BJOG: An International Journal of Obstetrics & Gynaecology

WILEY

BJOG An International Journal of Obstetrics and Gynaecology

SCIENTIFIC IMPACT PAPER

The Effect of Surgery on Endometriomas on Fertility (2025 Second Edition)

Scientific Impact Paper No 55

P. R. Supramaniam | M. Mittal | C. Becker | K. Jayaprakasan | on behalf of the Royal College of Obstetricians and Gynaecologists

Correspondence: on behalf of the Royal College of Obstetricians and Gynaecologists (clinicaleffectiveness@rcog.org.uk)

Funding: All those involved in the development of Scientific Impact Papers, including the Scientific Advisory Committee, Scientific Advisory Committee chair, developers, peer reviewers and other reviewers, are unpaid volunteers and receive no direct funding for their work in producing the paper. The only exception to this are the Scientific Advisory Committee members who receive reimbursement for expenses for attending Scientific Advisory Committee meetings for standard RCOG activities; this is standard as per Royal College of Obstetricians and Gynaecologist rules.

Plain Language Summary

Endometriosis is a condition where the lining of the uterus (womb) is found in other locations in the body such as, but not limited to, the ovaries, bowel and bladder. It is a common condition that can affect up to one in 10 women and can be found in between three to five in 10 women who have been diagnosed with subfertility.

Women with endometriosis often present with painful periods, heavy periods, pain while opening their bowels or passing urine, pain during sexual intercourse and difficulty in conceiving. A proportion of those with endometriosis remain asymptomatic of the disease. Care should be tailored to each individual.

The significant improvement in diagnostic technology has increased the detection rate of endometriosis. People with ovarian endometriosis, also known as an ovarian endometrioma, can be diagnosed using a transvaginal (internal) or transabdominal (via the tummy) ultrasound scan. Detection rates of up to 90% have been reported for routine ultrasound scans.

Ovarian endometriomas can impact fertility outcomes, and for these people a multidisciplinary approach to care is required. The presence of an ovarian endometrioma and endometriosis is known to have a negative impact on the ovarian reserve (egg count and quality) and overall, chance of successful conception. Women with known endometriosis should therefore be counselled about the various options available for fertility preservation.

The treatment for ovarian endometrioma(s) in those wanting to conceive can be broadly divided into two categories, expectant (watch-and-wait approach), and surgical which most commonly involves-keyhole surgery.

Expectant management avoids the risks of surgery, along with no further surgically related reduction in ovarian reserve. It also reduces the delay from diagnosis to starting fertility treatment. The disadvantages of this approach, however, would be the persistence of pain symptoms, and ongoing difficulty with accessing the ovaries during assisted fertility treatment such as in vitro fertilisation.

Surgical treatment for ovarian endometrioma(s) in the context of women trying to conceive is often approached with caution. Surgery has been shown to reduce the ovarian reserve further, and clinicians would attempt to limit the degree of impact by reducing the amount of surgical stress to an ovary. The benefits of this approach, however, would be an improvement in symptoms and access to the ovaries for fertility treatment.

This is the second edition of this paper. It replaces the earlier edition published September 2017.

1 | Background

Endometriosis is increasingly recognised as a systemic inflammatory condition extending beyond the pelvis [1]. It is characterised by the presence of endometrium-like epithelium and/or stroma outside of the endometrium and myometrium [2]. It is estimated that 5%–10% of women [1] mainly of reproductive age, have signs of endometriosis, with a reported higher prevalence in certain subgroups, such as those affected by subfertility, 30%–50% [3, 4]. Endometriotic ovarian cysts (known as endometriomas) can be found in up to 17%–44% of women with endometriosis and are often associated with the severe form of the disease [5, 6]. While the pathogenesis of endometriosis per se remain elusive, it was historically believed that immune dysfunction interfered with endometrial implant clearance [7]. Extrapelvic endometriosis is no longer explained by the theory of retrograde menstruation. Ovarian endometrioma(s) are mostly thought to occur through the invagination of endometriotic tissue/cells on the ovarian serosa, for example, during remodelling of the ovarian cortex after ovulation [8].

The presence of an endometrioma can often present a clinical dilemma during fertility treatment. For example, there can be uncertainty regarding the decision to operate or to manage conservatively, balancing the potential detrimental effect of surgery on ovarian reserve largely reflected by a lower anti-müllerian hormone (AMH) level, antral follicle count (AFC) and oocyte yield, against the potential benefit that may be gained from surgery, such as an improvement in symptoms aiding natural conception or improved follicular access during assisted reproductive techniques (ART). Ovarian reserve and its parameters, however, do not reflect the chances of natural conception but provide information and largely represent how the woman or person would respond to controlled ovarian stimulation in assisted reproductive treatments such as in vitro fertilisation (IVF) (Table 1).

The optimal intervention for the management of endometriomas is largely debated. Many different techniques exist, with the recommendation for treatment needing to be individualised to the individual's specific circumstances, such as the presence of concomitant pain, unilateral or bilateral disease and the location of the follicles in relation to the site of the endometrioma(s). Fertility- preserving surgical management options for an endometrioma include ultrasound-guided or laparoscopic-guided cyst aspiration, cystectomy or fenestration and coagulation. In the presence of bilateral disease, a more conservative approach may be favoured to help preserve as much normal ovarian tissue as possible. In an asymptomatic individual, as long as the endometrioma does not prevent access to the follicles, it can be left untreated [9].

Current guidelines often rely on evidence from historical studies, which tend to be either small and/or retrospective in design. This Scientific Impact Paper will review the current evidence for management of endometriomas within the context of subfertility treatment and offer an opinion of how best to counsel patients in their journey, taking into consideration improvements made with stimulation protocols and laboratory techniques as well as the advancements made in benign laparoscopic surgery.

This guidance is for healthcare professionals who care for women, non-binary and trans people with ovarian endometriosis, also known as an ovarian endometrioma.

Within this document we use the terms woman and women's health. However, it is important to acknowledge that it is not only women for whom it is necessary to access women's health and reproductive services to maintain their gynaecological health and reproductive wellbeing. Gynaecological and obstetric services and delivery of care must therefore be appropriate, inclusive and sensitive to the needs of those individuals whose gender identity does not align with the sex they were assigned at birth.

2 | Potential Mechanisms for Endometriosis-Associated Subfertility

Fecundity rates may be reduced in women with endometriosis, with a nearly two-fold increased risk of subfertility in women

TABLE 1 | Risks and benefits of expectant and surgical management of an endometrioma for women undergoing assisted reproductive treatment.

