ENDOMETRIOSIS

This document outlines the management of endometriosis related to fertility agreed by a combined patient and health provider committee. This is the result of many meetings discussing evidence based management and agreeing its relevance to investigation and treatment in the real world. We hope you find this document interesting. Wherever you access treatment for endometriosis related to fertility in Dorset your management should follow these guidelines that should be regarded as best practice guidelines.

The management focuses primarily on fertility as the prime goal rather than pain relief or period relief and therefore does not discuss in detail either hormonal suppression or destructive surgical procedures that might harm fertility. It does not discuss hysterectomy at all as this is clearly not a fertility preserving procedure.

THE INVESTIGATION AND MANAGEMENT OF ENDOMETRIOSIS

The Dorset Guidelines

INDEX

THE INVESTIGATION AND MANAGEMENT OF ENDOMETRIOSIS

Aim, Introduction and background

The aim of this guideline is to provide up-to-date information, based on clinical evidence, regarding the diagnosis and treatment of endometriosis. The options for treatment are examined in the light of presenting symptoms, including associated infertility. This document has been prepared using the RCOG greentop guideline as a basis and by adding local variations and practical suggestions as necessary.
This guideline is part of the Dorset Endometriosis Project which has been stimulated by locally identified needs and the NHS Modernisation Agency, Patient and Public Initiative (PPI) .

Endometriosis is a common condition but its epidemiology in the general population is uncertain as prevalence varies widely depending on the type of hospital-based population being studied. It is seen more frequently among women being investigated for infertility (21%) than among those undergoing sterilisation (6%). Among those being investigated for chronic abdominal pain, the incidence of endometriosis is 15%, while among those undergoing abdominal hysterectomy, it can be as high as 25%.[1]

Identification and assessment of evidence

The Cochrane Library and the Cochrane Register of Controlled Trials were searched for relevant RCTs, systematic reviews and meta-analyses. A search of MEDLINE and PUBMED (electronic databases) from 1966-1999 was also carried out. The databases were searched using the relevant MeSH terms including all sub-headings and this was combined with a Key-Words search.

The definitions of the types of evidence used in this guideline originate from the US Agency for Health Care Policy and Research. Where possible, recommendations are based on, and explicitly linked to the evidence that supports them. Areas lacking evidence are highlighted and annotated as ‘Good Practice Points’.

Diagnosis

The symptoms associated with endometriosis such as dysmenorrhoea and pelvic pain are common.[2,3] Establishing the diagnosis can be difficult because the presentation is so variable and there is considerable overlap with other conditions such as irritable bowel syndrome and pelvic inflammatory disease. As a result there is often delay between symptom onset and surgical diagnosis.

Endometriosis may present with any combination of the following: secondary dysmenorrhoea, deep dyspareunia, pelvic pain, infertility or a pelvic mass. However, the predictive value of any one symptom or set of symptoms remains uncertain. Furthermore, endometriosis is often found coincidentally in asymptomatic women

History and clinical examination remain as the cornerstones of diagnosis. It is important to emphasise the individuality of each patient. Speculum assessment of the vaginal vault is essential in order to identify the presence or otherwise of endometriotic nodules. If present, the location ie. anterior, central or lateral needs identifying as this has a bearing on the subsequent management plan (see algorithm).

B **Laparoscopy is the 'gold standard' diagnostic test in endometriosis.**

Laparoscopy is still regarded as the 'gold standard' diagnostic test in looking for evidence of all types and stages of endometriosis. However, diagnostic laparoscopy is associated with 0.06% risk of major complications (e.g. bowel perforation) whilst this risk is increased to 1.3% in operative laparoscopy.[5]	Evidence Level III

In early stage disease the diagnosis by laparoscopy can be elusive and requires a high degree of suspicion. It is important that individuals undertaking diagnostic laparoscopy for pelvic pain be aware of this difficulty and acquaint themselves with the identification of subtle appearances as described below.

To be complete this must use an effective uterine manipulator and a suprapubic probe. A lateral port may also be utilised if there is difficulty in gaining satisfactory access.

The Pouch-of –Douglas(POD) must be thoroughly inspected; the fallopian tubes mobilised and importantly, all surfaces of the ovary together with the ovarian fossae visualised. Vaginal examination should be performed under endoscopic control to assess possible POD tethering.

If endometriosis is suspected a biopsy should be performed, but this would not be necessary where the disease is obvious. An area needs to be identified away from potential damage by identifying the ureter first. The left pelvic sidewall is more likely to yield a positive result.

Detailed operative notes must be completed to include both negative and positive findings
.

SUBTLE APPEARANCES

Sometimes the subtle endometriotic lesions can be the only lesions seen at laparoscopy. These forms are more common and may be more active than the puckered black lesions (Table 1).

Table I: Different appearances of peritoneal endometriosis

Color	*Description*
Black	typical puckered black lesions
Red	red flame-like lesion glandular excrescence

	petechial peritoneal changes areas of hypervascularization
White	white opacification subovarian adhesions yellow-brown peritoneal patches circular peritoneal defects

The non-pigmented endometriotic peritoneal lesions include the following:

(1) White opacification of the peritoneum which appears as peritoneal scarring or as circumscribed patches, often thickened and sometimes raised

(2) Red flame-like lesions of the peritoneum or red vesicular excrescences, more commonly affecting the broad ligament and the uterosacral ligaments.

(3) Glandular excrescences on the peritoneal surface which in colour, translucency and consistency closely resemble the mucosal surface of the endometrium seen at hysteroscopy

(4) Subovarian adhesions or adhesions between the ovary and the peritoneum of the ovarian fossa, which are distinctive from adhesions characteristic of previous salpingitis or peritonitis.

(5) Yellow-brown peritoneal deposits; *café au lait* patches.

B **The use of transvaginal ultrasound may be helpful in diagnosis, particularly to detect ovarian endometriomas.**

A systematic review (unpublished) of the accuracy of ultrasound identified seven relevant studies, all using transvaginal scanning (TVS) to diagnose endometriomata.[6] TVS appears to be a useful test both to make and to exclude the diagnosis of an ovarian endometrioma. Magnetic resonance imaging may be a useful non-invasive tool in the diagnosis of deep endometriosis.[7] While it has limitations in the visualisation of small endometriotic implants and adhesions, it has the ability to characterise the lesions, to study extraperitoneal locations and the contents of pelvic masses.[8]	Evidence Level III

A **The use of serum CA-125 testing has limited value as a screening test for endometriosis.**

CA-125 has limited value as a screening test as well as a diagnostic test. It may however, serve as a useful marker for monitoring the effect of treatment once the diagnosis of endometriosis has been established, but again its use has not been evaluated systematically.	Evidence Level Ia

C **Rectal endoscopic ultrasonography is superior to MRI for the diagnosis of Rectosigmoid endometriosis.**

Intestinal endometriosis is difficult to diagnose and treatment remains complex. Until recently barium enema and colonoscopy have been the only diagnostic tools but suffer from limitations and drawbacks. Rectal ultrasound has a sensitivity approaching 100% although MRI offers a larger view of the pelvis. This test should be offered to patients presenting with symptoms suggestive of bowel involvement.	Evidence Level IIIa

C **Transvaginal and Transrectal ultrasonography are useful diagnostic tests for rectosigmoid endometriosis.**

TVS and TRS provide characteristic appearances for rectosigmoid endometriosis that correlate well with it's histological findings and are useful in pre-operative diagnosis.	Evidence Level II

See algorithm for further details.

