

Original Article

## Surgery for Inflammatory Bowel Disease Has Unclear Impact on Female Fertility: A Cochrane Collaboration Systematic Review

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### Abstract

**Background and Aims:** Surgical treatment of inflammatory bowel disease (IBD) may impair female fertility. We conducted a systematic review to determine the risk of infertility and pregnancy outcomes in women with IBD who underwent surgery.

**Methods:** We identified studies evaluating the impact of IBD surgery on infertility and pregnancy outcomes. Risk ratios (RR) and 95% confidence intervals (CIs) were pooled when data were presented using contingency tables. Odds ratios (OR) were pooled when raw numbers were not provided. GRADE was used to evaluate the certainty of evidence.

**Results:** Sixteen observational studies were included, comparing women with and without surgery, open and laparoscopic surgery and before and after surgery. All studies were of low quality. The effect of surgery on infertility at 12 months (RR 5.45, 95% CI 0.41 to 72.57) was uncertain. Similarly, the fertility effects of laparoscopic versus open surgery method were unclear (RR 0.70, 95% CI 0.38 to 1.27). The impact of IBD surgery on pregnancy outcomes should be interpreted with caution. Surgery was associated with miscarriage (OR 2.03, 95% CI 1.14 to 3.60), use of assisted reproductive technologies (RR 25.09, 95% CI 1.56 to 403.76) and caesarean section (RR 2.23, 95% CI 1.00 to 4.95), but not with stillbirth (RR 1.96, 95% CI 0.42 to 9.18), preterm birth (RR 1.91, 95% CI 0.67 to 5.48), low birth weight (RR 0.61, 95% CI 0.08 to 4.83) or small for gestational age (RR 2.54, 95% CI 0.80 to 8.01).

**Conclusion:** The effect of surgical therapy for IBD on rates of female infertility and pregnancy-related outcomes was uncertain due to poor quality of existing literature.

**Keywords:** Crohn's disease; Fertility; Infertility; Inflammatory bowel disease; Surgery; Ulcerative colitis

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## Background

Within 10 years, 50% of Crohn's disease (CD) and 15% of ulcerative colitis (UC) patients require surgery due to medically refractory or complicated disease (1). Ileal pouch-anal anastomosis (IPAA) following colectomy is common in UC patients. Between 44% and 82% of women are infertile following IPAA; in comparison, 0 to 38% of women without IPAA are infertile (2,3). The effect of other surgical procedures remains unknown.

Our review evaluated the effects of surgical interventions on female infertility and their impact on the need for assisted reproductive technology (ART), time to pregnancy and pregnancy outcomes. This report is based on a systematic review and meta-analysis conducted for the Cochrane Collaboration (4).

## METHODS

This systematic review was conducted based on a previously published protocol (5) and reported in accordance with the PRISMA guidelines (6).

### Study Identification and Selection

Interventional or observational studies of women of reproductive age ( $\geq 12$  years) with inflammatory bowel disease (IBD) published in any language were included. Eligible studies compared infertility and/or secondary outcomes between IBD patients with and without surgery or with different surgical techniques (e.g., open versus laparoscopic). Studies comparing IBD to non-IBD controls or combining IBD patients with those undergoing similar surgeries for non-IBD indications were excluded. Cross-over studies, case series and case reports were excluded.

MEDLINE, EMBASE, Cochrane CENTRAL and the Cochrane IBD Group Specialized Register were searched for eligible studies from inception to September 27, 2018 (Supplementary Appendix). Additional studies were identified from references of relevant articles, conference abstracts, trials registers and grey literature databases.

Two authors (S.L. and M.C.) independently screened abstracts for eligibility and independently reviewed full texts for inclusion. Disagreements were resolved by consensus with C.H.S., E.I.B. or M.E.K.

### Comparisons

We compared infertility and secondary outcomes in women with and without any previous IBD surgery (intra-abdominal or perianal) and with open and laparoscopic surgery (IPAA only). We also describe outcomes in women before and after surgery.

### Outcomes

Our primary outcome was infertility defined as an inability to become pregnant after 1 year of regular unprotected sexual

intercourse without birth control. Secondary outcomes included infertility at 6, 18 and 24 months, miscarriage, stillbirth, use of ART (hormonal or mechanical treatments and in vitro fertilization), mode of delivery, prematurity (delivery before 37 weeks of gestation), low ( $< 2500$  g) or very low ( $< 1500$  g) birth weight, small for gestational age ( $< 10$ th percentile), gestational diabetes, preeclampsia and time to pregnancy. Requirement for resuscitation and/or neonatal intensive care, antenatal and postpartum hemorrhage, retained placenta, postpartum depression and fertility rate were also of interest, but not reported in any identified studies.