	Expectant management	Surgical management
Potential benefit	• Avoidance of surgery and its associated complications • No further surgical compromise to ovarian reserve • Avoids delay in commencing assisted reproductive treatment	• Alleviation of symptoms • Histological confirmation of diagnosis (i.e., exclusion of malignancy) • Reduced risk of cyst complications • Facilitates ovarian access
Potential harm	• Symptoms (pain) • Spontaneous cyst rupture • Difficult ovarian access during oocyte retrieval procedures • Infection of an endometrioma • Follicular fluid contamination • No histological diagnosis • Accelerated progression of endometriosis	• Surgical risks • Reduced ovarian reserve • Development of new post operative pain symptoms • Postoperative adhesions • Potential delay of assisted reproductive treatment

aged under 35 years, with an approximately 2%–10% fecundity rate per month compared to 15%–20% per month in healthy couples [3, 10], potentially related to the severity of the disease (revised American Society for Reproductive Medicine [rASRM] classification) [11]. The presence of ovarian endometriomas is usually associated with rASRM staging of moderate or severe disease [5]. A number of theories for endometriosis-related subfertility have been proposed, including chronic inflammation and reduced endometrial receptivity, tuboperitoneal anatomic distortion, compromised oocyte and embryo quality, reduced ovarian reserve, but the precise mechanism has yet to be determined [12].

2.1 | Chronic Inflammation

Endometriosis is associated with dysregulation of the immune system. Peritoneal fluid from people with endometriosis has been found to contain increased numbers of immune cells, including macrophages, and mast, natural killer and T cells, as well as elevated levels of growth factors, chemokines and cytokines [13–15]. The enhanced inflammatory state might affect the quality of the oocytes and impair ovarian function, resulting in defective folliculogenesis and fertilisation [16].

2.2 | Endometrial Receptivity

Implantation and trophoblast invasion can be disrupted in the presence of endometriosis by the dysregulation of signalling pathways and molecules (proteins) in endometrial stromal cells, differential endometrial gene expression, alterations in cell physiology and vascular abnormalities. Inflammation, a consequence of endometriosis, is known to alter endometrial receptivity [17]. Implantation and clinical pregnancy rates have been shown to be significantly reduced by 7.67% and 13.33% respectively, in women with endometriosis compared to women without endometriosis [18]. This finding, however, has been shown to be overcome by employing the freeze-all strategy where all suitable embryos are cryopreserved and no fresh embryo transfer is undertaken, increasing both the clinical pregnancy rates (13.4%) and cumulative ongoing pregnancy rates (17%) in frozen cycles compared to fresh cycles [19, 20].

2.3 | Oocyte and Embryo Quality

Oocyte and embryo quality are key determinants of reproductive outcomes. Oocyte competence (growth and maturation) is influenced by the follicular fluid, which is composed of many substances, such as hormones, cytokines, immune cells (including natural killer cells, lymphocytes and macrophages), enzymes, anticoagulants, electrolytes, reactive oxygen species, lipids, cholesterol, and antioxidants. In endometriosis, dysregulation of molecular mechanisms may alter the follicular microenvironment, represented by elevated concentrations of progesterone and interleukin-6, and decreased concentrations of vascular endothelial growth factor [21], inhibiting embryonic development by affecting the mRNA, mitochondria, lipid and protein reserves. Furthermore, the degree of apoptosis of the granulosa cells surrounding the oocyte, alterations of the cell cycle and incidence of oxidative stress have been suggested to be greater in women with endometriosis than in women with other causes for their subfertility [3]. Embryo development with autologous oocytes is slower in women with endometriosis than in women with tubal factor subfertility [22]. However, women with moderate to severe disease who receive eggs from a donor without endometriosis have a similar pregnancy rate to other egg recipients [23, 24]. The implantation rate has been shown to be reduced by 4.2%–16.6% and the pregnancy rate by 16.7%–33% if oocytes are donated by women with endometriosis compared with no endometriosis [24].

2.4 | Ovarian Reserve

The presence of ovarian endometriomas, especially if bilateral, can affect the ovarian reserve, impacting the ovarian response to gonadotrophins during ART. A histological study [25] reported a significant reduction in the primordial follicle cohort in affected ovaries. Follicle depletion may be secondary to damage induced by the endometriosis-associated inflammatory reaction and by increased tissue oxidative stress leading to fibrosis [26]. A group of potentially toxic agents, such as free iron, that can diffuse through the cyst wall of the endometrioma, as well as long-lasting mechanical stretching of the ovarian cortex, might all detrimentally impact the ovarian reserve [27]. Most importantly, however, is the negative effect of ovarian surgery on ovarian reserve, especially if repeated surgical interventions are undertaken (see Sections 3.1.2 and 3.2.2).

3 | Management Options

While the options include expectant and surgical management in the context of fertility, the recommended treatment should be guided by: the woman's symptoms; fertility prognostic factors, including age and ovarian reserve; previous treatment history with specific reference to past surgical interventions; size and nature of the cyst; unilateral or bilateral, and the wishes of the woman or person [28]. Treatment of incidental disease in otherwise asymptomatic women is currently not recommended, as the development and natural progression of endometriomas is not well understood [29].

3.1 | Natural Conception

3.1.1 | Conservative Management for Natural Conception

Women with regular menstrual cycles and an incidental finding of an ovarian endometrioma without suspicion of malignancy, who wish to conceive, can be encouraged to try natural conception before seeking fertility treatment. While the evidence of the impact of an endometrioma on spontaneous conception is limited, a prospective observational study [30] ($n = 244$) reported a 43% spontaneous pregnancy rate during the 6-month follow-up period in the presence of unilateral endometriomas

of varying sizes (diameter 5.3 ± 1.7 cm [mean ± SD]). The study also reported similar ovulation rates in the affected ovary compared to the healthy ovary (49.7% versus 50.3%), not influenced by the position of the endometriomas, their number and size, or by the presence of deep endometriosis diagnosed by ultrasound scan. This finding contradicted previously reported data in a smaller prospective study ($n = 70$) [31], of reduced ovulation in the affected ovary (31% versus 69%). Conservative management for fertility should be weighed against the potential benefits and risks of surgery or fertility treatment. The dilemma is most acute for those who have a low ovarian reserve and are potential poor responders.

Women with known endometriosis can also be advised to attempt natural conception for 6 months and if they do not become pregnant, to seek specialist consultation. For those with a known diminished ovarian reserve, a 6-month delay to their IVF treatment has not been shown to detrimentally impact their overall outcome [32].

3.1.2 | Surgical Treatment for Natural Conception

There is controversy regarding surgical management of endometriomas in women with an incidental finding. Surgery in the form of laparoscopic excision or ablative treatment of peritoneal endometriosis (rASRM stage I [minimal endometriosis with a few superficial implants]/II [mild endometriosis with a greater number and deeper implants than stage I] endometriosis) has been shown to improve the clinical pregnancy rate compared to a diagnostic laparoscopy alone (odds ratio [OR] 1.89, 95% CI 1.25–2.86; three randomised controlled trials including 265 patients who underwent surgical intervention versus 263 who underwent a diagnostic laparoscopy only) [33]. However, by restoring pelvic anatomy, it remains unclear as to whether surgical intervention on the ovary itself is beneficial. It is not believed to reverse the inflammatory and biomolecular changes shown to influence fertilisation and implantation [34]. No comparative studies evaluating the spontaneous conception rate after surgery for an endometrioma or deep endometriosis compared to no surgical intervention have been identified [29].