Management

The choice of treatment will depend upon factors such as the woman's age, fertility plans, previous treatment, the nature and severity of the symptoms, and the location and severity of disease. Women with endometriosis-associated infertility and pain may have to decide which is the major priority as there is no evidence that hormonal therapy alone improves fertility.[4]

Optimum selection of drug therapy can make a difference to treatment outcome despite the complexity of pain management and the need to take account of various other factors (Grade C).

Medical management of Endometriosis associated pain

A **Non-steroidal anti-inflammatory drugs may be effective in reducing the pain associated with endometriosis.**

Some women prefer to avoid hormonal therapy and can manage their symptoms effectively with analgesia and/or a complementary medicine approach. Non-steroidal anti-inflammatory drugs may be effective, but the few RCTs assessing their effectiveness have involved small patient numbers.[10]	Evidence Level Ib

Advice on prescribing / advising on analgesics for endometriosis

The response to various analgesics varies widely between both individual and type of pain.
The following approach is very general and there are no known "best analgesics" for endometriosis.
Individuals must be advised to try the various recommendations in order to find the most suitable preparation/s for them
The following are suggested:

(I) PARACETAMOL
1g (2 tabs) 4 x / day
Should be used regularly (ie not prn) 4x/day for flare-ups.

(II) NSAID:
Safest & cheapest = **Ibuprofen**. (400mg tabs)
Dose: 1.2 - 1.8g daily in divided doses preferably after food.
May be increased to 2.4g daily for short periods

There is no evidence that one NSAID is better as an analgesic than any other.

Cox II type NSAIDS may be preferable in patients who have previously had upper GI side-effects from NSAIDS, but should not be used if upper GI symptoms persist. Cox II NSAIDS do not give better analgesia and are expensive.

NOTE**:** Paracetamol and NSAIDS have different modes of action and can be taken simultaneously. The analgesic effect is additive. There is no added risk**.** It is highly likely that taking them together will give better analgesia. (Synergistic effect)

Synergistic effect also appears strong for opioid/paracetamol combinations.
They can be bought as combination tabs

(III) WEAK ORAL OPIATES

Codeine(+ Paracetamol)	Co-codamol
Dextropropoxyphene(+ Paracetamol)	Co-proxamol
Dihydrocodeine (+ Paracetamol)	Co-dydramol

NOTE:

1) 13% of Caucasians cannot bio-convert codeine to its active form (morphine) and will therefore not notice any analgesic benefit but only side-effects.

2) Codeine and dihydrocodeine are poor analgesics on their own with several side-effects, including severe constipation, which may be very unhelpful to patients with endometriosis
.
3) Dextropropoxyphene has a bad side-effect profile, including confusion, sedation etc. and is not recommended. It performs no better than a full dose of paracetamol even when combined with this drug as co-proxamol.
4)

(IV) Other suggestions:

Encourage experimentation with alternative remedies in conjunction with the above analgesics rather than instead of. This is important as most people will not think of taking different analgesics simultaneously unless they are combined in one pill.

For very severe and prolonged pain when all other analgesia has failed consider replacing weak opioids with an oral strong opioid such as *oral morphine* (5-20mg prn) or the delayed release opiate such as *oxycontin* (10mg bd). These may be beneficial in the short term but there is no evidence available for endometriosis. If you wish to go down this path you may wish to refer to guidelines for management of opioids for chronic non malignant pain produced by the British Pain Society 2003 plus the booklet for patients via www.painsociety.org

If pain is causing disturbance of sleep, consider a trial of Amitriptyline 10-25mg at night. This is often useful in some chronic pain syndromes, but there is no evidence for endometriosis pain. Prescribing a drug classified as an antidepressant may not be appreciated by some patients.

If a woman is not trying to conceive and there is no evidence of a pelvic mass or vaginal nodule on examination, there may be a role for a therapeutic trial of a combined oral contraceptive or a progestogen to treat pain symptoms suggestive of endometriosis without performing a diagnostic laparoscopy first**.**

The use of Mirena (intra-uterine Levonorgestral system) can be a useful method of providing local progesterones in order to treat pain associated with menses.

Recommendations for clinical practice

1. There should be support for specialist obstetrics and gynaecology pain clinics and for a transdisciplinary approach with a true diversity of specialists involved (Grade C).

2. The setting in which consultations for pelvic pain take place need adequately to reflect the referral pattern: patients with long-standing or disabling symptoms require extended consultation time and access to other advice and treatment resources, as in a multidisciplinary model (Grade B).

3. Clinicians need to be aware of the importance of the initial medical consultation with women with chronic pelvic pain as a factor influencing the outcome from investigation and treatment. While consulting styles reflect the individual personality of the doctor, clinicians need to be aware of their own underlying attitudes and how these might enter into the dynamics of the consultation (Grade B).

4. Women presenting with pelvic pain in whom no clear diagnosis is present, or where diagnoses overlap, need to be given clear explanations which do not undermine the legitimacy of their experience of pain or convey a message of dismissal (Grade B).

5. The role of establishing whether pain is 'real' or not should be rejected, as chronic pain may be a diagnosis as well as a symptom

6. Health professionals should discard dualistic notions of pain being either physical or psychological, and adopt a biopsychosocial model of pain instead. This model of pain is especially important with regard to chronic pain in women, where there is been a greater tendency to label unexplained pains as manifestations of psychiatric illness.

Training

Gynaecologists should be taught psychological pain management theory and skills as part of their training *and* should take more time for in-depth assessment.

There should be dissemination of existing information from psychology sources to both clinicians and patients.

The RCOG and the British Psychological Society should set up a joint education committee to develop the content of a training programme in psychogynaecology, for trainees and staff in obstetrics, gynaecology and psychology.

Study guides need to emphasise the importance of attention to the patient's needs for treatment objectives and explanation, rather than an exclusive pursuit of a pathological diagnosis. Consulting styles that address these needs can be taught in role-play and evaluated in OSCE formats, as can the communication skills required to convey diagnostic uncertainty or negative findings without undermining the patient's confidence.

