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# Infertility management in patients with bowel endometriosis: the current landscape and the promise of randomised trials: a narrative review

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#### **ABSTRACT**

The management of infertility in women with bowel endometriosis remains a significant clinical challenge. The two primary therapeutic approaches include first-line medically assisted reproduction (MAR) and primary bowel surgery, with or without subsequent fertility treatments. While surgery can significantly improve fertility outcomes, the success of these interventions is influenced by several factors, and MAR may still be necessary for certain patients, especially those over 35 years or with complex disease patterns. In this narrative review, we assessed the outcomes of the main therapeutic strategies commonly offered to patients with bowel endometriosis-associated infertility and discussed the challenges inherent in evaluating reproductive outcomes in women with colorectal endometriosis.

Keywords: Bowel endometriosis, colorectal endometriosis, infertility, pregnancy rates, reproduction

#### Introduction

Bowel endometriosis affects approximately 8-12% of patients with deep endometriosis (DE) and is associated with severe pain and infertility. 1,2 Although medical therapies can alleviate pain in symptomatic patients, they are not suitable for patients seeking to conceive due to their contraceptive effects.3 Thus, treatment must be individualised based on symptom severity and reproductive goals.

Several mechanisms have been proposed to explain endometriosis-associated infertility, includina distorted pelvic anatomy, abnormal utero-tubal transport, immunological and peritoneal alterations, poor oocyte/embryo quality, impaired implantation,4 and reduced frequency of sexual intercourse due to dyspareunia.5

However, the mechanisms contributing to subfertility in patients with bowel DE remain poorly understood

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and seem related to the inflammatory environment produced by endometriotic nodules<sup>6,7</sup> and the presence of posterior cul-de-sac obliteration.<sup>8</sup> Nevertheless, the usual coexistence of bowel endometriosis with other infertility factors such as endometriomas, hydrosalpinx, and adenomyosis complicates the attribution of subfertility to bowel lesions alone.

To date, the management of infertility in women with bowel endometriosis remains a significant clinical challenge. The two primary therapeutic approaches include first-line medically assisted reproduction (MAR) and primary surgical intervention, which may involve intestinal procedures.

Since patients with untreated colorectal endometriosis achieve similar fertility outcomes after *in vitro* fertilisation (IVF) compared with those without endometriosis, infertile patients with minimal pain are typically advised to pursue MAR first to avoid surgical risks. On the other hand, for patients with severe symptoms, the predominant indication of surgical resection is the severity of pain.

Long-term benefits of laparoscopic resection of bowel endometriosis in relieving pelvic pain, improving bowel function, and enhancing quality of life (QoL) are well established; 8,10,11 however, its role in enhancing fertility remains uncertain. Observational data suggest that surgery may boost spontaneous conception and MAR success rates, 12-15, but no randomised trials have addressed this specifically.

This review evaluates fertility outcomes after different treatment options in patients with bowel DE, highlighting challenges in measuring reproductive efficacy in this population.

### Methods

#### Search Strategy

We conducted a narrative review of studies published between January 2009 and March 2025 in multiple databases, including PubMed, Google Scholar, Scielo, and ClinicalTrials.gov, to identify articles related to fertility and colorectal endometriosis. Only studies published in English, French, or Spanish were included.

Medical Subject Headings terms used included "colorectal endometriosis," "bowel endometriosis," and "intestinal endometriosis," in combination with "fertility," "infertility," "pregnancy rate (PR)," "live birth rate, (LBR)"

"in vitro fertilization (IVF)," "intracytoplasmic sperm injection (ICSI)," "assisted reproductive technology (ART)," "medically assisted reproduction (MAR)," and "intrauterine insemination (IUI)." The references of included studies were also screened to identify additional relevant publications.

#### **Definitions**

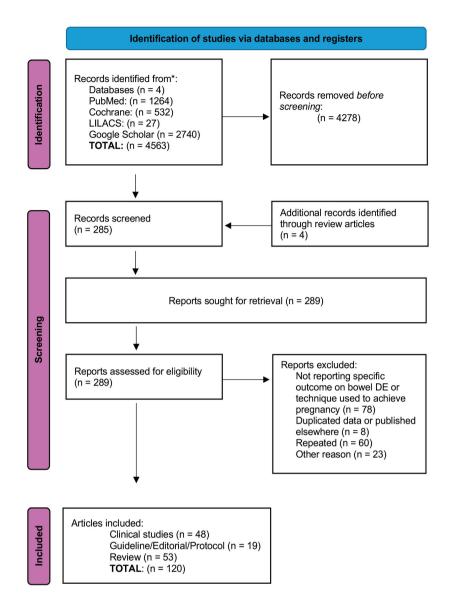
Definitions and outcomes were classified according to the 2017 International Glossary on Infertility and Fertility Care.<sup>4</sup> "Infertility" was defined as the failure to achieve a clinical pregnancy after ≥1 year of regular, unprotected intercourse. The term "MAR" comprised ART (e.g., IVF, ICSI) and IUI, while "ART" refers exclusively to procedures involving the *in vitro* gamete handling (e.g., IVF and IVF ± ICSI).

Surgical procedures for bowel endometriosis were defined based on the updated terminology proposed in the International Endometriosis Terminology. <sup>16</sup> "Shaving" refers to a partial-thickness excision without entry into the bowel lumen. "Discoid excision" indicated a full-thickness resection of the bowel wall with lumen entry. "Bowel resection" involved the removal of a bowel segment followed by re-anastomosis. Surgical complications were graded using the Clavien–Dindo classification. <sup>17</sup>

#### **Study Selection**

We considered observational, randomised, and review articles reporting reproductive outcomes in women with documented bowel DE who desired pregnancy (with or without proven infertility). Surgical videos and case reports were excluded. Both spontaneous and MAR-related outcomes were considered. Surgical techniques and patient fertility histories were also analysed. For review articles, methodological quality was assessed using the scale for the Assessment of Narrative Review Articles criteria (Supplementary Table 1).<sup>18</sup>

The following data were extracted from the included studies and entered into a datasheet: study characteristics (author, year of publication, study design, and whether data were collected prospectively or retrospectively), patient characteristics (definition of the included population and the total number of women initially included in the study), fertility outcomes [i.e., cumulative PR (CPR)] and the techniques used to achieve the pregnancies (spontaneous or MAR). Figure 1 depicts the review flow chart.



**Figure 1.** Flowchart for study selection reported in three studies. DE: Deep endometriosis.

## Optimising Fertility Outcomes in Women with Deep Endometriosis Affecting the Bowel

There are many challenges in understanding the best treatment options for patients desiring fertility affected by DE of the bowel. This is because assessing fertility outcomes in patients with bowel endometriosis is hindered by multiple confounding factors (Table 1).

# Spontaneous Conception in Patients with Untreated Colorectal Endometriosis

In comparison to the fecundity rate of 15% to 20% per month in healthy couples, the spontaneous PR (SPR) in patients with untreated endometriosis is notably lower (2%-10%).<sup>19</sup> Although previous studies have estimated SPR in patients with DE,<sup>20,21,</sup> these studies did not specifically focus on those with colorectal involvement.

To date, there is very limited data on spontaneous fertility outcomes in patients with untreated intestinal DE lesions (*in situ*) (Table 2). <sup>8,22,23</sup> However, the presence of intestinal endometriosis has been associated with the lowest fertility rates (0.84% per month) and the longest time to conception among infertile patients attempting natural conception. <sup>8</sup> Notably, Ferrero et al. <sup>22</sup> reported a 38.9% spontaneous conception rate in women with untreated colorectal endometriosis, following proper patient selection for those with a good reproductive prognosis.