Furthermore, there are concerns regarding the safety of surgical treatments, with a reported reduction in ovarian reserve [35, 36] and the small added risk of requiring an oophorectomy. In contrast, concerns have been raised about the effect of an endometrioma on oocyte quantity and quality. This conflict suggests that management should be individualised and based on clinical factors, including pain symptoms, size of the cysts and concerns over potential malignancy. Consideration should be given to surgical treatment being undertaken by a gynaecologist with specific expertise in endometriosis and fertility to minimise the impact on ovarian reserve and provide a holistic assessment regarding future fertility management.

When performing surgery, ovarian endometriomas can be managed by performing a cystectomy or drainage with adjuvant therapy such as coagulation or sclerotherapy. Preoperative assessment of AMH levels may be beneficial in knowing the baseline ovarian reserve before embarking on surgery and helping clinicians and women to make an informed decision, as a cystectomy may potentially reduce the ovarian reserve. A cystectomy is associated with an overall lower risk of recurrence and less endometriosis-associated pain, especially if the cyst is 3 cm or more in diameter [37]. The rate of recurrence after laparoscopic ovarian cystectomy is approximately 6%–67%, while the rate of recurrence after aspiration is 28%–98%, reducing to approximately 15% after surgery in conjunction with sclerotherapy [38]. Hart et al. [37] summarised two randomised controlled trials that demonstrated a beneficial effect of excisional surgery of an endometrioma compared to drainage or ablation on spontaneous pregnancy rates (OR 5.24, 95% CI 1.92–14.27; $n = 88$; two trials) in infertile women. This finding is further supported by a comparative study that demonstrated higher spontaneous pregnancy rates after a laparoscopic ovarian cystectomy (55.5%) compared with cyst vaporisation with CO_2 laser (35.9%) [39].

3.2 | Assisted Conception

3.2.1 | Effect of Endometriosis and Endometriomas on In Vitro Fertilisation Outcomes

Evidence of the impact of an endometrioma on ovarian response during IVF is equivocal. Systematic reviews including controlled studies have reported similar ovarian response in women with and without endometriosis [40]. Similar outcomes in ovarian response are also seen when a unilateral ovarian endometrioma is compared to a normal contra-lateral ovary in the same women [41]. The live birth rate (OR 0.96, 95% CI 0.82–1.12; 8 studies; $n = 4157$), clinical pregnancy rate (OR 0.84, 95% CI 0.69–1.03; 15 studies; $n = 9692$) and mean number of oocytes retrieved per cycle (−0.58, 95% CI 21.16–0.01; 11 studies) have been shown to be comparable in those with stage I/II endometriosis and no endometriosis. In contrast, the live birth rate (OR 0.77, 95% CI 0.64–0.92; 8 studies), clinical pregnancy rate (OR 0.60, 95% CI 0.44–0.81; 15 studies; $n = 9471$) and mean number of oocytes retrieved (21.76, 95% CI 22.73–0.79; 14 cycles; $n = 9172$) were significantly lower in women with stage III (moderate endometriosis with a number of deep implants, including small endometriomas on one or both ovaries and the presence of filmy adhesions)/IV (severe endometriosis with a number of deep implants, including large endometriomas on one or both ovaries and the presence of dense adhesions) endometriosis compared to no endometriosis [42]. However, the live birth rate (OR 0.98, 95% CI 0.71–1.36; 5 studies; $n = 928$ women), clinical pregnancy rate (OR 1.17, 95% CI 0.87–1.58; 5 studies; $n = 928$ women) and miscarriage rate (OR 1.70, 95% CI 0.86–3.35; 3 studies; $n = 171$ pregnancies) were similar between women with and without an endometrioma, but the mean number of oocytes retrieved (mean difference − 0.23, 95% CI −0.37– −0.10; 5 studies; $n = 941$ cycles) was significantly lower and the cycle cancellation rate (OR 2.83, 95% CI 1.32–6.06; 3 studies; $n = 491$) significantly higher in those with an endometrioma compared to those without [43]. Furthermore, studies [44–47] have reported on the potential detrimental effect of the size of the endometrioma on ovarian response, especially when it is 3 cm or more in diameter. These findings have been replicated by Alshehre et al. [47], who compared reproductive outcomes following ART in women with an endometrioma and controls, including those without an endometrioma, tubal factor or male subfertility. The number of oocytes ($n = 428$ women had an endometrioma and 523 controls)

(weighted means difference [WMD] −2.25, 95% CI −3.43 to −1.06) and the number of mature oocytes retrieved ($n = 140$ women had an endometrioma and 186 controls) (WMD −4.64, 95% CI −5.65 to −3.63) were significantly lower in the presence of an endometrioma compared to the control group. In contrast, the gonadotrophin dose ($n = 178$ women had an endometrioma and 249 controls) and total duration ($n = 173$ women had an endometrioma and 241 controls), number of high-quality embryos created ($n = 156$ women had an endometrioma and 185 controls), clinical pregnancy rate ($n = 152$ women had an endometrioma and 251 controls), implantation rate ($n = 241$ women had an endometrioma and 361 controls) and live birth rate ($n = 76$ women had an endometrioma and 134 controls) were comparable [47]. Of note, no pelvic abscesses were recorded in a series of 214 women undergoing oocyte retrieval in the context of endometriomas under antibiotic prophylaxis [48].

When comparing women with an intact endometrioma with those with peritoneal endometriosis only, no difference was seen in the live birth rate (OR 0.92, 95% CI 0.92–1.79; 2 studies; $n = 353$ women), clinical pregnancy rate (OR 0.87, 95% CI 0.56–1.35; 3 studies; $n = 518$ women), miscarriage rate (OR 0.86, 95% CI 0.18–4.17; 2 studies; $n = 175$ pregnancies), mean number of oocytes retrieved (mean difference −0.31, 95% CI −1.03–0.42; 3 studies; $n = 539$ cycles) and cancellation rate (OR 0.82, 95% CI 0.23–2.93; 1 study; $n = 46$ cycles) [43].

Different ovarian stimulation protocols in ART cycles have not been shown to affect the outcomes in women with stage III/IV disease. In contrast, an observational retrospective cohort study ($n = 386$) has demonstrated a higher biochemical, clinical pregnancy and live birth rate (42.8% vs. 26.7%) in women with stage I/II disease with gonadotrophin-releasing hormone (GnRH) agonist protocols compared to antagonist protocols [49].