The RCOG should create a subspecialty of benign gynaecological surgery and funding should be available to ensure an adequate number of such centres throughout the UK.

Gynaecologists need to be educated to take a full history, including a full gastroenterological history.

There should be an awareness of the ethical issues in the management of pain.

A **The choice between the combined oral contraceptive, progestogens, danazol and GnRH agonists depends principally upon their side-effect profiles because they relieve pain associated with endometriosis equally well.**

The aim of medical treatment is to induce atrophy in the ectopic endometrial tissue with the use of hormones. The drugs available are equally effective in relieving endometriosis-associated symptoms however, these drugs are associated with significant side-effects that limit their long-term use and often produce poor compliance.

In addition, hormonal manipulation probably does not affect any of the primary biological mechanisms responsible for the disease process. Consequently, medical treatment does not always provide complete pain relief and some patients fail to respond.

Evidence Level Ib

Symptom recurrence is common following medical treatment. Thus, in a follow-up study, the cumulative recurrence rates for the fifth year after the completion of GnRH agonist treatment were 37% for minimal disease and 74% for severe disease.[11] The following reviews have been considered:

Combined oral contraceptive (COC) v GnRH agonist (one RCT):[12.:] Ethinyloestradiol 20µgms/ Desogestrel 150mg was as effective as goserelin for the relief of symptoms.

Progestogens v other medical therapy or placebo (four RCTs):[13] The treatments Ethinyloestradiol 35µgms/Cyproterone acetate 27mg; Ethinyloestradiol 20µgms/Desogestrel 150mg,dydrogesterone and medroxyprogesterone acetate were as effective as placebo, goserelin or danazol in relieving symptoms.

Danazol (alone or as adjunctive therapy) v placebo (four RCTs):[14] Danazol was more effective than placebo in relieving symptoms and causing disease regression.

GnRH agonists v other medical therapy or placebo (26 RCTs):[15] GnRH agonists were as effective as other active comparators (principally Danazol) in relieving symptoms and causing disease regression.

GnRH agonist therapy given for three months may be as effective as treatment given for six months in relieving endometriosis-associated pain. If longer treatment is required, GnRH agonist use can be extended safely with 'add-back' therapy.

Duration of therapy is limited for some drugs due to the side-effect profile. COC and Depo-Provera may be used long-term, but generally the use of gestagens, Danazol and GnRH agonists is usually restricted to six months. GnRH agonist therapy is limited because up to 6% of bone mineral density may be lost in the first six months. However, the loss is restored almost completely two years after stopping treatment.[16]

'Add-back' therapy (i.e. progestogen with or without oestrogen) can be used (with no loss of efficacy) to relieve menopausal side-effects, to prevent bone loss and allow therapy to continue beyond six months. How long this regimen may safely be continued is unclear, but in a recent study using leuprolide acetate with hormonal add-back therapy, bone density was maintained at the same level over 12 months' treatment.[17]

Lastly, there is some evidence to suggest that GnRH agonist treatment for three months may be as effective as six months' treatment.[18]

Evidence Level III

Surgical management of Endometriosis associated pain

Laparoscopic approaches are the mainstay of surgical management of endometriosis but require training, skills, equipment and a steep "learning curve". The modalities utilised include diathermy, harmonic scalpel, excision and laser .Surgeons using these techniques must be familiar and confident in their application. Training of theatre staff is accepted as a pre-requisite.

Treatments need to be individualised and regularly reviewed on the basis of each patient's needs and aspirations. This takes place in some centres, which need to be identified to gynaecologists and to those in primary care. As well as offering the best available treatment for patients whose symptoms are proving difficult to manage, these would develop greater expertise in treatment and provide advanced training for the range of healthcare professionals involved in endometriosis care (Grade C).

Patients with severe endometriosis should be referred to specialist treatment centres with experience advanced laparoscopic surgery (Grade B).

Laparoscopic treatment of stage I - Ill endometriosis is a safe procedure and has been shown in a double blind randomised controlled trial to be effective in a large proportion of patients. It requires the complete removal of disease not only from the peritoneum but also from the utero-sacral ligaments (Grade B). The complete removal of deeply infiltrating disease particularly from the recto-vaginal septum and bowel wall is important utilizing if needed specialist colo-rectal assistance.

Surgical findings should be digitally recorded if possible with copies for patient held records.

A **Laparoscopic ablation of minimal-moderate endometriosis appears to relieve pain, although it is unclear whether uterine nerve ablation is required as well.**

The role of surgery in the management of both endometriosis-associated pain and infertility has been assessed in a recent systematic review.[19]

One double-blind RCT has compared the effects of laser ablation of minimal-moderate endometriosis plus uterine nerve ablation versus diagnostic laparoscopy alone for pain relief.[20] At six months' follow-up, 62.5% of the treated patients reported improvement or resolution of symptoms compared with 22.6% in the no-treatment group.

Outcome was poorest in patients with minimal endometriosis. However, 73.7% of women with mild-moderate disease experienced pain relief. Symptom relief continued at one year follow-up in 90% of those who initially responded.[21]

Although there are limited data available from RCTs assessing the effectiveness of surgery in relieving pain, it is clearly effective for many women. However, clinical experience shows that some women fail to respond to surgical treatment either because of incomplete excision or because of post-operative disease recurrence

There is evidence to suggest that post-operative medical treatment with GnRH agonists significantly prolongs the pain-free interval after conservative surgery in symptomatic women,[22,23] although in an earlier review it was suggested otherwise.[24] In the management of endometriomas, laparoscopic cystectomy may offer better results with regard to pain relief and cumulative post-operative pregnancy rates compared with drainage and coagulation.[26] In cases where no cyst wall is present, fenestration followed by GnRH agonists may prove beneficial.[27]	Evidence Level Ia-Ib

There appears to be no evidence at present that denervation procedures confer any additional benefit to the excellent results of laparoscopic ablation of ectopic endometriotic implants and deeply infiltrating disease (Grade A).

References : Appendix 1

Severe cases of endometriosis should be referred to centres of excellence where relevant clinical expertise is available. Patients treated according to the Dorset guidelines will in the first instance be referred to Princess Anne Hospital, Southampton

ENDOMETRIOSIS ASSOCIATED INFERTILITY

C **Endometriosis should be classified using the revised AFS system of classification, until such time as an alternative proven functional classification is approved** [1]

The mechanism of infertility associated with endometriosis is very complex and poorly understood and therefore optimal treatment of endometriosis as related to infertility is unclear. The options for treatment of endometriosis include no treatment, medical treatment and surgical treatment by laparoscopy or laparotomy.