Given that most spontaneous pregnancies in patients with untreated colorectal endometriosis occur in those under 35 years of age and within the first year of trying to conceive, <sup>21,23</sup> expectant management could be considered as an initial approach for a limited period (6-12 months). In our opinion, this approach may be offered to younger patients (<35 years) with an adequate ovarian reserve (Anti Mullerian Hormone serum level >2 ng/mL), patent tubes, no evidence of adenomyosis, and normal semen analysis. In other cases, expectant management is discouraged.

## Fertility Outcomes After "Medically Assisted Reproduction First" Approach in Patients with In Situ Colorectal Endometriosis

Current guidelines recommend that surgery should not be performed before ART in patients with colorectal endometriosis, with the primary goal of improving fertility.<sup>24</sup> As a result, primary MAR is often the first-line treatment for infertile women with bowel endometriosis who experience little or no pain. Several reasons support this approach:

Table 1. Confounders influencing the	interpretation of studies on fertility outcomes in patients with bowel endometrios is.
Possible confounders	Explanation
Comorbidity of endometriosis	Bowel DE often coexists with other forms of endometriosis and infertility factors like tubal occlusion, hydrosalpinx, pelvic adhesions, endometriomas, and adenomyosis, complicating attribution of fertility outcomes to bowel lesions alone.
Surgical goals and challenges	The primary aim of DE surgery is the radical excision of all lesions, including bowel nodules, while preserving reproductive function. As such, evaluating the specific impact of removing specific endometriotic lesions on fertility outcomes is inherently tricky.
Patient populations	Many studies do not distinguish between women with proven infertility and those simply wishing to conceive.
Surgical heterogeneity	Variability in techniques - shaving, discoid excision, segmental resection - makes comparisons difficult. Most data emphasise pain relief and functional outcomes over fertility metrics.
Inconsistent definitions and reporting	Definition of pregnancy, reporting of conception methods and time to pregnancy metrics vary widely.
Terminology and reporting variability	Inconsistent use of terms like ART and MAR and a lack of consensus on cumulative live birth definitions further complicate data synthesis.
Unclear surgical classifications	Terms like "deep shaving" or "partial-thickness excision" lack standardisation across studies, hindering reproducibility.
Lack of randomised trials	Most available studies are observational and heterogeneous, precluding strong recommendations for surgery or MAR as first-line treatment.
DE: Deep endometriosis, ART: Assisted repro	ductive technology, MAR: Medically assisted reproduction.

**Table 2.** Spontaneous pregnancy in patients desiring pregnancy reported in three studies with untreated (*in situ*) colorectal endometriosis (with or without documented infertility).

Author (year) (ref)	Study design	Intervention	n	Patients wishing to conceive	Infertility diagnosis	Mean follow-up (range)	Spontaneous pregnancy rate	Mean time to pregnancy	Live- birth rate
Ferrero et al. (2021) <sup>22</sup>	Retrospective	No surgery expectant management	215	167	NR	31 months (13-63)	65/167 * (38.9%)	10 months (2-34)	62/167 (37.1%)
Acién et al. (2013) <sup>23</sup>	Retrospective	Removal of non-bowel DE lesions	10	10	NR	7 years (1-23)	6 /10 * (60%)	NR	NR
Stepniewska et al. (2009) <sup>8</sup>	Prospective	Removal of non-bowel DE lesions	40	39	40	26.9 months	7/23 * (30.4%)	NR	6/23 (26.1%)
*Patients who a	attempted to conc	eive naturally. DE:	Deen e	ndometriosis N	IR: Not reporte	24			

- 1) Avoidance of surgical risks, such as anastomotic leakage, pelvic abscesses, rectovaginal fistula formation, neurogenic bladder/bowel dysfunction, and anastomosis stenosis, without strong evidence supporting the role of surgery in improving reproductive outcomes.<sup>25</sup>
- 2) Patients with untreated colorectal endometriosis achieve similar fertility outcomes after IVF compared with non-endometriosis patients. In addition, first-line ART offers favourable CPR and cumulative LBR (CLBR). A large retrospective study, spanning 12 years, compared IVF-ICSI outcomes between 120 patients with bowel DE undergoing primary ART and 69 patients managed surgically. No significant differences in CPR (56.7% vs. 58%, *P*=0.47) and CLBR (50.8% vs. 52.2%, *P*=0.43) were found. The authors concluded that IVF-ICSI outcomes were similar regardless of prior surgical intervention, suggesting no additional benefit from surgery in these patients. 26
- 3) Impact of uterine adenomyosis: The prevalence of adenomyosis in patients with bowel endometriosis ranges from 17% to 88%. 15,27-29 A systematic review identified adenomyosis as a strong predictor of reproductive failure in patients with colorectal endometriosis undergoing surgery, 27 suggesting that adenomyosis may play a more significant role in infertility than the intestinal endometriotic lesions themselves. Since adenomyosis is not corrected surgically, the role of bowel surgery in asymptomatic patients solely to improve fertility may be overestimated.
- 4) Quality of evidence: Most available data on the impact of bowel surgery on fertility outcomes in infertile women with colorectal endometriosis come from uncontrolled cohorts where fertility was a secondary outcome. Given that non-randomised studies often report larger treatment effects than randomised controlled trials (RCTs), and cohort studies are prone to bias, the actual impact of bowel surgery on fertility may be overestimated.<sup>25</sup>

We identified eight studies<sup>8,9,22,23,26,28-30</sup> involving 363 women with documented colorectal endometriosis and pregnancy intention undergoing primary MAR without prior bowel surgery (Table 3). Among these women, 170 became pregnant, resulting in a PR of 46.8 %. Time to pregnancy after MAR was reported in two studies<sup>8,22</sup>

and was considerably longer than the time reported for patients who conceived naturally.

Prognostic factors impacting reproductive outcomes in patients with bowel endometriosis undergoing first-line fertility treatments.

### Adenomyosis

In a prospective multicentre study involving 75 patients with *in situ* colorectal endometriosis, Ballester et al.<sup>28</sup> demonstrated that CPR were significantly lower after IVF-ICSI in women with concomitant adenomyosis (19%) compared to those with a healthy uterus (82.4%) (*P*=0.01). However, the detrimental impact of adenomyosis was not observed in a larger prospective study involving 89 patients with documented adenomyosis undergoing primary IVF.<sup>29</sup>

### History of Prior Surgery for Deep Endometriosis

Prior observational studies have suggested that a history of surgery for endometriosis negatively affects ART outcomes in patients with DE. $^{5,29,31}$  However, only two studies have specifically evaluated this effect in patients with bowel endometriosis. One study found no association between prior surgery for DE and worse IVF outcomes, $^8$  while another study reported significantly lower LBR for patients with a history of endometriosis surgery compared to those without prior surgery (64.4% vs. 41.3%, respectively; P=0.009). $^{29}$  Despite surgery may impair ovarian reserve and reduce IVF.

#### Diminished Ovarian Reserve

Low ovarian reserve, as indicated by low AMH levels (<2 ng/mL) and an antral follicle count <10, has been identified as an independent negative predictive factor for ART success in patients with *in situ* bowel endometriosis. <sup>28,29</sup> In these studies, low ovarian reserve parameters were associated with a significantly lower CPR (P=0.02)<sup>28</sup> and lower LBR (P=0.001). <sup>29</sup> However, it is noteworthy that the authors included in their analysis patients with and without concomitant endometrioma.

