds of the nerve was resected. **Participants** n=46 Mean age: 28 years (range, 24–36) Nulliparous: 86% Previous medical treatments: 100% Neuropathic sciatic pain, VAS score of 9–10 despite use of strong pain medication	**Pain score, VAS, mean** BL: 9.33±0.65 (range, 9–10) (while taking pain medication) 1 year: 1.91±1.92 (0–6) 2 years: 1.41±1.08 (0–3) 3 years: 1.25±1.05 (0–3) 4 years: 1.25±1.05 (0–3) 5 years: 1.25±1.05 (range, 0–3) **Complications** No perioperative or postoperative major complications occurred, and no blood transfusion was necessary	**Comments** Postoperative management included medical treatment with neuroleptic agents and intensive physiotherapy. All patients underwent postoperative intensive physiotherapy and pain treatment with pregabalin starting the day after surgery for a period of at least 6 months.

First author Year Country Reference	Study design Setting Recruitment Inclusion criteria Follow up time	Intervention Participants Dropout	Outcome/Result	Comments
Seracchioli et al 2010 Italy [221]	**Study design** Prospective cohort study **Setting** Single centre, Tertiary-care university hospital **Recruitment** Consecutive enrolment **Inclusion criteria** Laparoscopic diagnosis and histologic confirmation of urinary bladder or ureteral endometriosis **Follow up time** Mean 55±18 months (range 34–84 months)	**Intervention** Laparoscopic partial cystectomy for bladder endometriosis and uretric endometriosis laparoscopically managed by: uretrolysis only; segmental ureterectomy and terminoterminal anastomosis; or segmental ureterectomy and uretrocystoneostomy. **Participants** n=74 Mean age: 33.1±4.7 Previous surgery for endometriosis: 17 (30%) Nulliparous: 49 (87%) Bladder endometriosis: 26 (46%) Ureteral involvement: 15 (27%) Both bladder ad ureteral involvement: 15 (27%) **Dropout** 18 (5 got pregnant <6 months, 8 used hormonals after surgery, 5 did not show up)	**Recurrence, n** 8/56 **Dysuria, VAS, mean** Pre: 4.02 24 months: 0.11 36 months: 0.07 Disappeared or improved: 32/32 **Suprapubic pain, VAS, mean** Pre: 3.12 24 months: 0.73 36 months: 0.63 Disappeared or improved: 18/20	**Comments** All cases were operated by the same first surgeon The surgical team had consistent background in laparoscopic management of DIE
Seracchioli et al 2007 Italy [222]	**Study design** Prospective cohort study **Setting** Single centre, Endometriosis Clinic **Recruitment** Consecutive enrolment **Inclusion criteria**	**Intervention** Laparoscopic segmental rectosigmoid resection preoperative bowel preparation on the day before surgery with Selg-S 1000 **Participants** n=22 Mean age: 35.1±5.2 years	**Symptoms, VAS 0–10, median (range)** ***Dysmenorrhoea*** 24 months: 3 (0–10)* 26 months: 4 (0–10)* *p<0.05 ***Dyspareunia*** 24 months: 2 (0–9)* 36 months: 3 (0–9)* *p<0.05 ***Nonmenstrual pelvic pain***	**Comments**