In 1985, the American Fertility Society published the Revised AFS Classification of Endometriosis (R-AFS). The scores and location of the endometriosis are recorded on a standardised classification form which includes anatomical diagrams in an attempt to aid objectivity.

Reproducibility of the scoring system has been studied[2,3] and suggestions for improvements made especially in relation to the confirmation of ovarian endometriomas.[4,5]. Guzick et al [6] performed a retrospective analysis to describe the relationship between the revised AFS classification of endometriosis and pregnancy rates after treatment. No differences in pregnancy rates were found across the stages of endometriosis. However, in the absence of more functional, accepted classification systems, it would seem appropriate to use the most widely used classification system.	Evidence Level IIb

.

References : Appendix 2

A **Surgical ablation of minimal and mild endometriosis improves fertility in subfertile women. Women with minimal and mild endometriosis who undergo laparoscopy should be offered surgical ablation or resection of endometriosis as this improves the chance of pregnancy.**[1]

In a multicentre RCT[2] 341 infertile women with minimal or mild endometriosis were randomised to either diagnostic laparoscopy or surgical treatment of the endometriosis with destruction and removal of all visible endometriotic implants and lysis of adhesions.

Laparoscopic surgery increased the cumulative probability of a pregnancy that lasted more than 20 weeks by 73% in the first 36 weeks after the procedure (30.7% compared with 17.7% for diagnostic laparoscopy alone) This corresponds to an absolute increase in the 36-week probability of a pregnancy carried beyond 20 weeks attributable to laparoscopic surgery of 13% or one in eight women

.

A smaller randomised study by Parazzini 10/51 women (l9.6%) in the treatment group as opposed to 16/45 women (22.2 %) in the control group became pregnant within one year following laparoscopy suggesting no difference[3]

Pooled data from one quasi-randomised study, five cohort studies[4-9],and a recent systematic review (increased pregnancy and live birth rates [11])showed also suggest that laparoscopic surgery is superior to treatment with danazol or no treatment in terms of pregnancy rates as does a meta-analysis of non RCTs [10]. Although these studies were heterogeneous the results are generally favourable towards surgical treatment.

References: Appendix 3

A **Medical treatment of minimal and mild endometriosis does not enhance fertility in subfertile women**

The value of ovarian suppression with danazol, medroxyprogesterone acetate,. or gestrinone versus placebo/no treatment has been assessed in a Cochrane review (13 RCTs) 1 .The common odds ratio for pregnancy was 0.83 (95% CI 0.5-1.39).The results comparing Medroxyprogesterone acetate and placebo2. are similar.

Clearly there is no evidence to support the use of ovarian suppression agents in the treatment of endometriosis-associated infertility.

A **There is no role for medical therapy with hormonal drugs in the treatment of endometriosis associated infertility.**

References: Appendix 4

A **Ovarian stimulation with intrauterine insemination (IUI) is more effective than either no treatment or IUI alone in subfertile women with minimal or mild endometriosis**

Tummon et al.' evaluated the efficacy of superovulation with FSH and IUI versus no treatment for infertility associated with minimal or mild endometriosis. Live births were higher in the treated group (11 % vs 2%)

Fedele et al.2 evaluated the efficacy of superovulation in the treatment of primary or secondary infertility associated with minimal or mild endometriosis. There was no significant difference between the two groups.

Nuisen et al.3 studied the efficacy of hMG superovulation and IUI versus IUI alone when normal ovulation was present. The results reached statistical significance only for endometriosis and unexplained infertility.

Multiple pregnancy rates were 18-33% in these trials.

The evidence presented above suggests that ovarian hyperstimulation with IUI is better than no treatment or IUI alone for women with minimal or mild endometriosis. However a recent systematic review suggested otherwise[4]. A diagnosis of endometriosis reduced treatment effectiveness by approximately half.	Evidence Level

References: Appendix 5

A **There is no evidence that medical treatment of moderate and severe endometriosis either alone or as an adjunct to surgery improves fertility**

Three systematic reviews with meta-analysis[1-3], have consistently shown that there is no significant difference in crude pregnancy rates between medical treatment and no treatment in endometriosis.	Evidence Level Ia

Since the meta-analyses reported above, 2 RCTs found no difference in pregnancy rates with or without GnRH analogue therapy post surgery[4,5,6].Similar results were found with Danazol[7]

Medical treatment as a post-operative adjunct to surgery does not appear to change the pregnancy rates.

References: Appendix 6

B Surgical treatment of moderate and severe endometriosis may improve fertility but controlled studies and comparisons with assisted reproduction techniques are required

Studies of infertility associated with endometriosis use mainly changes in R-AFS score as end-point. It is assumed that a drug that makes the endometriotic implants less visible at second look laparoscopy should also increase the patient's fecundity[1]. Relatively few studies were found of advanced stage endometriosis associated infertility that used pregnancy rates as the endpoint and none were randomised placebo-controlled trials.

Two systematic reviews with meta-analyses have evaluated the role of surgical interventions for the treatment of endometriosis associated with infertility.
The main outcome measure was pregnancy rates. The 22 studies represent a total of 3879 patients. Basic data for the up-dated meta-analyses were mostly obtained from Hughes et al[3]. and from the published articles directly.

For some treatment comparisons the necessary information was calculated from the original data. Conclusions were:
i) Laparoscopic destruction of endometriotic implants improves fertility
ii) Surgical treatment is better than medical or no treatment.
iii) No difference between laparoscopy and laparotomy

Studies looking at surgery in moderate and severe endometriosis only

Four studies present results for moderate and severe endometriosis separately, although the different classification systems used make direct comparisons difficult.

Adamson et al[4,5] reported on a prospective cohort study of infertility patients with endometriosis. In moderate or severe disease the three-year life-table cumulative pregnancy rates were 62% ± 6% and 44% ± 6%, respectively. These were significantly lower than those with minimal or mild endometriosis who had surgery.

Federici et al.[6] treated 163 infertile women with endometriosis. There was a 55% pregnancy rate in the moderate endometriosis group and a 15.3% pregnancy rate in the severe endometriosis group.

Buttram et al.[7] retrospectively compared three groups of women who had surgery for endometriosis. The pregnancy rates after a minimum follow up of 15 months were 56% and 40% for moderate and severe endometriosis, respectively, in the surgery only group, 67% and 53% for the surgery with pre-operative danazol and 0% (group only contained one patient) and 32% for the surgery with post-operative danazol.

Paulson et al.[8] compared medical and surgical treatment in women with moderate endometriosis (stage II original AFS classification) 71% (126/177) became pregnant after surgery. This was significantly higher than those treated medically (39%, 23/59).