#### **Other Factors**

Other prognostic factors have been inconsistently associated with worse reproductive outcomes in patients with bowel endometriosis undergoing ART, including age over 35 years<sup>28</sup> and a duration of infertility exceeding 30 months.<sup>29</sup>

Table 3. Fertility outcomes after primary medically assisted reproduction in patients reported in eight studies with untreated (in situ) colorectal endometriosis (with or without documented infertility).

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Author (year) (Ref)	Study design	Study design Intervention	u	Infertility diagnosis	Mean follow- up	IUI pregnancy (%)	IVF-ICSI pregnancies (%)	MAR pregnancy rate	Mean time to pregnancy	Live-birth rate	Associated adenomyosis	Prior history of surgery for endometriosis
Ferrero et al. (2021) <sup>22</sup>	Retrospective	No surgery expectant management	83	Z Z	31 months (13-63)	9/32 (28%)	29/68 (42.6%) (51 directly and 17 after IUI failure)	42.6% (IVF) (CPR after 3 cycles) 28% (IUI)	17 months (4-37)	27/68 (39.7%) (CLBR after 3 IVF cycles) 8/32 (25%) (IUI)	Z Z	Z.
Acién et al. (2013) <sup>23</sup>	Retrospective	Removal of non-bowel DE lesions	10	Z Z	7 years (1-23)	1	1/4 (25%)	25%	N. N.	1/4 (25%)	<u>~</u> Z	4.3%
Stepniewska et al. (2009) <sup>8</sup>	Prospective	Removal of non-bowel DE lesions	40	40	26.9 months	6/3	1/13 (7.7%)	7.7%	1417 days	1/13 (7.7%)	Z	53%
Mathieu d`Argent et al. (2010)°	Retrospective	No surgery first-line ART	29	29	Z R	I	12/29 (41%)	41% (CPR after 1 cycle)	NR	8/29 (27.6% after 1 cycle)	Z	NR
Ballester et al. (2012) <sup>28</sup>	Prospective	No surgery first-line ART	75	75	I	I	32/75 (42.7%)	68.6% (CPR after 3 cycles)	NR	24/75 (32% after 3 cycles)	21 (28%)	74.7%
Rubod et al. (2024) <sup>26</sup>	Retrospective	No surgery first-line ART	120	120	N R	I	W Z	56.7% (CPR after 4 cycles)	N R	50.8% (CLBR after 4 cycles)	33 (27.5%)	%0
Maignien et al. (2021)™	Prospective	No surgery First-line ART	101	101	N R	I	74/101 (73.3%)	73.3% (CPR after 4 cycles)	NR	64.4% (CLBR after 4 cycles)	89 (88.1%)	%0
Bendifallah et al. (2017) <sup>30</sup>	Retrospective	No surgery first-line ART	55	55	N N	I	12/55 (21.8%)	56.6% (CPR after 3 cycles)	N R	54.9% (CLBR after 3 cycles)	19 (34.5%)	58.2%
CPR: Cumulative	CPR: Cumulative pregnancy rate, CLBR: Cumulative live birth rate, IUI: Intrauterine insemination, IVF: In vitro fertilisation, ICSI: Intracytoplasmic sperm injection, ART: Assisted reproductive technology, NR: Not reported,	LBR: Cumulative liv	ve birth	rate, IUI: Intraute	erine insem	ination, IVF: In v	itro fertilisation, IC	SI: Intracytoplasm	ic sperm injectio	n, ART: Assisted repr	oductive technolog	v. NR: Not reported,

CPR: Cumulative pregnancy rate, CLBR: Cumulative live birth rate, IUI: Intrauterine insemination, IVF: In vitro fertilisation, ICSI: Intracytoplasmic sperm injection, ART: Assisted reproductive technology, NR: Not reported, MAR: Medically assisted reproduction, DE: Deep endometriosis.

## Bowel Endometriosis-Related Complications in Women Undergoing First-Line Medically Assisted Reproduction

Although rare, infertile patients with bowel endometriosis who delay surgery should be informed about the potential complications that may arise after discontinuing hormonal therapies, 32,33 as well as during ovarian stimulation, 22 oocyte retrieval, 34 pregnancy, and even the postpartum period. 35 Theoretically, the resulting hyperestrogenism could stimulate the growth of intestinal nodules, leading to exacerbation of symptoms and even bowel obstruction or perforation. 32,36

The estimated risk of developing occlusive symptoms during primary MAR in patients with bowel endometriosis ranges from 5% to 11.8%,<sup>36,37</sup> and the risk is higher in patients with undiagnosed bowel stenosis (>60%).<sup>37</sup> Consequently, bowel imaging to assess stenosis is strongly recommended before advising patients with bowel DE to prioritise primary MAR.

# Fertility Outcomes After Primary Surgical Resection of Bowel Endometriosis

Observational studies conducted by experienced surgical teams have suggested the beneficial impact of complete resection of bowel DE on reproductive outcomes. In addition to improving the chances of natural pregnancy and LBR, 31,38 surgery may also enhance the MAR success rate, 14,30 while preventing potential complications associated with disease progression during ovarian stimulation. Surgery is also recommended after failed IVF, 39,40 and several studies have reported spontaneous conception following surgery in patients with previously failed IVF. 15,41,42 Studies reporting postoperative reproductive outcomes are summarised in Supplementary Table 2. 43-76

## Determinant Factors of Fertility Outcomes After Surgery in Patients Undergoing Surgical Excision of Bowel Endometriosis

Even though the results published by experienced surgeons may not be fully generalizable to all surgical teams, several key factors must be considered to maximise the chances of reproductive success (either naturally or through MAR) in patients with bowel endometriosis undergoing surgery.

### Surgical Route

A randomised trial comparing fertility outcomes after laparoscopic and open colorectal resection for bowel

endometriosis reported significantly higher SPR in patients who underwent laparoscopic surgery. <sup>41</sup> In another study by the same team, the authors demonstrated that conversion to open surgery negatively impacted PR in patients undergoing colorectal resection for DE. <sup>42</sup> Based on these findings, laparoscopy is considered the gold standard for treating bowel DE in patients wishing to conceive, and the procedure must be carried out in a specialised centre with a multidisciplinary team available.

### Completeness of Surgery

Four studies have evaluated the impact of incomplete surgical resection in infertile women with DE. In one study, patients with documented colorectal endometriosis underwent complete eradication of non-bowel DE lesions, but intestinal nodules were left behind.8 The authors reported both lower spontaneous and ART-induced PR in patients with residual bowel disease compared to those who had complete disease resection. Additionally, patients who underwent incomplete surgery had longer intervals to conception (P<0.05) and lower monthly fecundity rates (P<0.05).8 Similarly, a large retrospective study involving 230 patients with posterior DE compared three groups: complete surgery, incomplete surgery, and no surgery before ART. After logistic regression analysis, the presence of a rectouterine nodule was associated with a significantly lower chance of pregnancy after IVF.77

Other studies have shown no difference in fertility outcomes among patients with DE undergoing postoperative ART, regardless of whether surgery was complete or not. However, these studies included both colorectal and non-colorectal cases and did not specifically analyse fertility outcomes in the subgroup of patients with bowel disease. 31,78,79

Therefore, for patients with colorectal endometriosis, a complete macroscopic resection should be attempted, as it is associated with better fertility outcomes and pain relief compared to incomplete procedures, especially in patients with multiple DE lesions.<sup>31,80</sup>

However, in selected cases, incomplete resection may be justified (e.g., low rectal lesions, nerve supply involvement) to avoid complications. Tentini et al.  $^{31}$  found no significant impact on fertility outcomes (P=0.37) when small retroperitoneal nodules were left in place. Based on these data, the current recommendation is to aim for the complete removal of all macroscopic DE lesions when feasible, maintaining a balance between radical excision and functional preservation.