Basal follicle-stimulating hormone levels were higher in women with an endometrioma compared to women with no evidence of endometriosis (mean difference 0.20, 95% CI 0.02–0.38; three studies; $n = 491$ cycles) but similar to women with peritoneal endometriosis (mean difference 0.41, 95% CI −0.29–1.10; 2 studies; $n = 190$). The antral follicle count (mean difference −0.02, 95% CI −0.21–0.18; 2 studies; $n = 433$ cycles) and total stimulation dose (mean difference −0.07, 95% CI −0.27–0.12; 2 studies; $n = 433$ cycles) were comparable in those with an endometrioma and no evidence of endometriosis [43]. Although equivocal, most studies [50, 51] report that the observed reduced ovarian response, especially in the presence of larger endometriomas, is related to an overall reduced ovarian reserve in women with an endometrioma.

An adverse impact of endometriomas and endometriosis on oocyte quality has been suggested by Simón et al. [52] who reported on data from an oocyte donation programme. Within this, people with endometriosis were shown to have the same chance of implantation and pregnancy as other oocyte recipients, when the oocytes came from donors without known endometriosis. However, the implantation rates were reduced in healthy recipients when the oocytes came from donors with endometriosis, suggesting the condition had a negative effect on oocyte quality. Nevertheless, the European Society of Human Reproduction and Embryology (ESHRE) guideline for the management of endometriosis [29], published 20 years after Simón et al. [52], has not identified such differences. ESHRE is reassured by the reproductive outcomes demonstrated in large databases, such as those of the Human Fertilisation and Embryology Authority and the Society for Assisted Reproductive Technology, that include more recent IVF cycles.

3.2.2 | Surgical Treatment Prior to In Vitro Fertilisation

Surgical treatment of endometriomas prior to IVF is widely practised [53], although there is debate about its effect and need. The live birth rate (OR 0.90, 95% CI 0.63–1.28; 5 studies; $n = 655$), clinical pregnancy rate (OR 0.97, 95% CI 0.78–1.20; 11 studies; $n = 1512$) and miscarriage rate (OR 1.32, 95% CI 0.66–2.65; 4 studies; $n = 195$ pregnancies) were found to be comparable between women who underwent surgical treatment of an endometrioma prior to ART and conservative management of an intact endometrioma [43]. A further systematic review and meta-analysis did not demonstrate an advantage of surgical pre-treatment of an endometrioma on live birth rates (OR 1.08, 95% CI 0.80–1.45; 7 studies) [54]. While the mean number of oocytes retrieved (mean difference −0.17, 95% CI −0.38–0.05; 9 studies; $n = 810$ cycles) and the cancellation rate per cycle (OR 1.17, 95% CI 0.69–2.00; 4 studies; $n = 647$ cycles) were comparable, women who underwent surgical pre-treatment of an endometrioma had a lower antral follicle count (mean difference −0.53, 95% CI −0.88 to −0.18; 4 studies; $n = 558$ cycles) and required higher doses of gonadotrophins for ovarian stimulation (mean difference 1.45, 95% CI 0.23–2.68; 4 studies; $n = 635$ cycles) [43]. Women who had undergone surgical management of a unilateral endometrioma had a lower number of oocytes retrieved from the surgically treated ovary (mean difference −2.59, 95% CI −4.13 to −1.05; 4 studies; $n = 222$ cycles) [43] when compared with the contralateral normal ovary, indicating a reduction in the ovarian reserve following surgical intervention, as has been reported in several other studies [34, 44, 50]. The potential physiological compensation by the normal ovary for the compromised ovary, in conjunction with the higher follicle-stimulating hormone doses required for ovarian stimulation, may account for the similar IVF outcomes noted in women who have undergone surgical treatment for their endometriomas [45].

Furthermore, no difference in the live birth rate (OR 0.72, 95% CI 0.37–1.37; 2 studies; $n = 371$), clinical pregnancy rate (OR 0.99, 95% CI 0.71–1.38; 6 studies; $n = 893$) and miscarriage rate (OR 0.80, 95% CI 0.17–3.72; 2 studies; $n = 69$ pregnancies) was seen between women who had undergone surgical pre-treatment of an endometrioma versus peritoneal endometriosis. The total gonadotrophin dose required for ovarian stimulation (mean difference 0.18, 95% CI −0.25–0.61; 2 studies; $n = 167$ cycles) was not different, but the mean number of oocytes retrieved (mean difference −0.33, 95% CI −0.53 to −0.13; 7 studies; $n = 1101$ cycles) was significantly lower in those who underwent surgical pre-treatment of an endometrioma compared to peritoneal endometriosis [43].

Different surgical techniques have been employed to manage an endometrioma with no superiority demonstrated for one approach over another [29]. A Cochrane review incorporating two

small randomised controlled trials has reported similar pregnancy rates for surgical (cystectomy or aspiration) and expectant management [55]. While no differences in pregnancy rates have been shown between a cystectomy and aspiration of an endometrioma, a cystectomy is associated with a lower ovarian response following controlled stimulation, with a lower number of mature oocytes retrieved, raising concern about the potential adverse influence of a cystectomy on ovarian reserve. A retrospective cohort study found a higher cancellation rate following an ovarian cystectomy compared to conservative management [42]. In contrast, a meta-analysis incorporating controlled studies (including non-randomised controlled trial studies) reported similar ovarian responses (mean difference in the number of oocytes retrieved −0.17, 95% CI −0.56–0.22; 4 studies; $n = 289$ cycles) and clinical pregnancy rates (OR 0.98, 95% CI 0.57–1.69; 3 studies; $n = 232$ women) [43] following IVF in women with an endometrioma surgically managed with a cystectomy compared to transvaginal aspiration. The total gonadotrophin dose required to achieve ovarian stimulation (mean difference −0.02, 95% CI −0.42–0.38; 2 studies; $n = 100$ cycles) was also comparable [43].

Ethanol sclerotherapy is a potential adjuvant to the management of endometriomas that are aspirated. In this treatment, the endometrioma is first aspirated, followed by the instillation and flushing through of the cyst with 96% ethanol for 10 minutes. The ethanol is then re-aspirated and removed [56]. A systematic review and meta-analysis evaluating the effect of ethanol sclerotherapy with ovarian cystectomy demonstrated a similar clinical pregnancy rate (OR 1.63, 95% CI 0.91–2.9; 3 studies; $n = 214$ women) but significantly higher oocyte yield (mean difference 2.7, 95% CI 0.98–4.4; 3 studies; $n = 178$ women) with sclerotherapy. No difference was seen in the clinical pregnancy rate (OR 1.1, 95% CI 0.57–2.12; 3 studies; $n = 164$ women) and oocyte yield (mean difference −0.51, 95% CI −2.23–1.21; 3 studies; $n = 148$ women) between those treated with sclerotherapy or conservatively [57]. In contrast, a small retrospective study reported a more than two-fold higher chance of a woman birthing a live baby following ethanol sclerotherapy compared to conservative management (OR 2.68, 95% CI 1.13–6.36; $n = 74$) [58].