Comparisons showed that surgical treatment was superior in terms of pregnancy rates However, there is a need for properly controlled prospective studies for different stages of endometriosis using a comparable classification system . Comparisons with assisted reproduction techniques are also required, it is not known whether assisted reproduction techniques or surgery is the best option for women with moderate or severe endometriosis.	Evidence IIB

References: Appendix 7

C In cases of moderate and severe endometriosis, assisted reproduction techniques should be considered, as an alternative to, or following unsuccessful surgery

It is not known whether *in vitro* fertilisation (IVF) or gamete intrafallopian transfer (GIFT) may be better than medical or surgical treatment for moderate or severe endometriosis as there are no direct comparisons. There are only the following two trials that compare IVF and GIFT with conventional infertility treatment, which included some women with endometriosis. No studies have compared IVF with GIFT for women with endometriosis.

Soliman et al[1]. evaluated the effectiveness of immediate vs six-month delayed IVF. The respective clinical pregnancy rates were 8% and 13.1 %, which was not statistically significant.

Pagidas et al.[2] retrospectively evaluated the efficacy of re-operation for stage 11 or IV endometriosis related infertility in comparison with IVF. The cumulative pregnancy rate nine months after re-operation was 24.4% compared 33.3% after 1 cycle of IVF and 69.9% after two cycles of IVF (the latter is significant).

A systematic review of 22 observational studies of patients undergoing IVF treatment, suggested that those with endometriosis-associated infertility compared with couples with other causes of infertility, had a lower pregnancy rate.

Marcus and Edwards[4] found significantly higher pregnancy rates per embryo transfer after IVF in women with severe endometriosis (grades Ill and IV) when women had several months of down-regulation with a GnRH analogue compared with a standard short protocol regimen (42.8% versus 12.7%).

Wessels et al.[5] compared the effectiveness over a period of two years of GIFT with that of conventional infertility treatment. In women endometriosis, significantly more women (31.6%) became pregnant per cycle with GIFT compared to 5.26% per cycle with conventional therapy.

Evidence is not yet available to support either IVF/GIFT or surgery preferentially for the treatment of moderate to severe endometriosis.

A meta-analysis of all published studies analysing outcome following IVF in women with endometriosis (1,070 cycles) compared to those with tubal infertility (2,619 cycles) showed that pregnancy rates per cycle were significantly lower in the endometriosis group (26% v 36%, $p<0.005$)[6]. However, analysis of large databases indicates that there is no difference in outcome[7].

References: Appendix 8

A Women with ovarian endometriomas should be offered laparoscopic cystectomy as this may improve the chance of spontaneous pregnancy

Ovarian endometriomas do not respond very well to medical therapy[1-5]and drainage is not effective for large endometriomas, as the cysts regrow[1].

One RCT found that laparoscopic cystectomy increased cumulative pregnancy rates at 24 months when compared with drainage and coagulation in the treatment of large ovarian endometrioma (66.7% vs 23.5%)[6]

Donnez et al.[7] report on the management of large endometriomas (> *3 c*m) treated with GnRH analogues and C02 laser laparoscopy A cumulative pregnancy rate, of 51% at one year was achieved with a recurrence rate of 8%.

Laparoscopic treatment is as effective as laparotomy

Cohort studes of patients with moderate and severe endometriosis having operative treatment with laparoscopy or laparotomy suggest pregnancy rates may be the same or increased in those treated by laparoscopy. (54%-66% with operative laparoscopy vs 36%-45% with laparotomy).[8-11]

Do endometriomas affect IVF?

Isolated case reports and a case series have suggested that the presence of ovarian endometriomas can cause morbidity after transvaginal egg collection either because of rupture[12] or infection after the procedure.[13] It is not clear if the presence of endometriomas affects IVF outcomes. Diugi et al.[14] found it did but others found no difference in the clinical pregnancy rates[15,16].

Surgical treatment of ovarian endometriomas may enhance spontaneous pregnancy rates [6]Further research into the extent which endometriomas contribute to endometriosis associated infertility is required.. Further research is also required into how endometriomas affect IVF outcomes.	Evidence Level IB

References: Appendix 9

APPENDICES

References : Appendix 1

1. Mahmood TA, Templeton A. Prevalence and genesis of endometriosis. Human Reprod 1991; 6:544-9.
2. Zondervan KT, Yudkin PL, Vessey MP, Dawes MG, Barlow DH, Kennedy SH. The prevalence of chronic pelvic pain in women in the United Kingdom: a systematic review. Br J Obstet Gynaecol 1998; 105:93-9.
3. Zondervan K, Yudkin PL, Vessey MP, Dawes M, Barlow DH, Kennedy SH. Prevalence and incidence in primary care of chronic pelvic pain in women: evidence from a national general practice database. Br J Obstet Gynaecol 1999; 106:1149-55.
4. Hughes E, Fedorkow D, Collins J, Vandekeckhove P. Ovulation suppression vs. placebo in the treatment of endometriosis (Cochrane Review). In: The Cochrane Library 1999, Issue 3. Oxford:Update Software.
5. Harkki-Siren P, Sjoberg J, Kurki T. Major complications of laparoscopy: a follow-up Finnish study. Obstet Gynecol 1999; 94:94-8.
6. Moore J, Wadsworth S, Lindsell D, Golding S, Morris J, Kennedy S. A systematic review of the accuracy of ultrasound in the diagnosis of endometriosis (submitted for publication).
7. Kinkel K, Chapron C, Balleyguier C, Fritel X, Dubuisson JB, Moreau JF. Magnetic resonance imaging characteristics of deep endometriosis. Hum Reprod 1999; 14:1080-6.
8. Manfredi R, Valentini AL. Magnetic resonance imaging of pelvic endometriosis. Rays 1998; 23:702-8.
9. Mol BW, Bayram N, Lijmer JG, et al. The performance of CA-125 measurement in the detection of endometriosis: a meta-analysis. Fertil Steril 1998; 70:1101-8.
10. Waller KG, Shaw RW. Endometriosis, pelvic pain and psychological functioning. Fertil Steril 1995; 63:796-800.

11. Moore J, Kennedy S, Prentice A. Modern combined oral contraceptives for the treatment of painful symptoms associated with endometriosis (Cochrane Review). In: The Cochrane Library 1999, Issue 3. Oxford:Update Software.

12. Vercellini P, Trespidi L, Colombo A, Vendola N, Marchini M, Crosignani PG. A gonadotropin-releasing hormone agonist versus a low-dose oral contraceptive for pelvic pain associated with endometriosis. Fertil Steril 1993; 60:75-9.

13. Vercellini P, Cortesi I, Crosignani PG. Progestins for symptomatic endometriosis: a critical analysis of the evidence. Fertil Steril 1997; 68:393-401.

14. Selak V, Farquhar C, Prentice A, Singla A. Danazol vs. placebo for the treatment of endometriosis (Cochrane Review). In: The Cochrane Library 1999, Issue 3. Oxford:Update Software.