#### Other Factors

Other prognostic factors have been inconsistently associated with worse postoperative fertility outcomes in patients with bowel endometriosis, like age over 35 years, higher American Society for Reproductive Medicine (ASRM) scores, and the presence of concomitant adenomyosis.<sup>27,30,42</sup>

## The Impact of Bowel Endometriosis Resection on Spontaneous Fertility

To accurately evaluate whether surgery improves fertility in patients with bowel DE, the preferred outcome should be the postoperative SPR. Theoretically, DE excision restores normal anatomy and significantly increases the chance of spontaneous conception, 31,81 enabling patients to avoid ART and minimise associated healthcare costs. However, assessing the impact of bowel DE excision on spontaneous pregnancy is challenging because ART is often indicated immediately after surgery (without allowing time for spontaneous conception to occur). In addition, comparative studies evaluating postoperative spontaneous fertility in patients with DE have not focused on patients with bowel involvement. 21,82

To date, postoperative spontaneous fertility in patients with colorectal endometriosis wishing to conceive (with or without documented infertility) has been evaluated in four systematic reviews. Iversen et al.<sup>83</sup> reported a 21% SPR among 490 patients from three prospective studies, and 49% SPR from four retrospective studies involving 415 women. Daraï et al.<sup>39</sup> reported a 31.4% SPR among 855 patients wishing to conceive from 24 studies published between 1990 and 2015. Cohen et al.<sup>84</sup> reviewed 1320 patients with bowel DE who underwent surgery. They identified 171 spontaneous pregnancies among 597 women, resulting in a SPR of 28.6%.

Recently, a comprehensive review by Daniilidis et al.<sup>85</sup> estimated a 24.9% postoperative SPR in patients with bowel endometriosis. However, this estimate included two studies focusing solely on ART outcomes (which reported 0% spontaneous pregnancies), making the reported SPR potentially inaccurate.

In our study, spontaneous fertility after bowel surgery for DE was reported in 35 studies published from 2009 to the present, involving 2405 patients with pregnancy intention (with or without infertility diagnosis). 12,13,15,41,43-74 We identified 783 spontaneous pregnancies, resulting in a 32.6% SPR. Most available studies were observational and failed to report how many patients underwent

surgery due to pain, infertility, or both. Three RCTs were identified, 41,43,86 though their primary outcomes were not fertility-related.

# Selecting Candidates for Attempting Natural Conception After Surgery

Several factors have been associated with a lower postoperative chance of spontaneous pregnancy in patients with bowel DE, emphasising the importance of patient selection in estimating postoperative reproductive success.<sup>87</sup> These factors should always be considered during perioperative counselling.

### **Preoperative Infertility Diagnosis**

Although satisfactory postoperative SPRs are reported in patients with bowel DE wishing to conceive, when only patients with documented infertility are analysed, the estimated SPR is significantly lower. A systematic review by Vercellini et al.,87 aimed at defining SPR specifically in patients with documented infertility before surgery, reported a mean postoperative SPR of 24% among 510 infertile women with rectovaginal endometriosis from 11 studies. However, this review was not restricted to patients with bowel DE. We identified sixteen studies reporting SPR in patients with colorectal DE according to their preoperative fertility status. Among 824 infertile women undergoing digestive surgery (shaving, disc excision, segmental resection), 190 achieved a spontaneous pregnancy, resulting in an SPR of 23.1% (Table 4). It is important to note that in most studies, limited information is available on the duration of infertility and the coexistence of additional infertility factors other than endometriosis. Indeed, duration of preoperative infertility may be a determining factor of postoperative SPR after colorectal resection for endometriosis.44

#### Age at the Time of Surgery

Patient age has been consistently associated with postoperative SPR in patients with bowel DE. Stepniewska et al.<sup>45</sup> reported a cumulative SPR after laparoscopic segmental resection of 58% for patients younger than 30 years, and 45% for those aged 30-34 years. No pregnancies were achieved in patients older than 35 years. This result aligns with findings from Daraï et al.,<sup>41</sup> who observed no spontaneous pregnancies after colorectal resection in women older than 35 years. Based on these data, IVF may be prioritised for women over 35 years. Since fertility outcomes after IVF in women under 35 years were similar to those of women trying to

conceive naturally,<sup>45</sup> postoperative natural conception should be attempted in young women with normal tubal function and normal semen analysis.

### **Endometriosis Fertility Index**

The Endometriosis Fertility Index (EFI) is a validated tool to predict the likelihood of natural conception after endometriosis surgery.<sup>88</sup> Although the EFI score has been demonstrated to correlate well with the chance of live birth and fertility prognosis after surgical resection of moderate to severe endometriosis (ASRM stage III-IV),<sup>89</sup> it has not been explicitly validated among women with bowel endometriosis. Then, the place of the EFI in the decision-making process after surgery in patients with bowel DE remains to be established.

# Fertility Outcomes According to the Surgical Procedure Performed for Bowel Endometriosis

Postoperative SPR after rectal "shaving" has been evaluated in six retrospective studies. 13,46-50 Among 654 women with pregnancy wishes or proven infertility, 295 spontaneous pregnancies were observed, resulting in a 45.1% SPR. The mean time to pregnancy after surgery was reported in two studies 12,51 and varied from 9.4 to 14 months.

Seven studies, including 348 patients desiring pregnancy (with or without documented infertility), specifically reported fertility outcomes after "disc excision" of colorectal endometriosis. 12,50,52-56 In the entire group, 109 spontaneous pregnancies were observed after surgery, resulting in a 31.3% SPR. Time to pregnancy was reported in three studies, 12,52,55 ranging from 5 to 20.6 months.

"Segmental resection" remains the most widely performed procedure for the surgical treatment of colorectal endometriosis. Fertility outcomes were retrieved from eighteen studies, 41,43,44,46,47,50,52,55,57-66 including 675 patients with pregnancy intention in whom segmental resection was the only technique performed to treat colorectal endometriosis. In the entire group, 207 spontaneous pregnancies were observed after surgery, resulting in a 30.7% SPR.

Total pregnancy rates according to the surgical procedure performed for bowel endometriosis.

Seven studies, 13,14,47,52,55,86,90 and one meta-analysis 91 evaluated postoperative PR (both spontaneous and after MAR) by surgical approach among patients with pregnancy intention.