### Data Extraction

Two authors (S.L. and M.C.) used a standardized data extraction form to extract independently extract data in duplicate. Disagreements were resolved by consensus with C.H.S., E.I.B. or M.E.K. Extracted data included study design, identification, recruitment and characteristics of study participants, inclusion/exclusion criteria, descriptions of interventions and comparators and details of infertility and pregnancy-related outcomes.

### Risk of Bias and Certainty of the Evidence

Two authors (S.L. and M.C.) independently assessed risk of bias using the Newcastle-Ottawa Scale (7). Overall quality of evidence was assessed using the GRADE approach and rated as high, moderate, low or very low quality. Observational studies were initially rated low quality but could be upgraded based on large magnitude of effect, judgement that all plausible confounding reduced a demonstrated effect or suggested a spurious effect when results showed no effect, or a dose response gradient (8).

### Statistical Analysis

Our primary analysis combined women of all IBD subtypes. Studies comparing women with and without surgery and women with open and laparoscopic surgical procedures were pooled using random-effects meta-analyses. Where possible, we calculated risk ratios (RRs) with 95% confidence interval (CI) to compare outcomes for each comparison. We pooled odds ratios (ORs) instead of RRs using the generic inverse variance method when individual studies reported ORs with corresponding CIs that were adjusted for confounding variables and did not provide contingency tables. Studies comparing women before and after surgery were summarized qualitatively due to concerns about the statistical validity of pooling data without accounting for the paired nature of the data.

We did not construct a funnel plot nor test for funnel plot asymmetry as no analysis included more than 10 studies (8). Analyses were conducted using Review Manager (RevMan) 5.3 (The Cochrane Collaboration).

## Sensitivity and Subgroup Analyses

We conducted subgroup analyses based on IBD subtype (CD or UC) and age at surgery (<18 years, 18–34 years, ≥35 years). A sensitivity analysis excluding women with active disease at conception or a diagnosis of IBD during pregnancy or postpartum was also conducted.

## RESULTS

### Description of Included Studies

Database searching identified 1092 records; 151 underwent full-text review and 16 (all observational) were included (Supplementary Figure S1, Table 1). Ten studies included our prespecified comparisons and were meta-analyzed. Nine compared women with and without previous surgery. One compared open and laparoscopic IPAA. Seven compared the risk of infertility and/or secondary outcomes before and after surgery. One included comparisons of women with and without IPAA and women before and after IPAA. No studies evaluated the impact of perianal surgery on infertility or pregnancy outcomes.

### Risk of Bias of Included Studies

The risk of bias of included studies is summarized in Supplementary Figure S2. Overall, studies were at high risk of selection and misclassification bias. Most studies included unadjusted estimates and were at risk of confounding.

### Any Previous Surgery Versus No Previous Surgery

#### Infertility

Previous surgery was not associated with infertility at 12 months (RR 5.45, 95% CI: 0.41 to 72.57; Figure 1). Both studies evaluating this association only included UC patients; one compared women with and without IPAA (9) and the other compared women with and without restorative proctocolectomy with ileorectal anastomosis (10).

One study reported infertility at 24 months was associated with previous surgery (RR 3.59, 95% CI: 1.32 to 9.73) with a significant association in UC patients (RR 5.28, 95% CI: 2.09 to 13.34), but not in CD (RR 2.03, 95% CI: 0.56 to 7.33). No detailed information about surgical procedures was reported (11).

Based on GRADE analyses, the overall certainty of evidence was downgraded from low to very low due to high risk of bias and imprecise estimates.

#### Miscarriage

Surgery was associated with miscarriage (OR 2.03, 95% CI: 1.14 to 3.60; Figure 2A). Findings were consistent when limiting the analysis to women with CD (OR 2.56, 95% CI: 1.19 to 5.51) and UC (OR 7.14, 95% CI: 1.02 to 50.18) and in a sensitivity analysis excluding women with active disease at conception (RR 2.38, 95% CI: 1.11 to 5.11; Supplementary Figure

S3). Studies evaluating this association did not describe the type of surgery women underwent. The overall certainty of evidence was downgraded from low to very low due to high risk of bias.