15. Prentice A, Deary AJ, Goldbeck-Wood S, Farquhar C, Smith SK. Gonadotrophin-releasing hormone analogues for pain associated with endometriosis (Cochrane Review). In: The Cochrane Library 1999 Issue 3. Oxford:Update Software.

16. Paoletti AM, Serra GG, Cagnacci A, et al. Spontaneous reversibility of bone loss induced by gonadotropin-releasing hormone analogue treatment. Fertil Steril 1996; 65:707-10.

17. Hornstein MD, Surrey ES, Weisberg GW, Casino LA. Leuprolide acetate depot and hormonal add-back in endometriosis: a 12-month study. Lupron Add-Back Study Group. Obstet Gynecol 1998; 91:16-24.

18. Hornstein MD, Yuzpe AA, Burry KA, Heinrichs LR, Buttram-VL J, Orwoll ES. Prospective randomized double-blind trial of 3 versus 6 months of nafarelin therapy for endometriosis associated pelvic pain. Fertil Steril 1995; 63:955-62.

19. Farquhar C, Sutton C. The evidence for the management of endometriosis. Curr Opin Obstet Gynecol 1998; 10:321-32.

20. Sutton CJ, Ewen SP, Whitelaw N, Haines P. Prospective, randomized, double-blind, controlled trial of laser laparoscopy in the treatment of pelvic pain associated with minimal, mild, and moderate endometriosis. Fertil Steril 1994; 62:696-700.

21. Sutton CJ, Pooley AS, Ewen SP, Haines P. Follow-up report on a randomized controlled trial of laser laparoscopy in the treatment of pelvic pain associated with minimal to moderate endometriosis. Fertil Steril 1997; 68:1070-4.

22. Hornstein MD, Hemmings R, Yuzpe AA, Heinrichs W.LeRoy. Use of nafarelin versus placebo after reductive laparoscopic surgery for endometriosis. Fertil Steril 1997; 68:860-4.

23. Vercellini P, Crosignani PG, Fadini R, Radici E, Belloni C, Sismondi P. A gonadotrophin-releasing hormone agonist compared with expectant management after conservative surgery for symptomatic endometriosis. Br J Obstet Gynaecol 1999; 106:672-7.

24. Parazzini F, Fedele L, Busecca M, et al. Postsurgical medical treatment of advanced endometriosis: results of a randomized clinical trial. Am J Obstet Gynecol 1994; 171:1205-7.

25. Vercellini P, De Giorgi O, Pesole A, Zaina B, Pisacreta A, Crosignani PG. Endometriosis: drugs and adjuvant therapy. In: Templeton A, Cooke I, O'Brien PMS, editors. *Evidence-based fertility treatment*. London: RCOG Press, 1998; 225-45.

26. Beretta P, Franchi M, Ghezzi F, Busacca M, Zupi E, Bolis P. Randomized clinical trial of two laparoscopic treatments of endometriomas: cystectomy versus drainage and coagulation. Fertil Steril 1998; 70:1176-80.

27. Donnez J, Nisolle M, Gillerot S, Anaf V, Clerckx-Braun F, Casanas-Roux F. Ovarian endometrial cysts: the role of gonadotropin-releasing hormone agonist and/or drainage. Fertil Steril 1994; 62:63-6.

28. Adamson GD, Pasta DJ. Surgical treatment of endometriosis-associated infertility: meta-analysis compared with survival analysis. Am J Obstet Gynecol 1994; 171:1488-504.

29. Marcoux S, Maheux R, Berube S. Laparoscopic surgery in infertile women with minimal or mild endometriosis. Canadian Collaborative Group on Endometriosis. N Engl J Med 1997; 337:217-22.

30. Parazzini F. Ablation of lesions or no treatment in minimal-mild endometriosis in infertile women: a randomized trial. Gruppo Italiano per lo Studio dell'Endomeriosi. Hum Reprod 1999; 14:1332-4.

31. Hughes EG. The effectiveness of ovulation induction and intrauterine insemination in the treatment of persistent infertility: a meta-analysis. Hum Reprod 1997; 12:1865-72.

32. Nulsen JC, Walsh S, Dumez S, Metzger DA. A randomized and longitudinal study of human menopausal gonadotrophin with intrauterine insemination in the treatment of infertility. Obstet Gynecol 1993; 82:780-6.

33. Tummon IS, Asher LJ, Martin JSB, Tulandi T. Randomized controlled trial of superovulation and insemination for infertility associated with minimal or mild endometriosis. Fertil Steril 1997; 68:8-12.

34. Landazábal A, Díaz I, Valbuena D, et al. Endometriosis and in-vitro fertilization: a meta-analysis. Hum Reprod 1999; 14(Abstract Book 1):181-2.

35. Templeton A, Morris JK, Parslow W. Factors that affect outcome of in-vitro fertilisation treatment. Lancet 1996; 348:1402-6.

References:Appendix 2

1. The American Fertility Society. Revised American Fertility Society Classification of Endometriosis: 1985. Fertility *and* Sterility 1985;43:351-352.

2. Rock JIA, Zoladex Endometriosis Study Group. The revised American Fertility Society classification of endometriosis: reproducibility of scoring. Fertility *and* Sterility 1995;63:1108-1110.

3. Hornstein MD, Gleason RE, Orav J, Haas ST, Friedman AJ, Rein MS. The reproducibility of the American Fertility Society classification of endometriosis. Fertility *and* Sterility 1993;59:1015-1021.

4. Candiani GB, Vercellini P, Fedele L. Laparoscopic ovarian puncture for correct staging of endometriosis. Fertility *and* Sterility 1990;53:994-997.

5. Vercellini P, Vendola N, Bocciolone 1, Rognoni MT, Carinelli SG, Candiani GB. Reliability of the visual diagnosis of ovarian endometriosis. Fertility *and* Sterility 1991;56:1198-1200.

6. Guzick DS, Silliman NP, Adamson GD, et al. Prediction of pregnancy in infertile women based on the American Society for Reproductive Medicine's revised classification of endometriosis. Fertility *and* Steriliiy 1997;67:822-829.

References: Appendix 3

1 Marcoux S, Maheux R, Berube S. Laparoscopic surgery in infertile women with minimal or mild endometriosis. *New England Journal of Medicine* 1997;337:217-222.

2 Hughes EG, Fedorkow DM, Collins J. A quantitative overview of controlled trials in endometriosis-associated infertility *Fertility and Sterility* 1993;59:963-970.

3.Parazzini F. Ablation of lesions or no treatment in minimal-mild endometriosis in infertile women: a randomized trial. Gruppo Italiano per lo Studio dell'Endometriosi. Hum Reprod 1999; 14:1332-4.