• Lapointe et al.<sup>13</sup> compared fertility outcomes of patients undergoing shaving with those undergoing

Table 4. Postoperative spontaneous conception in infertile women reported in 16 studies with bowel endometriosis
who wished to conceive (2009 – present) at the end of follow-up

Author (year) (Ref)	Spontaneous pregnancies	Infertile women wishing to conceive	SPR	Mean length of follow-up
Daraï et al. (2011) <sup>41</sup>	3	15	20%	29 months (6-52)
Daraï et al. (2010) <sup>42</sup>	12	39	30.8%	34 months (6-68)
Hezer et al. (2023) <sup>15</sup>	16	60	26.7%	47.2 months
Minelli et al. (2009) <sup>76</sup>	13	113	11.5%	19.6 (6-48)
Meuleman et al. (2011) <sup>61</sup>	8	28	28.6%	27 months (16-40)
Raos et al. (2023) <sup>67</sup>	39	193	20.2%	NR
Hudelist et al. (2023) <sup>52</sup>	15	52	28.8%	42.27±17.59 months
Ferrero et al. (2009) <sup>44</sup>	2	21	9.5%	49.9±21.1 months
Stepniewska et al. (2010) <sup>45</sup>	12	50	24%	19.6 months (6-48)
Hudelist et al. (2018) <sup>55</sup>	26	61	42.6%	NR
Abo et al. (2018) <sup>50</sup>	8	64	12.5%	40 ± 22 months
Neme et al. (2013) <sup>65</sup>	4	6	66.7%	12 months
Jelenc et al. (2012) <sup>72</sup>	8	14	57.1%	NR
Roman et al. (2018) <sup>51</sup>	9	23	39.1%	50-79 months
Dobó et al. (2023) <sup>43</sup>	4	34	11.8%	14 ± 2.6 months
Gordts et al. (2013) <sup>68</sup>	11	51	21.6%	776 ± 465 days
TOTAL	190	824	23.1%	
SPR: Spontaneous pregnancy ra	ate, NR: Not reported.			

digestive resection (discoid or segmental). While there was no difference in the overall PR between groups, spontaneous conception was significantly higher in the resection group than in the shaving group (73.6% vs. 33.3%, *P*=0.0086).

- In a prior prospective study, Ballester et al. 14 assessed fertility outcomes after IVF in infertile women following the complete removal of colorectal endometriosis. A decreased CPR was observed for women who required segmental resection compared to those who underwent shaving or disc excision (P=0.04). Additionally, all patients who underwent more conservative bowel surgery (n=18) became pregnant after two IVF cycles, suggesting that patients requiring shaving or disc excision may be good candidates for first-intention surgery.
- Conversely, Bourdel et al.<sup>47</sup> reported no differences between groups when comparing shaving to segmental resection in terms of fertility. These findings were corroborated by Roman et al.,<sup>86</sup> who reported similar PR in patients undergoing segmental resection compared to those who underwent shaving or disc excision (*P*=0.99) after a 7-year follow-up.
- In a previous study, Hudelist et al.<sup>55</sup> evaluated fertility results as a secondary outcome among 102 patients who underwent segmental resection and 32 women undergoing disc excision. No differences were found between groups. Similar results were obtained in more recent studies.<sup>52,90</sup>
- In a recent systematic review and meta-analysis including 13 studies and 2131 patients with pregnancy information, old colorectal resection was associated with a lower PR compared with the other surgical techniques [35.5% vs. 42.6%, odds ratio (OR): 0.64 (95% confidence interval (CI): 0.52-0.79), P<0.001]. There was a similar result when comparing colorectal resection with shaving [n=952, 17.3% vs. 38.8%, OR: 0.51 (95% CI: 0.36-0.73), P<0.001] and no differences were found when comparing colorectal resection with disc excision [n=432, 29.2% vs. 35.8%, OR: 0.65 (95% CI: 0.37-1.13), P=0.13]. However, when SPR was specifically evaluated, there was no difference between colorectal resection and the other techniques.

Nevertheless, the question of which approach is best for removing bowel DE to improve reproductive outcomes in these women remains difficult to answer. Most of the aforementioned studies used fertility outcome as a secondary result, and the decision to perform one technique over another is largely based on the characteristics of the endometriotic bowel lesions.<sup>1</sup>

# Complications After Surgery and Their Impact on Fertility Outcomes

Although surgical resection of bowel endometriosis exposes patients to serious complications, the impact of such complications (Clavien-Dindo III-IV) on fertility outcomes is not well-defined. Kondo et al. 92 evaluated fertility outcomes in 23 patients who experienced major postoperative complications following DE resection. Although the study was not specifically focused on patients with bowel involvement, overall PR was significantly lower among women who experienced intestinal complications, compared with those who presented urinary complications (33.3% vs. 83.3%, P=0.04).

Specifically, the reproductive outcome of patients who underwent colorectal surgery for bowel endometriosis and experienced severe complications has been reported in four studies. 12,42,50,67 In a recent study by Raos et al.,67 16.6% of patients experienced Clavien-Dindo grade III complications. Notably, the presence of such complications did not affect the chances of pregnancy, time-to-pregnancy, or LBR. These findings align with previous reports on women who developed severe surgical complications after bowel endometriosis resection. 12,42,50 However, the occurrence of postoperative complications was associated with a longer delay in achieving pregnancy. 12,50

Ferrier et al. 93 retrospectively analysed reproductive outcomes in 48 patients who experienced major complications (Clavien-Dindo  $\geq$  grade III) after colorectal surgery for endometriosis. After a median follow-up of 5 years, the CPR was 46%, and the LBR was 29.2%. Although the occurrence of such complications seemed to have little impact on fertility outcomes, a significantly lower CPR was observed in patients who developed septic complications such as deep pelvic abscesses (P=0.04) and anastomotic leakage (P=0.02). Additionally, the median time between surgery and the first pregnancy was longer than that observed in patients without complications.

Hence, surgery should not be avoided due to the risk of complications affecting pregnancy chances. However, efforts should be made to achieve pregnancy during the first postoperative year. For patients experiencing septic complications, rapid ART may be a good option.

# First-line Surgery Followed by Assisted Reproductive Technologies

The potential influence of surgical excision of bowel endometriosis before IVF on fertility outcomes has been evaluated in three studies, <sup>14,26,30</sup> and one systematic review, <sup>94,</sup> providing conflicting results.

Casals et al.<sup>94</sup> reported a benefit of surgery before ART in patients with colorectal endometriosis (OR: 2.43, 95% CI: 1.13-5.52). However, this result was based on a single retrospective study.<sup>30</sup> This study compared the impact of first-line ART versus first-line colorectal surgery followed by ART on fertility outcomes in 110 women with proven infertility and documented bowel DE using propensity score matching analysis to reduce bias. Patients were allocated into two groups: 55 in the first-line IVF arm and 55 in the first-line colorectal surgery arm. The authors reported significantly higher PR (21.8% vs. 49%, P=0.003), CPR (56.6% vs. 79.7%, P=0.037), and CLBR after 3 IVF cycles (54.9% vs. 70.6%, P=0.008) in women who underwent first-line surgery. Additionally, a subgroup of patients with a worse reproductive prognosis (those over 35 years old, with AMH  $\geq$  2 ng/mL, and with concomitant adenomyosis) was identified. For patients with at least one negative factor, first-line surgery resulted in significantly higher PR (P=0.01). However, no significant differences were found between the two strategies in patients over 35 years or those with adenomyosis.

In a separate analysis from the same cohort (n=60), Ballester et al. <sup>14</sup> reported a 78.1% CPR after 3 IVF cycles. However, a trend toward a decreased CPR was observed for women who received their first IVF cycle more than 18 months following surgery (*P*=0.07). Interestingly, a 44% (4/9 patients) postoperative PR was found after the first IVF cycle in a group of patients with previous IVF failure. Similarly, prior data indicated no benefit after three IVF cycles in patients with *in situ* colorectal endometriosis, reinforcing the indication for colorectal surgery after IVF failure. <sup>28</sup>

A third study,<sup>26</sup> not included in the meta-analysis, was published in 2024. The authors retrospectively compared fertility outcomes in 189 patients with colorectal endometriosis and proven infertility: 120 patients undergoing IVF alone and 69 patients undergoing surgery followed by IVF. Both the CPR and CLBR were similar between the groups.