#### Stillbirth

Stillbirth and previous IBD surgery were not associated (RR 1.96, 95% CI: 0.42 to 9.18; Figure 2B). Results were consistent in women with CD (RR 1.98, 95% CI: 0.32 to 12.16) and UC (RR 1.91, 95% CI: 0.10 to 36.02). One study presenting data specific to women with quiescent disease reported no events in either group (11) and no association in a second study (RR 1.26, 95% CI: 0.07 to 23.54) (12). These studies did not describe the surgical procedures women underwent. The overall certainty of evidence was downgraded from low to very low due to high risk of bias and imprecise estimates.

#### Use of ART

In one study, female UC patients with an IPAA were more likely to use ART (RR 25.09, 95% CI: 1.56 to 403.76) compared to those without. The overall certainty of evidence was downgraded from low to very low due to high risk of bias and imprecise estimates.

#### Caesarean Section

The association between previous surgery and caesarean section was reported in one study (RR 2.23, 95% CI: 1.00 to 4.95), which also presented disease-specific associations (CD, RR 3.60, 95% CI: 0.98 to 13.19; UC, RR 1.67, 95% CI: 0.61 to 4.59). All women with UC had IPAA. Women with CD underwent a variety of surgical procedures. The overall certainty of evidence was downgraded from low to very low due to high overall risk of bias.

#### Prematurity

Preterm birth was not associated with previous surgery (RR 1.91, 95% CI: 0.67 to 5.48; Figure 2C); this was consistent in women with CD (RR 2.32, 95% CI: 0.75 to 7.21) and UC (RR 0.56, 95% CI: 0.03 to 9.73). Results were consistent in an analysis limited to women with remission (RR 1.17, 95% CI: 0.11 to 12.38) (11). In one study, all women with UC who had previous surgery had IPAA while those with CD underwent various surgical procedures. The remaining studies did not describe the surgeries women underwent. The overall certainty of evidence was downgraded from low to very low due to high risk of bias and imprecise estimates.

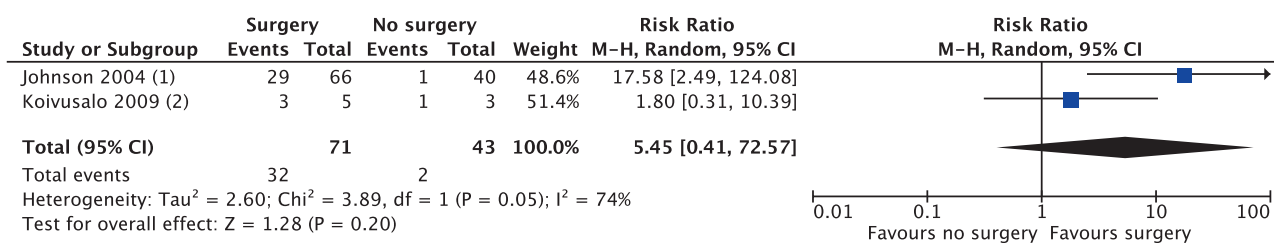
#### Low Birth Weight

One study reported no association between previous surgery and giving birth to a low birthweight infant (RR 0.61, 95% CI: 0.08 to 4.83), with similar findings in women with CD (RR 0.67, 95%