4.Nowroozi K, Chase JS, Check JH, Wu CH. The importance of laparoscopic coagulation of mild endometriosis in infertile women. *International Journal of Fertility* 1987;32:442-444.

5.Chong AP, Keene ME, Thornton ML. Comparison of three modes of treatment for infertility patients with minimal pelvic endometriosis. *Fertility and Sterility* 1990;53:407-410.

6.Fayez JA, Collazo LM, Vernon C. Comparison of different modalities of treatment for minimal and mild endometriosis. *American Journal of Obstetrics and Gynecology* 1988;159:927-932.

7.Paulson JD, Asmar P, Saffan DS. Mild and moderate endometriosis: comparison of treatment modalities for infertile couples. *Journal of Reproductive Medicine* 1991;36:151155.

8.Seiler JC, Gidwani G, Ballard L. Laparoscopic cauterization of endometriosis for fertility: a controlled study. *Fertility and Sterility* 1986;46:1098-1100.

9.Levinson CJ. Endometriosis therapy: rationale for expectant or minimal therapy in minimal/mild cases (AFSI). *Proceedings of the Second World Congress on Gynecologic Endoscopy.* Clermont-Ferrand, France 1989.

10 Adamson GD, Pasta DJ. Surgical treatment of endometriosis-associated infertility: meta-analysis compared with survival analysis. *American Journal of Obstetrics and Gynecology* 1994;171:1488-1504.

11. Jacobson, T. Z., Barlow, D. H., Koninckx, P. R., Olive, D., and Farquhar, C. Laparoscopic surgery for subfertility associated with endometriosis. TheCochrane Library (1). 2003.

Rerences: Appendix 4

1. Hughes E, Fedorkow D, Collins J, Vandelreckhove P. Ovulation suppression vs. placebo in the treatment of endometriosis (Cochrane Review). In: The Cochrane Library 1999, Issue 3. Oxford:Update Software.
2. Harrison RF,.Barry-Kinsella C. Efficacy of medroxyprogesterone treatment in infertile women with endometriosis: a prospective, randomized, placebo-controlled study. *Fertility and Sterility* 2000;74:24-30.

.References: Appendix 5

1.Tummon IS, Asher W, Martin JBS, Tulandi T. Randomised controlled trial of superovulation and insemination for infertility associated with minimal or mild endometriosis. *Fertility and Sterility 1997;68:8A2.*

2. Fedele L, Bianchi S, Marchini M, Villa L, Brioschi D, Parazzini F Superovulation with human menopausal gonadotrophins in the treatment of infertility associated with minimal or mild endometriosis: a controlled randomised study *Fertility and Sterility 1992;58:28-31.*

3. Nulsen JC, Walsh S, Dumez S. A randomised and longitudinal study of human menopausal gonadotrophin with intrauterine insemination in the treatment of infertility. *Obstetrics and Gynecology 1993;82:780-786.*

4. Hughes EG. The effectiveness of ovulation induction and intrauterine insemination in the treatment of persistent infertility: a meta-analysis. *Human Reproduction 1997;12:18651872.*

References: Appendix 6

1 Hughes E, Fedorkow DIVI, Collins J, Vandekerckhove P. Ovulation suppression versus placebo in the treatment of endometriosis (Cochrane Review). In: *The Cochrane Library,* Issue 2 Oxford: Update Software, 1998.

2 Hughes EG, Fedorkow DM, Collins J. A quantitative overview of controlled trials in end ometriosis-associated infertility *Fertility and Sterility* 1993;59:963-970.

4. Vercellini P, Crosignani PG, Fadini R, Radici E, Belloni C, Sismondi P. A gonadotrophin-releasing hormone agonist compared with expectant management after conservative surgery for symptomatic endometriosis. *British Journal of Obstetrics and Gynaecology* 1999;106:672-7.

5. Busacca M, Somigliana E, Bianchi S, De Marinis S, Calia C, Candiani M *et al*. Post-operative GnRH analogue treatment after conservative surgery for symptomatic endometriosis stage III-IV: a randomized controlled trial. *Human Reproduction* 2001;16:2399-402.

6 Parazzini F, Fedele L, Busacca M, et al. Postsurgical medical treatment of advanced endometriosis: Results of a RCT. *American Journal of Obstetrics and Gynecology* 1994;171:1205-1207.

7. Bianchi S, Busacca M, Agnoli B, Candiani M, Calia C, Vignali M. Effects of 3 month therapy with danazol after laparoscopic surgery for stage III/IV endometriosis: a randomized study. *Human Reproduction* 1999;14:1335-7.

References: Appendix 7

1.Evers JLK The pregnancy rate of the no-treatment group in RCTs of endometriosis therapy. *Fertility and Sterility 1989;52:906-907.*

2 Adamson GD, Pasta DJ. Surgical treatment of endometriosis-associated infertility: meta-analysis compared with survival analysis. *American Journal of Obstetrics and Gynecology 1994;171:1488-1504.*

3 Hughes EG, Fedorkow DM, Collins J. A quantitative overview of controlled trials in endometriosis-associated infertility. *Fertility and Sterility 1993;59:963-970.*

4 Adamson GR Hurd SJ, Pasta DJ, Rodriguez BD. Laparoscopic endometriosis treatment: is it better? *Fertility and Sterility 1993;59:35-44.*

5 Adamson GD, Frison L, Lamb EJ, Endometriosis: studies of a method for the design of a surgical staging system. *Fertility and Sterility 1982;38:659-666.*

6.Federici D, Conti E, Constantini W, et al. Endometriosis and infertility: our experience over *5* years. *Human Reproduction 1988;3:109-111*

.

7.Buttram V, Reiter R, Ward S. Treatment of endometriosis with danazol: report of a 6-year prospective study. *Fertility and Sterility* 1985;43:353-360

8.Paulson JD, Asmar *P,* Saffan DS. Mild and moderate endometriosis: comparison of treatment modalities for infertile couples. *Journal of Reproductive Medicine 1991;36:151155*

.

Arumugam K, Urquhart R. Efficacy of laparoscopic electrocoagulation in infertile patients with minimal or mild endometriosis. *Acta Obstetrica et Gynecologica Scandinavica 1991;70:125-127.*

Nowroozi K, Chase JS, Check JH, Wu CH. The importance of laparoscopic coagulation of mild endometriosis in infertile women. *International Journal of Fertility 1987;32:442-444.*

.