### **Ongoing Trials**

The ENDOFERT study (NCT0294897) is an open, multicentre, parallel-group, controlled trial aimed to

evaluate the impact of complete surgery of colorectal DE on IVF outcomes. Patients are randomised into two groups: one group undergoing complete surgery of colorectal DE before IVF and the other group undergoing IVF alone (ratio 1:1). The Primary outcome will be the occurrence of a clinical pregnancy (6 weeks of gestation with ultrasound confirmation) after 2 IVF cycles.

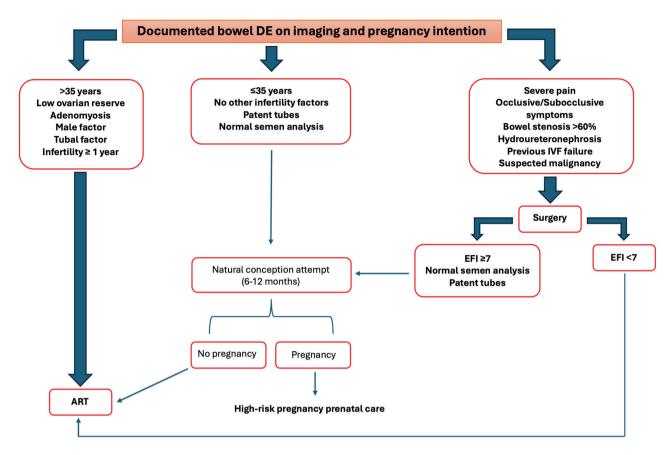
The TOSCA study (NCT05677269)95 is a multicentre prospective observational cohort study that will compare surgery (potentially combined with IVF/ICSI) versus IVF/ICSI-only treatment in women with colorectal endometriosis and subfertility, in order to provide evidence on the value of surgery as a fertility-enhancing procedure. The duration of time to allow natural conception will be determined based on the EFI score. The primary outcome will be the cumulative ongoing PR resulting in a live birth, measured by CLBR. The total follow-up time per patient will include 40 months unless the study endpoint is achieved earlier. The endpoint criteria of the study are: 1) live birth or 2) no live birth after 40 months of follow-up despite IVF/ICSI (maximum three cycles), colorectal resection surgery, or a combination of both treatments. The choice between surgery and IVF/ICSI treatment will be determined through shared decision-making while considering the patient's current QoL.

The EFFORT study (NCT 04610710)% is a multicentre, parallel-group, controlled trial aimed at determining the CPR and LBR after first-line surgery compared with first-line IVF for women with colorectal endometriosis and pregnancy intention. Patients are randomised 1:1 to either surgical management or IVF (at least two cycles if not pregnant after the first cycle). Women in the surgical intervention group will attempt to get pregnant after surgery, by either spontaneous conception or ART, depending on the EFI score.

### Conclusion

Bowel endometriosis-associated infertility remains a complex condition requiring individualised management. Laparoscopic surgical excision can improve fertility outcomes - especially in younger patients, those without adenomyosis, and those with minimal additional infertility factors.

Completeness of resection, surgical expertise, and proper candidate selection are key determinants of reproductive success. However, the evidence base is primarily observational. The benefit of surgery in improving outcomes - especially when performed



**Figure 2.** Proposed algorithm for the management of patients with bowel deep endometriosis and pregnancy intention. DE: Deep Endometriosis, ART: Assisted Reproductive Technology, EFI: Endometriosis Fertility Index.

before ART - remains uncertain. In patients with a good reproductive prognosis (age <35, no adenomyosis, patent tubes, normal ovarian reserve), natural conception after surgery is a reasonable goal. Conversely, for older patients or those with diminished ovarian reserve or prior ART failures, IVF should not be delayed (Figure 2).

Surgical complications, though infrequent, may delay conception but do not necessarily reduce LBRs - except in cases of septic events. Notably, the timing between surgery and ART initiation appears to impact outcomes, with earlier treatment yielding better results.

First-line ART remains a viable option in patients without obstructive bowel disease or pain, although fertility outcomes are influenced by adenomyosis and prior surgeries.

Ongoing trials are expected to provide needed clarity. Until randomised trials are published, the choice between surgery-first or ART-first must be guided by

shared decision-making, individual clinical profiles, and a balance between fertility goals, surgical risk, and symptom burden.

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Supplementary Table 1	I. SANRA- qua	lity assessme	nt of the include	ded reviews.			
	Importance for readership	Statement of aims or questions	Description of literature search	Referencing	Scientific reasoning	Appropriate presentation of data	Total score
brão et al. (2015)¹	2	2	2	2	2	2	12
Vercellini et al. (2021) <sup>3</sup>	2	2	2	2	2	2	12
Yin et al. (2023) <sup>6</sup>	1	1	0	2	2	2	8
Habib et al. (2020) <sup>7</sup>	2	1	0	2	2	2	9
Barra et al. (2021) <sup>32</sup>	2	1	0	2	1	1	7
Vercellini (2014) <sup>27</sup>	2	2	2	2	2	2	12
Melado et al. (2024) <sup>34</sup>	1	1	0	2	1	1	6
Grigoriadis et al. (2024) <sup>38</sup>	2	2	0	2	2	2	10
Daraï et al. (2017) <sup>39</sup>	2	2	2	2	2	1	11
Cohen et al. (2014) <sup>84</sup>	2	2	2	2	2	2	12
Daniilidis et al. (2022) <sup>85</sup>	2	2	2	2	2	2	12
Vercellini et al. (2012) <sup>87</sup>	2	2	2	2	2	2	12

	Prior history of surgery for endometriosis	100% (16.4% laparotomy)	%		17.6%	64.5% (13.6% laparotomy)	45.7%
	Complications Pri (Clavien-Dindo of ≥ 3)	10 (16 Jac	%86	%0	17	64 (13	45
	Comp (Clavi ≥ 3)	7.3%	%9	16.7%	1.4%	6.4%	3.7%
	Associated adenomyosis	N R	44%	R	N.	Z.	14.8%
	Live- birth rate	N N	100%	100%	100%	Z Z	77.8%
resent).	Mean time to pregnancy	N R	N R	Z Z	Z Z	11.4 ± 7.4 months	N R
iosis (2009-p	Total PR (SP+MAR)	36.6%	%05	33.3%	NR	53.1%	34.6%
endometri	MAR PR	4 (13.3%) (IVF)	5 (31.3%) (IVF)	1 (33.3%) (IVF)	N.	12 (37.5%) (IVF)	4 (15.4%) (IVF)
th colorectal	SP (SPR)	7 (23.3%)	3 (18.8%)	NR	11 (21.6%)	5 (15.7%)	5 (19.2%)
in patients wi	Mean follow-up	94 months (34-114)	42.5 months (12-157)	20 months	776 ± 465 days	1 and 3 years	21 months (12-29)
I in 42 studies	Women with pregnancy intention	17 (56.7%)	16 (32%)	3 (50%)	51 (79.7%)	32 (29.1%)	26 (32.1%)
vere reported	Infertility diagnosis	42 (76.4%)	NR	6 (100%)	51 (79.7%)	44 (40%)	38 (46.9%)
bowel surgery v	u	55 (25 lost to follow-up)	20	9	64	110	18
Supplementary Table 2. Fertility outcomes after primary bowel surgery were reported in 42 studies in patients with colorectal endometriosis (2009-present).	Intervention	Segmental resection	Segmental resection	Segmental resection	Shaving (n=59), Disc excision (n=1), No treatment (n=4)	Shaving	Segmental resection with transanal NOSE
y Table 2. Fertility ou	Study design	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Ambispective
Supplementary	Author (year) (ref)	Kavallaris et al. (2011) <sup>38</sup>	Turco et al. (2020)≅	Juhasz-Böss et al. (2010) <sup>75</sup>	Gordts et al. (2013) <sup>46</sup>	Marty et al. (2017)*	Malzoni et al. (2025) <sup>®</sup>