First author Year Country Reference	Study design Setting Recruitment Inclusion criteria Follow up time	Intervention Participants Dropout	Outcome/Result	Comments
	Severely symptomatic women with deep infiltrating intestinal endometriosis **Follow up time** Up to 36 months	Nulliparous: 20/22 Pain on defecation: 15 Pain on bowel movement: 12 Constipation: 14 Diarrhoea: 5 Low back pain: 13 Cyclic rectal bleeding: 6 Severe dysmenorrhoea: 21 Severe dyspareunia: 18 Noncyclic chronic pelvic pain: 16 Previous surgery for endometriosis: 15 Infertility: 10 **Dropout** 0	24 months: 6 (0–9) 36 months: 6.5 (0–9) ***Pain at defecation*** 24 months: 2 (0–5)* 36 months: 2 (0–5)* *p<0.05 ***Lower back pain*** 24 months: 1 (0–8)* 36 months: 1 (0–8)* *p<0.05 ***Pain on bowel movement*** 24 months: 1 (0–8)* 36 months: 1 (0–8)* *p<0.05 **Recurrence** Clinical recurrences of bowel endometriosis: 0	
Silveira da Cunha Araujo et al 2014 Brazil [223]	**Study design** Prospective cohort study **Setting** Singe centre, Central Hospital **Recruitment** Unclear **Inclusion criteria** Bowel Endometriosis as diagnosed by MRI and transrectal ultrasound **Follow up time** 48 months	**Intervention** Laparoscopic surgery **Participants** n=45 Mean age: 39±5.1 years Stage IV: 100% Endometriomas: 16 (40%) Dysrnenorrhea: 11 (30.6%) Dispareunia: 7 (19.4%) Dyschezia: 3 (8.3%) Use of hormonal drugs: 22 (61%) Previous surgery: 7 (19.4%) Hysterectomy: 3 **Dropout** 5	**Symptoms, n (%)** ***Dysmenorrhea:*** 11 (31%) ***Dyspareunia:*** 7 (19%) Pain with defecation: 3 (8.3%) Changes in bowel rhythm:17 (46.2%) Second surgical procedure due to pain: 7 (19.4%) **Pregnancy n (%)** 6 (16.6%) **QoL, SF-36, mean (range)** ***Physical component*** Physical functioning: 85.56 (30–100), p<0.001 Role-physical: 75.69 (0–100), p<0.001 Bodily pain: 64.11 (0–100), p<0.001	**Comments** All patients received a single dose of goserelin acetate at a dosage of 10.8 mg after surgery.

First author Year Country Reference	Study design Setting Recruitment Inclusion criteria Follow up time	Intervention Participants Dropout	Outcome/Result	Comments
			General health: 69.28 (25–97), p<.001 ***Mental component*** Vitality: 64.03 (10–95), p<0.001 Social functioning: 73.61 (0–100), p<0.001 Role-emotional: 65.72 (0–100), p<0.001 Mental health: 67.08 (20–100), p<0.001	
Stepniewska et al 2009 Italy [224]	**Study design** Prospective cohort study **Setting** Single centre, referral centre for endometriosis **Recruitment** Unclear **Inclusion criteria** Age ≤40 years Suffered from infertility ≥1 year underwent laparoscopic surgery between May 2000–May 2005, indication for endometriosis surgery was severe pelvic pain refractory medical treatments or severe bowel or ureteral stenosis due to endometriosis **Follow up time** Each year up to 4 years after surgery	**Intervention** Laparoscopy **Participants** n=155 Previous surgery: 62.5% Infertility: 85% ***Group A*** n=60 Colorectal segmental resection because of strong pain often associated with a relevant bowel stenosis ***Group B*** n=40 Endometriosis eradication without bowel resection ***Group C*** n=55 Stage III–IV endometriosis (r-ASRM) with ≥1 endometrioma and DIE but without bowel involvement **Dropout** 0	**Pregnancy, n** Group A: 17 (35%) (IVF: 5, spontaneous: 12) Group B: 8 (21%) (IVF: 1, spontaneous: 7) Group C: 32 (70%) (IVF: 4, UI: 4, spontaneous: 24) **Miscarriage, n** Group A: 1 Groups B: 1 Group C, UI: 6 **Recurrence (%)** Group A: 7% Group B: 15% Group C: 0	**Comments**

BFLUTS = Bristol Female Lower Urinary Tract Symptoms; **BMI** = Body mass index; **DEI** = Deep infiltrating endometriosis; **DEL** = Deep endometriotic lesions; **MRI** = Magnetic resonance imaging, **NR** = Not reported; **r-ASRM** = Revised American Society for Reproductive Medicine; **TVS** = Transvaginal ultrasound; **VAS** = Visual analogue scale; **USL** = Uterosacral ligaments