References: Appendix 8

1. Soliman S, Daya S, Collins J, Jarrell J. A randomised trial of *in vitro* fertilisation versus conventional treatment for infertility. *Fertility and Sterility 1993;59:1239-1244.*

2. Pagidas K, Falcone T, Hemmings R, Miron P. Comparison of reoperation for moderate (stage 111) and severe (stage IV) endometriosis- related infertility with *in vitro* fertilisationembryo transfer. *Fertility and Sterility 1996;65:791-795.*

3. Barnhart K, Dunsmoor-Su R, Coutifaris C. Effect of endometriosis on in vitro fertilization. *Fertility and Sterility* 2002;77:1148-55.

4. Marcus SF, Edwards RG. High rates of pregnancy after long-term down-regulation of women with severe endometriosis. *American Journal of Obstetrics and Gynecology 1994;171:812-817.*

5. Wessels PH, Cronje HS, Oosthuizen AP, Trumpelmann MD, Grobler S, Hamlett DK. Costeffectiveness of gamete intrafalliopian transfer in comparison with induction of ovulation with gonadotrophins in the treatment of female infertility: a clinical trial. *Fertility and Sterility 1992;57:163-167.*

6. LandazAbal A, Diaz 1, Valbuena D, et al. Endometriosis and in-vitro fertilization: a meta-analysis. Hum Reprod 1999; 14(Abstract Book 1): 18 1 2.

7.Templeton A, Morris *M* Parslow W. Factors that affect outcome of in-vitro fertilisation treatment. Lancet 1996; 348:1402-6.

References: Appendix 9

1. Donnez J, Nisolle M, Gillerot S, Anaf V, Clerckx-Braun F, Casanas-Roux F Ovarian endometrial cysts: the role of gonadotropin-releasing hormone agonist and/or drainage. *Fertility and Sterility* 1994;62:63-66.

2..Federici D, Conti E, Constantini W, et al. Endometriosis and infertility: our experience over 5 years. *Human Reproduction* 1988;3:109-111.

3. Donnez J, Nisolle-Pochet M, Casanas-Roux F. Endometriosis-associated infertility: evaluation of pre-operative use of danazol, gestrinone and buserelin. *International Journal of Fertility* 1990;35:297-301.

4. Nisolle M, Casanas-Roux F, Donnez J. Histologic study of ovarian endometriosis after hormonal therapy. *Fertility and Sterility* 1988;49:423-426.

5. Shaw RW. The role of GnRH analogues in the treatment of endometriosis. *British Journal of Obstetrics and Gynaecology* 1992;99:9A2.

6. Beretta P, Franchi M, Ghezzi F, Busacca M, Zupi E, Bolis P.Randomized clinical trial of two laparoscopic treatments of endometriomas:cystectomy versus drainage and coagulation. *Fertility and Sterility*1998;70:1176-80.

7. Donnez J, Nisolle M, Gillet N, Smets M, Bassi] S, Casanas-Roux F Large ovarian endometriomas. *Human Reproduction* 1996;11:641-646.

8. Adamson GD, Hurd SJ, Pasta DJ, Rodriguez BD. Laparoscopic endometriosis treatment: is it better? *Fertility and Sterility* 1993;59:35-44.

9. Fayez JA,.Collazo LM. Comparison between laparotomy and operative laparoscopy in the treatment of moderate and severe stages of endometriosis. *International Journal of Fertility* 1990;35:272-9.

10. Crosignani PG, Vercellini P, Biffignandi F, Costantini W, Cortesi I, Imparato E. Laparoscopy versus laparotomy in conservative surgical treatment for severe endometriosis. *Fertility and Sterility* 1996;Vol 66:-711.

11. Busacca M, Fedele L, Bianchi S, Candiani M, Agnoli B, Raffaelli R *et al*. Surgical treatment of recurrent endometriosis: laparotomy versus laparoscopy. *Human Reproduction* 1998;13:2271-4.

12. Dicker D, Ashkenazi J, Feldberg D, Levy T, Dekel A, Ben-Rafael Z. Severe abdominal complications after transvaginal ultrasonographically guided retrieval of oocytes for *in vitro* fertilisation and embryo transfer. *Fertility and Sterility* 1993;59:1313-1315.

13. Younis JS, Ezra Y, Laufer N, Ohel G. Late manifestation of pelvic abscess following oocyte retrieval, for *in vitro* fertilisation, in patients with severe endometriosis and ovarian endometriomata. *Journal of Assisted Reproduction and Genetics* 1997;14:343-346.

14.Dlugi AM, Loy RA, Dieterle S, Bayer SR, Seibel MM. The effect of endometriomas on *in vitro* fertilisation outcome. *Journal of In Vitro Fertilisation and Embryo Transfer* 1989;6:338341.

15. Isaacs JD, Jr., Hines RS, Sopelak VM, Cowan BD. Ovarian endometriomas do not adversely affect pregnancy success following treatment with in vitro fertilisation. *Journal of Assisted Reproduction and Genetics 1997;14:551-553.*

16. Olivennes F Feldberg D, Liu H, Cohen J, Moy F, Rosenwaks Z. Endometriosis: a stage by stage analysis - the role of *in vitro* fertilisation. *Fertility and Sterility* 1995;64:392-398.

Clinical guidelines are: 'systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions'. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in 'Guidance for the development of RCOG green-top guidelines' (available on the RCOG website). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

Classification of evidence levels

Ia	*Evidence obtained from meta-analysis of randomised controlled trials.*
Ib	*Evidence obtained from at least one randomised controlled trial.*
IIa	*Evidence obtained from at least one well-designed controlled study without randomisation.*
IIb	*Evidence obtained from at least one other type of well-designed quasi-experimental study.*
III	*Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.*
IV	*Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.*

Grades of recommendations

A *Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)*

B *Requires the availability of well controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)*

C *Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)*

Good Practice Point

☆ *Recommended best practice based on the clinical experience of the guideline development group.*

This Dorset Guideline was produced in part from the Guidelines and Audit Committee of the Royal College of Obstetricians and Gynaecologists by Mr S H Kennedy MRCOG, Oxford and was revised with the help of Dr M R Gazvani MRCOG, Aberdeen.

The remainder of the Guideline was produced by contributions from Mr.J.N.T.Edwards, Mr.J.S..Pampiglione, Dr.B. Newman,; Mrs E. Mann,; Miss N. Soliman,& Mrs. J. Jansen, on behalf of the Poole Hospital Public & Patient Involvement Project under the auspices of Mrs. Janice Beavan. Acknowledgement is also given to the Dorset Patient support groups & particularly to PEGASUS & to Mrs. L.Woodward who has acted as facilitator.

Peer reviewed by:
Ms A Barnard, National Endometriosis Society; Professor J L H Evers, Maastricht;
Mr N G B Haddad FRCOG, Chester; Dr C Overton MRCOG, London; Mr A J Rutherford FRCOG, Leeds; Professor C J G Sutton FRCOG, Guildford; Professor E J Thomas MRCOG, Southampton;
Dr P Vercellini, Milan.