Supplementar	Supplementary Table 2. Continued.													
Author (year) (ref)	Study design	Intervention	5	Infertility diagnosis	Women with pregnancy intention	Mean follow-up	SP (SPR)	MAR PR	Total PR (SP+MAR)	Mean time to pregnancy	Live- birth rate	Associated adenomyosis	Complications (Clavien-Dindo ≥ 3)	Prior history of surgery for endometriosis
Dobó et al. (2023)⁴³	Randomized	Segmental resection with transanal NOSE (n=42), conventional laparoscopic segmental resection (n=49)	91	34 (37.4%)	34 (37.4%)	14 ± 2.6 months	4 (11.8%)	18 (52.9%)	64.7%	N R	63.6%	N R	2.2%	68.1%
Wills et al. (2017) <sup>69</sup>	Retrospective	Segmental resection (n=136), Disc excision (n=146), Other (n=25)	307	107 (34.9%)	122 (39.7)	N R	28 (22.9%)	39 (32%)	54.9%	N R	N R	N N	11.4%	N N
Bafort et al. (2020) <sup>70</sup>	Retrospective	Segmental resection (n=171), Shaving (n=33), Disc excision (n=28)	232	203 (87.5%)	152 (65.5%) (9 missed data)	41.2 ± 29 months	26 (18.2%)	70 (49%)	67.1%	N R	N R	S S	%5.6	53.4%
Bendifallah et al. (2017) <sup>30</sup>	Retrospective (propensity score matching analysis)	Shaving, Disc excision, Segmental resection (n=NR)	35	55 (100%)	55 (100%)	N R	,	27 (49%) (IVF)	N R	N R	CLBR 70.6% after 3 cycles	45.5%	NR N	58.2%
Hudelist et al. (2023) <sup>52</sup>	Prospective	Segmental resection (n=125) Disc excision (n=37)	162 (20 lost to follow-up)	52 (43%)	52 (43%)	42.27 months (±17.59)	15 (28.8%)	15 (28.8%) (IVF)	57.7%	10 months (3-24)	63.3%	52%	4.3%	NR
Rubod et al. (2024) <sup>26</sup>	Retrospective	Shaving (n=18), Segmental resection (n=48), Disc excision (n=3)	69	(%001) 69	(%001) 69	NR	,	58% CPR after 4 IVF cycles	NR	N.	CLBR 52.2%	37.7%	8.7%	%0
Lapointe et al. (2022) <sup>13</sup>	Retrospective	Shaving (n=55) Resection (disc or segmental) (n=39)	94	37 (39.4%)	94 (100%)	24 months	24 (25.5%)	25 (26.6%) (IVF)	52.1%	15.8 months	NR	6.4%	4.3%	55.3%
Bourdel et al. (2018) <sup>47</sup>	Retrospective	Shaving (n=172) Segmental resection (n=23)	195	89 (45.6%)	138 (70.8%)	60 ± 42 months	51 (37%)	49 (35.5%) (IVF/IUI)	72.5%	13 ± 12 months	83%	N N	6.7%	29.7% (2.6% laparotomy)

Supplementar	Supplementary Table 2. Continued.	Ti-												
Author (year) (ref)	Study design	Intervention	c	Infertility diagnosis	Women with pregnancy intention	Mean follow-up	SP (SPR)	MAR PR	Total PR (SP+MAR)	Mean time to pregnancy	Live- birth rate	Associated adenomyosis	Complications (Clavien-Dindo ≥ 3)	Prior history of surgery for endometriosis
Dabi et al. (2024)¹²	Retrospective	Disc excision	49	28 (57.1%)	49 (100%)	15 months (1-57)	15 (30.6%)	10 (20.4%) (IVF)	51%	N.	75%	N.	2%	38.8%
Stepniewska et al. (2010) <sup>45</sup>	Retrospective	Segmental resection (n=60) lleal resection (n=2)	62	62 (100%)	50 (80.6%)	19.6 months (6-48)	12 (24%)	5 (10%) (IVF/IUI)	34%	NR	%76	20%	%8	63%
Hezer et al. (2023) <sup>15</sup>	Retrospective	Shaving (n=25) Disc excision (n=1) Segmental resection (n=53)	77	(%6.77) 09	77 (100%)	47.2 months	26 (33.8%)	22 (28.6%) (IVF)	62.3%	8.4 months (1.48-61)	89.1%	26.7%	6.5%	37.7%
Raos et al. (2023) <sup>67</sup>	Retrospective	Disc excision (n=44) Segmental resection (n=149)	193	193 (100%)	193 (100%)	N R	39 (20.2%)	78 (40.4%) (IVF/IUI)	%9:09	12.2 months (0.4-58)	53.9%	14.5%	16.6%	38.9%
Meuleman et al. (2014) <sup>60</sup>	Prospective	Segmental resection	76	N R	54 (71%)	20 months (1-45)	18 (33%)	30 (55.6%) (IVF/IUI)	88.9%	N.	NR	<u>د</u> 2	2%	Z.
Ferrero et al. (2009) <sup>44</sup>	Prospective	Segmental resection (laparoscopy n=33, laparotomy n=13)	46	21 (45.7%)	46 (100%)	49.9 ± 24.1 months	9 (19.6%)	13 (28.3%) (IVF/IUI)	47.8%	12.5 months (6-46)	86.4%	17.4%	8.7%	93%
Millochau et al. (2018) <sup>71</sup>	Retrospective	Multiple bowel nodules removal (Disc excision + segmental resection)	21	11 (52.4%)	9 (42.9%)	30 ± 25.4 months	2 (22.2%)	4 (44.4%) (IVF)	%9.99	<u>«</u> Z	83%	<u>«</u> Z	28%	66.7% (4.8% laparotomy)
Darai et al. (2011) <sup>41</sup>	Randomized	Segmental resection (laparoscopy n=26, laparotomy n=26)	52	23 (44.2%)	28 (53.8%)	29 months (6-52)	6 (21.4%)	5 (17.9%) (IVF)	39.3%	14 months (1-24)	ω Z	<u>«</u> Z	11.5%	67.3%
Roman et al. (2018) <sup>51</sup>	Randomized	Shaving (n=3), Disc excision (n=11), Segmental resection (n=22)	38	23 (63.9%)	36 (100%)	50-79 months	17 (47.2%)	12 (33.3%) (IVF/ IUI)	%9:08	W Z	œ Z	Z Z	Z Z	25%