Included qualitative studies, alphabetic order

First author Year Country Reference	Aim of study Underpinning theory	Setting Participants	Sampling	Data collection	Analysis	Measures to support trustworthyness
Ballard 2006 UK [225]	**Aim of study** To investigate the reasons women experience delays in diagnosis of endometriosis and the impact of this **Underpinning theory** Not described	**Setting** Hospital pelvic pain clinic **Participants** 32 women Age: 16–47 years; median 32 years Years with pelvic pain: median 15 years	**Sampling** ***Method*** Not described ***Inclusion criteria*** Confirmed or suspected endometriosis	**Data collection** ***Methods*** Semi structured, face-to-face interviews, most often conducted in the home of the interviewee; 60–120 minutes ***Interviewer*** The author, social scientist	**Analysis** ***Methods*** Thematic analysis where experiences and beliefs that women expressed were interpreted for key themes. Only women with confirmed endometriosis were included in the analysis ***Analysts*** Initial analysis by the author (a social scientist), refined after discussions with a pelvic pain specialist (gynaecologist) and a social scientist	**Measures to support trustworthyness**
Denny 2008 UK [226]	**Aims of study** Explore experiences from primary care. Reanalysis of data from Denny 2004 [227]. **Underpinning theory** Not described	**Setting** A clinic for endometriosis at a specialist women's hospital **Participants** 30 women Age: 19 to 44 years, mean age 31 years Diagnostic delay: mean 5.65 years (0–18 years)	**Sampling** ***Method*** Purposeful. ***Inclusion criteria*** Laparoscopically verified endometriosis	**Data collection** ***Methods*** Semi structured interview based on a story-telling approach, in their home or at the clinic; 30–50 minutes Probing for primary care if not mentioned spontaneously ***Interviewer*** The author, a social scientist	**Analysis** ***Methods*** Thematic analysis (Bryman) ***Analysts*** The two authors, one social scientist and one gynecologist	**Measures to support trustworthyness** Both authors and the women who participated in the study agreed the analytical themes as relevant and arising from the data.

First author Year Country Reference	Aim of study Underpinning theory	Setting Participants	Sampling	Data collection	Analysis	Measures to support trustworthyness
Denny 2009 UK [228]	**Aim of study** Explore women's experience of living with endometriosis. One-year follow-up from Denny 2004 [227]. **Underpinning theory** Feminist approach	**Setting** See Denny 2008 **Participants** Interviews: 27 women; see Denny 2008 Diary: 19 other women	**Sampling** ***Method*** Purposeful (interviews) Not reported (diaries)	**Data collection** ***Methods*** Interview: see Denny 2008 Diary on endometriosis for one menstrual cycle; completed by 7 women ***Interviewer*** See Denny 2008	**Analysis** ***Methods*** Narrative analysis ***Analysts*** Only one author, social scientist	**Measures to support trustworthyness** See Denny 2008, [226], regarding respondent validation.
Facchin 2017 Italy [229]	**Aim of study** Provide a broader understanding on how endometriosis affects psychological health **Underpinning theory** Grounded theory	**Setting** Tertiary level referral center for treatment of endometriosis **Participants** 74 women Age: 24 to 50 years	**Sampling** ***Method*** Theoretical sampling Consecutively recruited ***Inclusion criteria*** Self-referred for treatment, surgically verified diagnosis, different forms of endometriosis	**Data collection** ***Methods*** Face-to face interviews with a story-telling approach, conducted at the hospital Time: average 45 minutes ***Interviewer*** Trained psychologists including the first author	**Analysis** ***Methods*** Constant comparative (Corbin & Strauss 2008) ***Analysts*** Three, working independently	**Measures to support trustworthyness** All emergent themes were continuously discussed in the research team Findings were presented to expert gynecologists and female members of a non-for-profit endometriosis association Discrepancies were discussed until consensus was reached