A review based on the combined results of eight studies ($n = 553$ women) demonstrated no significant difference in the clinical pregnancy rate of women with endometriosis managed with either surgery alone (43.8%, 95% CI 22.5–66.4), surgery plus ART (38.3%, 95% CI 32.3–44.7), aspiration with or without sclerotherapy plus ART (40.8%, 95% CI 27.7–54.6) or ART alone (32%, 95% CI 15.0–52.0) [38].

Based on the available evidence, the ESHRE guideline concluded that surgery for ovarian endometriomas prior to ART does not improve live birth rates and is likely to have a negative impact on ovarian reserve [29, 59]. However, surgery before ART can be considered for the management of endometriosis-associated pain, for increasing the accessibility of the follicles during the oocyte retrieval procedures, or to ameliorate any concern for malignancy. No one surgical technique is considered superior in terms of reproductive outcomes. Ovarian reserve is largely said to be impacted by repeated surgical procedures on the same ovary compared to the first surgical intervention [60]. The management of bilateral endometriomas can have a greater negative effect on ovarian reserve compared to surgical treatment of unilateral disease [61].

Despite the lack of evidence of the clear benefit of surgical treatment for the management of an endometrioma on reproductive outcomes, and the various potential drawbacks and risks, conservative management in women with an endometrioma undergoing IVF treatment has been questioned. The presence of an endometrioma may theoretically interfere with ovarian responsiveness to controlled stimulation and oocyte competence, as well as pose potential risk and technical difficulties during oocyte retrieval, including the associated risks to injury to adjacent organs due to altered pelvic anatomy with the presence of adhesions, infection and abscess formation, follicular fluid contamination with endometrioma content, progression of endometriosis, further growth and rupture of the endometrioma, missed occult malignancy and cancer development in later life. A systematic review and meta-analysis, with acknowledgement of both heterogeneity and publication bias across the studies, has suggested a 1.9-fold greater risk of ovarian cancer development, specifically clear cell cancer of the ovary (3.4-fold) and ovarian endometrioid cancer (2.3-fold), in women with endometriosis compared to those without endometriosis, with the degree of risk potentially driven by those with an endometrioma, although the exclusion of risk for other endometriosis phenotypes could not be determined. A summary relative risk was also documented with thyroid cancer (SRR 1.39, 95% CI 1.24–1.57; $n = 5$ studies) and breast cancer (SRR 1.04, 95% CI 1.00–1.09; $n = 20$ studies) [62].

A systematic review evaluating the potential risks of conservative management in women with a known endometrioma undergoing IVF concluded that there was insufficient evidence on the risks of reduced ovarian responsiveness and reduced oocyte competence [41]. Furthermore, surgery for an endometrioma may potentially reduce ovarian reserve, as evidenced by a decrease in the AMH levels [36] and subsequent responsiveness to gonadotrophin stimulation [63].

While the risk of technical difficulties during oocyte retrieval is low, based on limited reports, there are no data to suggest that surgery for an endometrioma will prevent adhesion reformation and facilitate oocyte retrieval effectively. While the available data exclude a clinically relevant effect of IVF on progression of pelvic endometriosis and ovarian endometriomas [64], the risks of infection from an endometrioma (0%–1.9%) and follicular fluid contamination (2.8%–6.1%) are very small, and do not justify surgery for the presence of an endometrioma before IVF treatment. It must be acknowledged that there are difficulties in being able to conduct a randomised controlled trial to answer this fully, with no clear comparator group available for observational studies.

The ESHRE guideline discusses the importance of providing appropriate counselling to women about the risk of reduced ovarian function following surgical intervention and even the possible risk of an oophorectomy [29]. The decision to proceed with surgery for an endometrioma should be carefully considered, including the various prognostic factors that can influence the success of an ART cycle, such as age, ovarian reserve status, unilaterality or bilaterality of the disease, number and size of

the cysts, symptoms, presence or absence of suspicious radiological features, extent of extraovarian disease and history of previous ovarian surgery [65]. Asymptomatic women, those of advanced reproductive age, with reduced ovarian reserve, bilateral endometriomas or a history of prior ovarian surgery may benefit from proceeding directly with IVF treatment, as surgery may further compromise ovarian function and delay the start of treatment. Surgery may be considered as the first-line treatment in highly symptomatic women and people, those with an intact ovarian reserve, unilateral and large cysts, and should be considered for cysts with suspicious radiological and clinical features. Endometriomas may be associated with extraovarian disease, including bowel involvement and deep endometriosis. Reproductive outcomes have not been shown to be improved by the excision of deep endometriosis in randomised trials, with surgical excision of endometriotic nodules providing symptomatic benefit albeit potentially exposing the woman or person to significant surgical risks, for which appropriate counselling should be given [27].

4 | Fertility Preservation in the Presence of Endometriosis

Fertility preservation in the context of a cancer-related diagnosis or treatment that is likely to render women infertile is well established. Recent advancements in the field have seen fertility preservation using ovarian tissue cryopreservation with now successful pregnancies following orthotopic transplantation in women who have been cured of their disease [66].

Fertility preservation, however, for those with endometriosis is less well explored and discussed. The negative impact of endometriosis on ovarian reserve and the associated subfertility has been greatly discussed. Women with known endometriosis who are not planning to conceive imminently should be offered an early opportunity to discuss reproductive planning.

While AMH has not been shown to be a viable predictor of spontaneous pregnancy [67]; a baseline fertility assessment can be considered to inform this discussion. Discussion regarding the various forms of fertility preservation such as oocyte and embryo cryopreservation should be included [32]. There is increasing awareness and engagement around this issue including some employers offering women the option for early fertility preservation in the context of social oocyte or embryo freezing due to an age-related decline in fertility. Therefore, clinicians treating women with endometriosis will need to allow a pragmatic approach to consider women with this diagnosis to explore this further with an appropriate specialist [68].

5 | Opinion

- Endometriomas are associated with reduced monthly fecundity rates, although a direct causal relationship has not been well established.
- Endometriomas are known to impact the ovarian reserve and as such, women in the reproductive age group considering surgical treatment should have their ovarian reserve parameters assessed before surgery to aid fertility-related discussions.
- The surgical management option of a cystectomy, drainage with adjuvant therapy such as coagulation or sclerotherapy, should be individualised to the woman's circumstances and health requirements.
- Repeated or extensive ovarian surgery can have a detrimental impact on ovarian reserve, and this should be considered when deciding on treatment and specifically, further surgery.
- Surgery may reduce endometriosis-associated pain. The theoretical benefit of performing surgery to improve pelvic anatomy and accessibility is plausible but has not been supported with substantive scientific evidence.
- Surgery can be used as an adjunct to aid fertility treatment when transvaginal access to the ovaries for egg collection is suboptimal and likely to impact the IVF outcome. Surgery performed in this setting would be fertility optimising, with the risk of disease recurrence and persistence remaining.
- Until robust evidence from large randomised controlled trials incorporating modern treatment modalities is available, many uncertainties will remain on the optimal treatment of an endometrioma. Meanwhile, management decisions should be based on individual circumstances, such as patient choice, age, ovarian reserve and associated symptoms.
- Women with endometriosis who are considering fertility-preserving treatment should be offered an opportunity to discuss reproductive planning with a specialist in the field.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

References

1. H. S. Taylor, A. M. Kotlyar, and V. A. Flores, "Endometriosis Is a Chronic Systemic Disease: Clinical Challenges and Novel Innovations," *Lancet* 397, no. 10276 (2021): 839–852.