Supplementar	Supplementary Table 2. Continued													
Author (year) (ref)	Study design	Intervention	c	Infertility diagnosis	Women with pregnancy intention	Mean follow-up	SP (SPR)	MAR PR	Total PR (SP+MAR)	Mean time to pregnancy	Live- birth rate	Associated adenomyosis	Complications (Clavien-Dindo ≥ 3)	Prior history of surgery for endometriosis
Meuleman et al. (2011) <sup>61</sup>	Retrospective	Segmental resection	45	40 (88.9%)	28 (62.2%)	27 months (16-40)	8 (28.6%)	5 (17.8%) (IVF)	46.4%	Z. R.	Z Z	Z Z	%0	87%
Malzoni et al. (2016) <sup>62</sup>	Retrospective	Segmental resection	248 (56 excluded from follow-up)	72 (29%)	72 (29%)	12 months	44 (61.1%)	6 (8.3%) (IVF)	69.4%	8.4 ± 4.1 months	48%	<u>«</u> Z	8.1%	84%
Roman et al. (2015) <sup>53</sup>	Prospective	Disc excision	20	19 (38%)	20 (40%)	& Z	10 (50%)	6 (30%) (IVF/ IUI)	%08	Z R	%09	<u>«</u> ح	26%	<u>«</u> Z
Jelenc et al. (2012) <sup>72</sup>	Retrospective	Segmental resection (n=52) Disc excision (n=4)	26	14 (25%)	14 (25%)	N R	8 (57.1%)	2 (14.3%) (IVF)	71.4%	Z Z	64.3%	<u>«</u> 2	11.5%	Z Z
Meuleman et al. (2009) <sup>63</sup>	Retrospective	Segmental resection	26	49 (87.5%)	33 (59%)	29 months (6-76)	7 (21.2%)	9 (27.3%) (IVF/ IUI)	48.5%	N R	œ Z	<b>∝</b> Z	11%	75%
Donnez et al. (2010) <sup>48</sup>	Prospective	Shaving	200	324 (64.8%)	388 (78%)	3.1 years (2-6)	221 (57%)	107 (27.5%) (IVF)	84.5%	N. R.	œ Z	<u>«</u> Z	3%	Z Z
Minelli et al. (2009) <sup>76</sup>	Retrospective	Segmental resection	357 (71 lost to follow- up)	129 (36.1%)	113 (31.7%)	19.6 months (6-48)	N R	Z Z	41.6%	N. R.	Z R	& Z	9.8%	36.7%
Roman et al. (2016) <sup>49</sup>	Retrospective	Shaving	122 (4 lost to follow- up)	40 (32.8%)	26 (38.2%)	36 months (12-60)	10 (38.5%)	7 (26.9%) (IVF/ IUI)	65.4%	N. R.	Z R	& Z	%6	W Z
Koh et al. (2012) <sup>73</sup>	Retrospective	Segmental resection (n=26), Disc excision (n=66)	92	30 (38%)	28 (30.4%)	16 months (0.5-116)	8 (26.6%)	5 (16.7%) (IVF)	43.3%	Ϋ́Z	ж Z	<u>α</u> Ζ	7.1%	80.2% (2.2% laparotomy)

Supplementar	Supplementary Table 2. Continued	तं												
Author (year) (ref)	Study design	Intervention	c	Infertility diagnosis	Women with pregnancy intention	Mean follow-up	SP (SPR)	MAR PR	Total PR (SP+MAR)	Mean time to pregnancy	Live- birth rate	Associated adenomyosis	Complications (Clavien-Dindo ≥ 3)	Prior history of surgery for endometriosis
Fanfani et al. (2010) <sup>s4</sup>	Case-control	Disc excision (n=48)	48 (12 lost to follow- up)	22 (45.8%)	Z R	33 months (16-46)	6 (27.3%)	Z R	Z Z	N. R.	Z Z	Z Z	4.4%	41.6%
Darai et al. (2010) <sup>42</sup>	Prospective	Segmental resection	83	39 (47%)	55 (66.2%)	34 months (6-68)	N R	Z Z	43.6%	11 months (2-68)	Z Z	20%	12%	54.2%
Ballester		Shaving (n=15), Disc						36 (60%) (IVF)						
et al. (2017) <sup>14</sup>	Prospective	excision (n=3), Segmental resection (n=42)	90	(100%)	(100%)	Z Z	I	78.1% CPR after 3 cycles	N N	Z Z	œ Z	43.5%	Z Z	45%
Hudelist et al. (2018) <sup>55</sup>	Prospective	Segmental resection (n=102), Disc excision (n=32)	134 (22 lost to follow- up)	72 (53.7%)	73 (54.5%)	36.5 ± 21.9 months	30 (41.1%)	16 (21.9%) (IVF)	63%	7 months (2-51)	46.6%	47%	5.9%	31.3%
Parra et al. (2021) <sup>74</sup>	Retrospective	Segmental resection (n=36), Disc excision (n=23), Shaving (n=18)	77	47 (61%)	45 (58%)	27.6 months (6-78)	10 (22.2%)	12 (26.7%) (IVF/ IUI)	48.9%	요 고	œ Z	19.5%	<u>ч</u> Z	45.5%
Ceccaroni et al. (2021) <sup>56</sup>	Retrospective	Disc excision	371 (9 lost to follow- up)	207	232 (64.1%)	60 months (1-168)	67 (28.9%)	31 (13.4%) (IVF)	42.2%	N R	Z Z	Z Z	20.8%	40.4%
Rocha et al. (2018)⁴	Prospective	Segmental resection	46	21 (45.6%)	26 (56.5%)	28.4 months	7 (26.9%)	8 (30.8%) (IVF)	27.6%	Z Z	œ Z	<b>∝</b> Z	8.7%	Z Z

Supplementar	Supplementary Table 2. Continued.	7												
Author (year) (ref)	Author (year) Study design (ref)	Intervention	٤	Infertility diagnosis	Women with pregnancy intention	Mean follow-up	SP (SPR)	MAR PR	Total PR (SP+MAR)	Mean time to pregnancy	Live- birth rate	Associated adenomyosis	Complications (Clavien-Dindo ≥ 3)	Prior history of surgery for endometriosis
Abo et al. (2018) <sup>50</sup>	Retrospective	Segmental resection (n=139), Disc excision (n=80), Shaving (n=145)	364	128 (35.2%) (35 lost to follow- up)	64 (17.6%)	40 ± 22 months	8 (25%) (17.5%)		37.5%	ж Z	31.3%	ж Z	14.8%	Z Z
Neme et al. (2013) <sup>65</sup>	Retrospective	Segmental resection	10	(%09) 9 (%09) 9	(%09) 9	12 months	s (66.7%) 2 100% (IVF)	2 (33.3%) (IVF)	100%	N R	Z R	æ Z	%0	Z R
Tuominen et al. (2021) <sup>66</sup>	Retrospective	Segmental resection	132	Z R	74 (56.1%)	4.9 ± 3.5 years	38 18 (51.4%) (24.3%) (IVF/ IUI)	38 (51.4%) (IVF/ IUI)	75.7%	2.6 years	96.2%	Z 2	17.5%	43.2%

CPR: Cumulative pregnancy rate, CLBR: Cumulative live birth rate, IUI: Intrauterine insemination, IVF: In vitro fertilisation, ICSI: Intracytoplasmic sperm injection, ART: Assisted reproductive technology, SP: Spontaneous pregnancy, SPR: Spontaneous pregnancy rate, MAR: Medically assisted reproduction, NOSE: Natural orifice specimen extraction, NR: Not reported.