First author Year Country Reference	Aim of study Underpinning theory	Setting Participants	Sampling	Data collection	Analysis	Measures to support trustworthyness
Gilmour 2008 Huntingdon 2005 New Zealand [230,231]	**Aim of study** Explore the perceptions of living with endometriosis **Underpinning theory** Feminist research principles	**Setting** Local endometriosis support group **Participants** 18 women Age: 16 to 45 years Diagnostic delay: 5–10 years	**Sampling** ***Method*** Interested women from the support group contacted the researchers after information about the project	**Data collection** ***Methods*** Unstructured, interactive interview ***Interviewer*** Not described, but familiar with endometriosis and knowledgeable how to handle emotional reactions during the interview	**Analysis** ***Methods*** Thematic analysis ***Analysts*** The authors, with a nursing background and working as researchers at a department for health and social services	**Measures to support trustworthyness** Continuous collaboration with the support group Emerging themes were presented at two meetings and verified by the participants
Grundstrom 2017 Sweden [232]	**Aim of study** Identify and describe the experiences of health care encounters for women with endometriosis **Underpinning theory** Phenomenology	**Setting** A university and a central hospital clinic **Participants** 9 women consecutively invited by three gynecologists in charge of their endometriosis treatment Age: 23–55 years (median 37 years)	**Sampling** ***Method*** Purposive sampling ***Inclusion criteria*** Age >18 years Laparoscopy-verified endometriosis	**Data collection** ***Methods*** Semi-structured interviews in the home or a separate room at the hospital library Length: 33–113 min (median 64 min) ***Interviewer*** Midwife and Doctoral student	**Analysis** ***Methods*** Moustaka's modification of the Stevick-Colaizzi-Keen method (adding interpretation) ***Analysts*** Three researchers (two with midwife background, one a PhD student and the other a researcher, the third with a nursing background and researcher)	**Measures to support trustworthyness** Reporting the audit trail (i.e.,describing every step of the data collection and analysis.) The researchers analysed the data independently from each other, discussed the analysis and arrived at a consensus.
Jones 2004 UK [233]	**Aim of study** Explore and describe the impact of endometriosis on quality of life **Underpinning theory**	**Setting** Gynecology outpatient clinic **Participants** 24 women (until theoretical saturation)	**Sampling** ***Method*** Theoretical sampling to cover different disease stages and symptom profiles	**Data collection** ***Methods*** Semi-structured, in depth interviews at the hospital Mean time: 55 min	**Analysis** ***Methods*** Constant comparative method ***Analysts*** Not described	**Measures to support trustworthyness** The same themes were identified and the interviewees' dialogues were interpreted in the same way.

First author Year Country Reference	Aim of study Underpinning theory	Setting Participants	Sampling	Data collection	Analysis	Measures to support trustworthyness
	Grounded theory to generate categories and concepts	Age: 21.5 to 44 years; mean age 32.5 years	***Inclusion criteria*** Laparoscopically verified endometriosis	***Interviewer*** The researcher had no personal experience of endometriosis and only very basic knowledge of its symptoms before the interviews were started		
Young 2016 Australia [234]	**Aim of study** Explore experiences of health care related to endometriosis and fertility **Underpinning theory** Not described	**Setting** Non-clinical **Participants** 26 women, the majority in their 30s	**Sampling** ***Method*** invitation by advertisements. After 20 interviews, purposeful sampling was applied to ensure diversity ***Inclusion criteria*** At least 18 years Surgically verified endometriosis	**Data collection** ***Methods*** In depth, semi-structured interviews, face-to face or over the phone Mean time: 63 minutes ***Interviewer*** First author	**Analysis** ***Methods*** Thematic analysis (Braun & Clarke) ***Analysts*** Initial analysis by the first author. Then all authors participated in the analysis and interpretation of data.	**Measures to support trustworthyness**