2. International Working Group of AAGL, ESGE, ESHRE and WES, C. Tomassetti, N. Johnson, et al., "An International Terminology for Endometriosis," *Minimally Invasive Gynecology* 28 (2021): 1849–1859.

3. A. Boucher, G. Brichant, V. Gridelet, et al., "Implantation Failure in Endometriosis Patients: Etiopathogenesis," *Journal of Clinical Medicine* 11 (2022): 5366.

4. T. Dalsgaard, M. V. H. Hansen, D. Hartwell, and Ø. Lidegaard, "Reproductive Prognosis in Daughters of Women With and Without Endometriosis," *Human Reproduction* 28 (2013): 2284–2288.

5. D. B. Redwine, "Ovarian Endometriosis: A Marker for More Extensive Pelvic and Intestinal Disease," *Fertility and Sterility* 72, no. 2 (1999): 310–315.

6. D. L. Olive and A. F. Haney, "Endometriosis-Associated Infertility: A Critical Review of Therapeutic Approaches," *Obstetrical & Gynecological Survey* 41, no. 9 (1986): 538–555.

7. L. C. Giudice, "Clinical Practice. Endometriosis," *New England Journal of Medicine* 362, no. 25 (2010): 2389–2398.

8. J. Scurry, J. Whitehead, and M. Healey, "Classification of Ovarian Endometriotic Cysts," *International Journal of Gynecological Pathology* 20, no. 2 (2001): 147–154.

9. C. Ünlü and G. Yıldırım, "Ovarian Cystectomy in Endometriomas: Combined Approach," *Journal of the Turkish-German Gynecological Association* 15 (2014): 177–189.

10. The Practice Committee of the American Society for Reproductive Medicine, "Endometriosis and Infertility: A Committee Opinion," *Fertility and Sterility* 98, no. 3 (2012): 591–598.

11. American Society for Reproductive Medicine, "Revised American Society for Reproductive Medicine Classification of Endometriosis: 1996," *Fertility and Sterility* 67, no. 5 (1997): 817–821, https://doi.org/10.1016/S0015-0282(97)81391-X.

12. S. E. Bulun, "Endometriosis," *New England Journal of Medicine* 360, no. 3 (2009): 268–279.

13. I. P. Ryan, J. F. Tseng, E. D. Schriock, O. Khorram, D. V. Landers, and R. N. Taylor, "Interleukin-8 Concentrations Are Elevated in Peritoneal Fluid of Women With Endometriosis," *Fertility and Sterility* 63, no. 4 (1995): 929–932.

14. Y. Taketani, T. M. Kuo, and M. Mizuno, "Comparison of Cytokine Levels and Embryo Toxicity in Peritoneal Fluid in Infertile Women With Untreated or Treated Endometriosis," *American Journal of Obstetrics and Gynecology* 167, no. 1 (1992): 265–270.

15. J. Halme, S. Becker, M. G. Hammond, M. H. Raj, and S. Raj, "Increased Activation of Pelvic Macrophages in Infertile Women With Mild Endometriosis," *American Journal of Obstetrics and Gynecology* 145, no. 3 (1983): 333–337.

16. D. de Ziegler, B. Borghese, and C. Chapron, "Endometriosis and Infertility: Pathophysiology and Management," *Lancet* 376, no. 9742 (2010): 730–738.

17. B. A. Lessey and J. J. Kim, "Endometrial Receptivity in the Eutopic Endometrium of Women With Endometriosis: It Is Affected, and Let Me Show You Why," *Fertility and Sterility* 108 (2017): 19–27.

18. Y. Prapas, M. Goudakou, I. Matalliotakis, et al., "History of Endometriosis May Adversely Affect the Outcome in Menopausal Recipients of Sibling Oocytes," *Reproductive Biomedicine Online* 25, no. 5 (2012): 543–548.

19. M. Bourdon, P. Santulli, C. Maignien, et al., "The Deferred Embryo Transfer Strategy Improves Cumulative Pregnancy Rates in Endometriosis-Related Infertility: A Retrospective Matched Cohort Study," *PLoS One* 13 (2018): e0194800.

20. J. Wu, X. Yang, J. Huang, Y. Kuang, and Y. Wang, "Fertility and Neonatal Outcomes of Freeze-All vs. Fresh Embryo Transfer in Women With Advanced Endometriosis," *Frontiers in Endocrinology* 10 (2019): 770.

21. N. Garrido, J. Navarro, J. Remohi, C. Simón, and A. Pellicer, "Follicular Hormonal Environment and Embryo Quality in Women With Endometriosis," *Human Reproduction Update* 6, no. 1 (2000): 67–74.

22. A. Pellicer, N. Oliveira, A. Ruiz, J. Remohí, and C. Simón, "Exploring the Mechanism(s) of Endometriosis-Related Infertility: An Analysis of Embryo Development and Implantation in Assisted Reproduction," *Human Reproduction* 10, no. Suppl 2 (1995): 91–97.

23. N. Garrido, J. Navarro, J. Garcia-Velasco, J. Remoh, A. Pellice, and C. Simón, "The Endometrium Versus Embryonic Quality in Endometriosis-Related Infertility," *Human Reproduction Update* 8, no. 1 (2002): 95–103.

24. C. Simón, A. Gutiérrez, A. Vidal, et al., "Outcome of Patients With Endometriosis in Assisted Reproduction: Results From In-Vitro Fertilization and Oocyte Donation," *Human Reproduction* 9 (1994): 725–729.

25. M. Kitajima, K. N. Khan, K. Hiraki, T. Inoue, A. Fujishita, and H. Masuzaki, "Changes in Serum Anti-Müllerian Hormone Levels May Predict Damage to Residual Normal Ovarian Tissue After Laparoscopic Surgery for Women With Ovarian Endometrioma," *Fertility and Sterility* 95, no. 8 (2011): 2589–2591.

26. A. M. Sanchez, P. Viganò, E. Somigliana, P. Panina-Bordignon, P. Vercellini, and M. Candiani, "The Distinguishing Cellular and Molecular Features of the Endometriotic Ovarian Cyst: From Pathophysiology to the Potential Endometrioma-Mediated Damage to the Ovary," *Human Reproduction Update* 20, no. 2 (2014): 217–230.

27. E. Somigliana, P. Viganò, F. Filippi, et al., "Fertility Preservation in Women With Endometriosis: For All, for Some, for None?," *Human Reproduction* 30, no. 6 (2015): 1280–1286.

28. G. A. Dunselman, N. Vermeulen, C. Becker, et al., "ESHRE Guideline: Management of Women With Endometriosis," *Human Reproduction* 29, no. 3 (2014): 400–412.

29. C. M. Becker, A. Bokor, O. Heikinheimo, et al., "ESHRE Guideline: Endometriosis," *Human Reproduction Open* 2022, no. 2 (2022): hoac009.

30. U. Leone Roberti Maggiore, C. Scala, P. L. Venturini, V. Remorgida, and S. Ferrero, "Endometriotic Ovarian Cysts Do Not Negatively Affect the Rate of Spontaneous Ovulation," *Human Reproduction* 30, no. 2 (2015): 299–307.

31. L. Benaglia, E. Somigliana, P. Vercellini, A. Abbiati, G. Ragni, and L. Fedele, "Endometriotic Ovarian Cysts Negatively Affect the Rate of Spontaneous Ovulation," *Human Reproduction* 24, no. 9 (2009): 2183–2186.

32. P. A. Romanski, P. Bortoletto, Z. Rosenwaks, and G. L. Schattman, "Delay in IVF Treatment up to 180 Days Does Not Affect Pregnancy Outcomes in Women With Diminished Ovarian Reserve," *Human Reproduction* 35, no. 7 (2020): 1630–1636.

33. C. Bafort, Y. Beebeejaun, C. Tomassetti, J. Bosteels, and J. M. Duffy, "Laparoscopic Surgery for Endometriosis," *Cochrane Database of Systematic Reviews* 10 (2020): CD011031.

34. E. Somigliana, L. Benaglia, P. Vigano, M. Candiani, P. Vercellini, and L. Fedele, "Surgical Measures for Endometriosis-Related Infertility: A Plea for Research," *Placenta* 32, no. Suppl 3 (2011): S238–S242.

35. W. Hirokawa, A. Iwase, M. Goto, et al., "The Post-Operative Decline in Serum Anti-Mullerian Hormone Correlates With the Bilaterality and Severity of Endometriosis," *Human Reproduction* 26, no. 4 (2011): 904–910.

36. F. Raffi, M. Metwally, and S. Amer, "The Impact of Excision of Ovarian Endometrioma on Ovarian Reserve: A Systematic Review and Meta-Analysis," *Journal of Clinical Endocrinology and Metabolism* 97, no. 9 (2012): 3146–3154.

37. R. J. Hart, M. Hickey, P. Maouris, and W. Buckett, "Excisional Surgery Versus Ablative Surgery for Ovarian Endometriomata," *Cochrane Database of Systematic Reviews* , no. 2 (2008): CD004992.

38. S. Alborzi, Z. Zahiri Sorouri, E. Askari, T. Poordast, and K. Chamanara, "The Success of Various Endometrioma Treatments in Infertility: A Systematic Review and Meta-Analysis of Prospective Studies," *Reproductive Medicine and Biology* 18, no. 4 (2019): 312–322.

39. M. Candiani, S. Ferrari, L. Bartiromo, M. Schimberni, I. Tandoi, and J. Ottolina, "Fertility Outcome After Co_2 Laser Vaporization Versus Cystectomy in Women With Ovarian Endometrioma: A Comparative Study," *Journal of Minimally Invasive Gynecology* 28, no. 1 (2021): 34–41.

40. K. Barnhart, R. Dunsmoor-Su, and C. Coutifaris, "Effect of Endometriosis on In Vitro Fertilization," *Fertility and Sterility* 77, no. 6 (2002): 1148–1155.

41. E. Somigliana, L. Benaglia, A. Paffoni, A. Busnelli, P. Vigano, and P. Vercellini, "Risks of Conservative Management in Women With Ovarian Endometriomas Undergoing IVF," *Human Reproduction Update* 21, no. 4 (2015): 486–499.

42. Y. E. Sukur, B. Ozmen, B. Yakistiran, et al., "Endometrioma Surgery Is Associated With Increased Risk of Subsequent Assisted Reproductive Technology Cycle Cancellation; a Retrospective Cohort Study," *Journal of Obstetrics and Gynaecology* 41, no. 2 (2021): 259–262.

43. M. Hamdan, S. Z. Omar, G. Dunselman, and Y. Cheong, "Influence of Endometriosis on Assisted Reproductive Technology Outcomes: A Systematic Review and Meta-Analysis," *Obstetrics and Gynecology* 125, no. 1 (2015): 79–88.

44. M. E. Coccia, F. Rizzello, S. Barone, et al., "Is There a Critical Endometrioma Size Associated With Reduced Ovarian Responsiveness in Assisted Reproduction Techniques?," *Reproductive Biomedicine Online* 29, no. 2 (2014): 259–266.

45. I. Esinler, G. Bozdag, I. Arikan, B. Demir, and H. Yarali, "Endometrioma </=3 cm in Diameter Per Se Does Not Affect Ovarian Reserve in Intracytoplasmic Sperm Injection Cycles," *Gynecologic and Obstetric Investigation* 74, no. 4 (2012): 261–264.

46. E. Somigliana, N. Berlanda, L. Benaglia, P. Viganò, P. Vercellini, and L. Fedele, "Surgical Excision of Endometriomas and Ovarian Reserve: A Systematic Review on Serum Antimullerian Hormone Level Modifications," *Fertility and Sterility* 98, no. 6 (2012): 1531–1538.

47. S. M. Alshehre, B. F. Narice, M. A. Fenwick, and M. Metwally, "The Impact of Endometrioma on In Vitro Fertilisation/Intra-Cytoplasmic Injection IVF/ICSI Reproductive Outcomes: A Systematic Review and Meta-Analysis," *Archives of Gynecology and Obstetrics* 303, no. 1 (2021): 3–16.

48. L. Benaglia, E. Somigliana, R. Iemmello, E. Colpi, A. E. Nicolosi, and G. Ragni, "Endometrioma and Oocyte Retrieval-Induced Pelvic Abscess: A Clinical Concern or an Exceptional Complication?," *Fertility and Sterility* 89, no. 5 (2008): 1263–1266.

49. P. Drakopoulos, J. Rosetti, N. Pluchino, et al., "Does the Type of GnRH Analogue Used, Affect Live Birth Rates in Women With Endometriosis Undergoing IVF/ICSI Treatment, According to the rAFS Stage?," *Gynecological Endocrinology* 34, no. 10 (2018): 884–889.

50. C. P. Biacchiardi, L. D. Piane, M. Camanni, et al., "Laparoscopic Stripping of Endometriomas Negatively Affects Ovarian Follicular Reserve Even if Performed by Experienced Surgeons," *Reproductive Biomedicine Online* 23, no. 6 (2011): 740–746.

51. G. Uncu, I. Kasapoglu, K. Ozerkan, A. Seyhan, A. O. Yilmaztepe, and B. Ata, "Prospective Assessment of the Impact of Endometriomas and Their Removal on Ovarian Reserve and Determinants of the Rate of Decline in Ovarian Reserve," *Human Reproduction* 28, no. 8 (2013): 2140–2145.

52. C. Simon, A. Gutierrez, A. Vidal, et al., "Outcome of Patients With Endometriosis in Assisted Reproduction: Results From In-Vitro Fertilization and Oocyte Donation," *Human Reproduction* 9, no. 4 (1994): 725–729.

53. T. A. Gelbaya, S. Gordts, T. M. D'Hooghe, M. Gergolet, and L. G. Nardo, "Management of Endometrioma Prior to IVF: Compliance With ESHRE Guidelines," *Reproductive Biomedicine Online* 21, no. 3 (2010): 325–330.

54. M. Nickkho-Amiry, R. Savant, K. Majumder, E. Edi-O'sagie, and M. Akhtar, "The Effect of Surgical Management of Endometrioma on the IVF/ICSI Outcomes When Compared With no Treatment? A Systematic Review and Meta-Analysis," *Archives of Gynecology and Obstetrics* 297, no. 4 (2018): 1043–1057.

55. L. Benschop, C. Farquhar, N. van der Poel, and M. J. Heineman, "Interventions for Women With Endometrioma Prior to Assisted Reproductive Technology," *Cochrane Database of Systematic Reviews* , no. 11 (2010): CD008571.

56. L. Miquel, L. Preaubert, A. Gnisci, et al., "Transvaginal Ethanol Sclerotherapy for an Endometrioma in 10 Steps," *Fertility and Sterility* 115, no. 1 (2021): 259–260.

57. A. Cohen, B. Almog, and T. Tulandi, "Sclerotherapy in the Management of Ovarian Endometrioma: Systematic Review and Meta-Analysis," *Fertility and Sterility* 108, no. 1 (2017): 117–124.

58. L. Miquel, L. Preaubert, A. Gnisci, et al., "Endometrioma Ethanol Sclerotherapy Could Increase IVF Live Birth Rate in Women With Moderate-Severe Endometriosis," *PLoS One* 15, no. 9 (2020): e0239846.

59. K. Skorupskaite, M. Hardy, H. Bhandari, E. Yasmin, W. Saab, and S. Seshadri, "Evidence Based Management of Patients With Endometriosis Undergoing Assisted Conception: British Fertility Society Policy and Practice Recommendations," *Human Fertility* 27, no. 1 (2024): 2288634, https://doi.org/10.1080/14647273.2023.2288634.

60. L. Muzii, C. Achilli, F. Lecce, et al., "Second Surgery for Recurrent Endometriomas Is More Harmful to Healthy Ovarian Tissue and Ovarian Reserve Than First Surgery," *Fertility and Sterility* 103, no. 3 (2015): 738–743.

61. J. S. Younis, N. Shapso, R. Fleming, I. Ben-Shlomo, and I. Izhaki, "Impact of Unilateral Versus Bilateral Ovarian Endometriotic Cystectomy on Ovarian Reserve: A Systematic Review and Meta-Analysis," *Human Reproduction Update* 25, no. 3 (2019): 375–391.

62. M. Kvaskoff, Y. Mahamat-Saleh, L. V. Farland, et al., "Endometriosis and Cancer: A Systematic Review and Meta-Analysis," *Human Reproduction Update* 27, no. 2 (2021): 393–420.

63. E. Somigliana, M. Arnoldi, L. Benaglia, R. Iemmello, A. E. Nicolosi, and G. Ragni, "IVF-ICSI Outcome in Women Operated on for Bilateral Endometriomas," *Human Reproduction* 23, no. 7 (2008): 1526–1530.

64. E. Somigliana, P. Vigano, L. Benaglia, A. Busnelli, A. Paffoni, and P. Vercellini, "Ovarian Stimulation and Endometriosis Progression or Recurrence: A Systematic Review," *Reproductive Biomedicine Online* 38, no. 2 (2019): 185–194.

65. S. Alborzi, P. Keramati, M. Younesi, A. Samsami, and N. Dadras, "The Impact of Laparoscopic Cystectomy on Ovarian Reserve in Patients With Unilateral and Bilateral Endometriomas," *Fertility and Sterility* 101, no. 2 (2014): 427–434.

66. M. M. Dolmans, M. von Wolff, C. Poirot, et al., "Transplantation of Cryopreserved Ovarian Tissue in a Series of 285 Women: A Review of Five Leading European Centers," *Fertility and Sterility* 115 (2021): 1102–1115.

67. A. Z. Steiner, D. Pritchard, F. Z. Stanczyk, et al., "Association Between Biomarkers of Ovarian Reserve and Infertility Among Older Women of Reproductive Age," *JAMA* 318 (2017): 1367–1376.

68. S. Latif, E. Saridogan, and E. Yasmin, "FOR: Fertility Preservation for Women With Ovarian Endometriosis: It Is Time to Adopt It as Routine Practice," *British Journal of Obstetrics and Gynaecology* 129 (2022): 1935–1936.

This Scientific Impact Paper was produced on behalf of the Royal College of Obstetricians and Gynaecologists by: **Dr PR Supramaniam MRCOG, Oxford; Dr M Mittal MRCOG, London; Dr C Becker, Nuffield Department of Obstetrics and Gynaecology, University of Oxford; and Dr K Jayaprakasan FRCOG, Derby**.

The following individuals submitted comments at peer review: Dr. M Benjamin, Sussex; Dr. R Hughes FRCOG, Edinburgh; M Madhra, MRCOG, Edinburgh; Professor L Rombauts, FRANZCOG, Melbourne Australia; Dr. E Tsakos FRCOG, Thessaloniki, Greece

The Scientific Advisory Committee lead reviewers were Miss L Webber MRCOG, Singapore; Dr. J Rafi MRCOG, Ipswich; Professor S Quenby MRCOG, Warwickshire
The chair of the Scientific Advisory Committee was Professor K Morris, FRCOG Birmingham. The Vice Chairs were Dr. V Bills, MRCOG and Dr. S Sawan, FRCOG
All RCOG guidance developers are asked to declare any conflicts of interest. A statement summarising any conflicts of interest for this Scientific Impact Paper is available from: rcog.org.uk/sip55.
The final version is the responsibility of the Scientific Advisory Committee of the RCOG.

The guideline will be considered for update 3 years after publication, with an intermediate assessment of the need to update 2 years after publication.

Interested in CPD credits? You can answer CPD questions on this paper at the RCOG CPD ePortfolio.