**Table 1.** Characteristics of studies included in the meta-analysis

Study	Study design	Years of study	Comparison	Type of IBD	Outcomes
Banks 1957 (12)	Retrospective cohort	1931–1950	Previous surgery vs. no previous surgery	UC	Miscarriage Stillbirth
Bartels 2012 (29)	Cross-sectional	2010–2011 (surgery: 1993–2009)	Open vs. laparoscopic IPAA	UC	Infertility (12 months)
Bortoli 2011 (30)	Prospective cohort	2003–2006	Previous surgery vs. no previous surgery	CD	Miscarriage
Gorgun 2004 (13)	Cross-sectional	1983–2011	Before and after restorative proctocolectomy with IPAA	UC	Infertility (12 months) Use of ART
Hahnloser 2004 (31)	Cross-sectional	1981–1995	Before and after IPAA	UC	Miscarriage Stillbirth Gestational diabetes Preeclampsia
Hudson 1997 (11)	Cross-sectional	1967–1986	Previous surgery vs. no previous surgery	CD, UC	Infertility (24 months) Miscarriage Stillbirth Preterm birth
Johnson 2004 (9)	Cross-sectional	Unknown	IPAA vs. no previous surgery Before and after IPAA	UC	Infertility (12 months) Use of ART
Koivusalo 2009 (10)	Cross-sectional	1985–2005	Restorative proctocolectomy with ileoanal anastomosis vs. no previous surgery	UC	Infertility (12 months)
Mortier 2006 (15)	Cross-sectional	2003 (surgery: 1962–1999)	Before and after total colectomy with ileorectal anastomosis	UC	Infertility (6, 12, 24 months) Time to pregnancy
Moser 2000 (32)	Retrospective cohort	1993–1997	Previous surgery vs. no previous surgery	CD	Small for gestational age
Naganuma 2011 (33)	Cross-sectional	1989–2008	Previous surgery vs. no previous surgery	IBD	Miscarriage
Nielsen 1984 (34)	Retrospective cohort	1968–1980	Previous surgery vs. no previous surgery	CD	Miscarriage Stillbirth Preterm birth
Olsen 2002 (35)	Prospective cohort	1982–1998	Before and after restorative proctocolectomy with IPAA	UC	Infertility (12, 24 months)
Ravid 2002 (36)	Cross-sectional	1982–1998	Before and after IPAA	UC	Miscarriage Stillbirth Caesarean section
Tulchinsky 2013 (14)	Cross-sectional	Not specified	Before and after restorative proctocolectomy	UC	Infertility (12 months) Miscarriage Use of ART Caesarean section Time to pregnancy
Zavorova 2017 (37)	Restrospective cohort	2014–2016	Previous surgery vs. no previous surgery	CD, UC	Caesarean section Low birth weight Very low birth weight Prematurity

ART, Assisted reproductive technology; CD, Crohn's disease; IBD, Inflammatory bowel disease; IPAA, Ileal pouch-anal anastomosis; UC, Ulcerative colitis.



#### Footnotes

(1) Type of Surgery: IPAA

(2) Type of Surgery: Restorative proctocolectomy with ileorectal anastomosis

**Figure 1.** Risk of infertility at 12 months in women with inflammatory bowel disease (IBD) who did and did not have previous IBD-related surgery.

CI: 0.03 to 13.60) and UC (RR 0.56, 95% CI: 0.03 to 9.73). No infants were very low birth weight. All women with UC requiring surgery underwent IPAA. Women with CD underwent a variety of procedures. The overall certainty of evidence was downgraded from low to very low due to high risk of bias and imprecise estimates.

#### Small for Gestational Age

In women with CD, one study demonstrated no association between previous surgery and small for gestational age infants (RR 2.54, 95% CI: 0.80 to 8.01). Details of the surgical procedure(s) required were not provided. The overall certainty of evidence was downgraded from low to very low due to high risk of bias and imprecise estimates.

### Laparoscopic Versus Open Surgery

#### Infertility

One study reported no difference in the risk of infertility at 12 months in women with UC who underwent laparoscopic versus open surgery (RR 0.70, 95% CI: 0.38 to 1.27). All women in this study underwent IPAA. The overall certainty of evidence was downgraded from low to very low due to high risk of bias and imprecise estimates.

### Before and After Surgery

#### Infertility

The rates of infertility at 6, 12 and 24 months in women before and after surgery were described in one, five and two studies, respectively (Table 2). Infertility at 12 months was reported in 20.8% (68/327) of women before surgery compared to 63.4% (239/277) of women afterwards. Similar proportions reported infertility at 6 and 24 months. Age-stratified comparisons from a single study suggested rates of infertility were similar before and after surgery in women who were younger at the time of surgery, with larger differences noted in women who were older at surgery (Supplementary Table S1) (13). The overall certainty of evidence was downgraded from low to very low due to high risk of bias.

#### Miscarriage

Three studies reported miscarriage rates before and after surgery in females with UC; miscarriage occurred in 15.4%

(19/123) of pregnancies before and 15.7% (21/134) of pregnancies after surgery (Table 3). The overall certainty of evidence was downgraded from low to very low due to high risk of bias.

#### Stillbirth

In two studies, 5.3% (2/38) of pregnancies in women with UC before IPAA resulted in stillbirth compared to 3.8% (3/80) of pregnancies after IPAA (Table 3). The overall certainty of evidence was downgraded from low to very low due to high risk of bias.

#### Use of ART

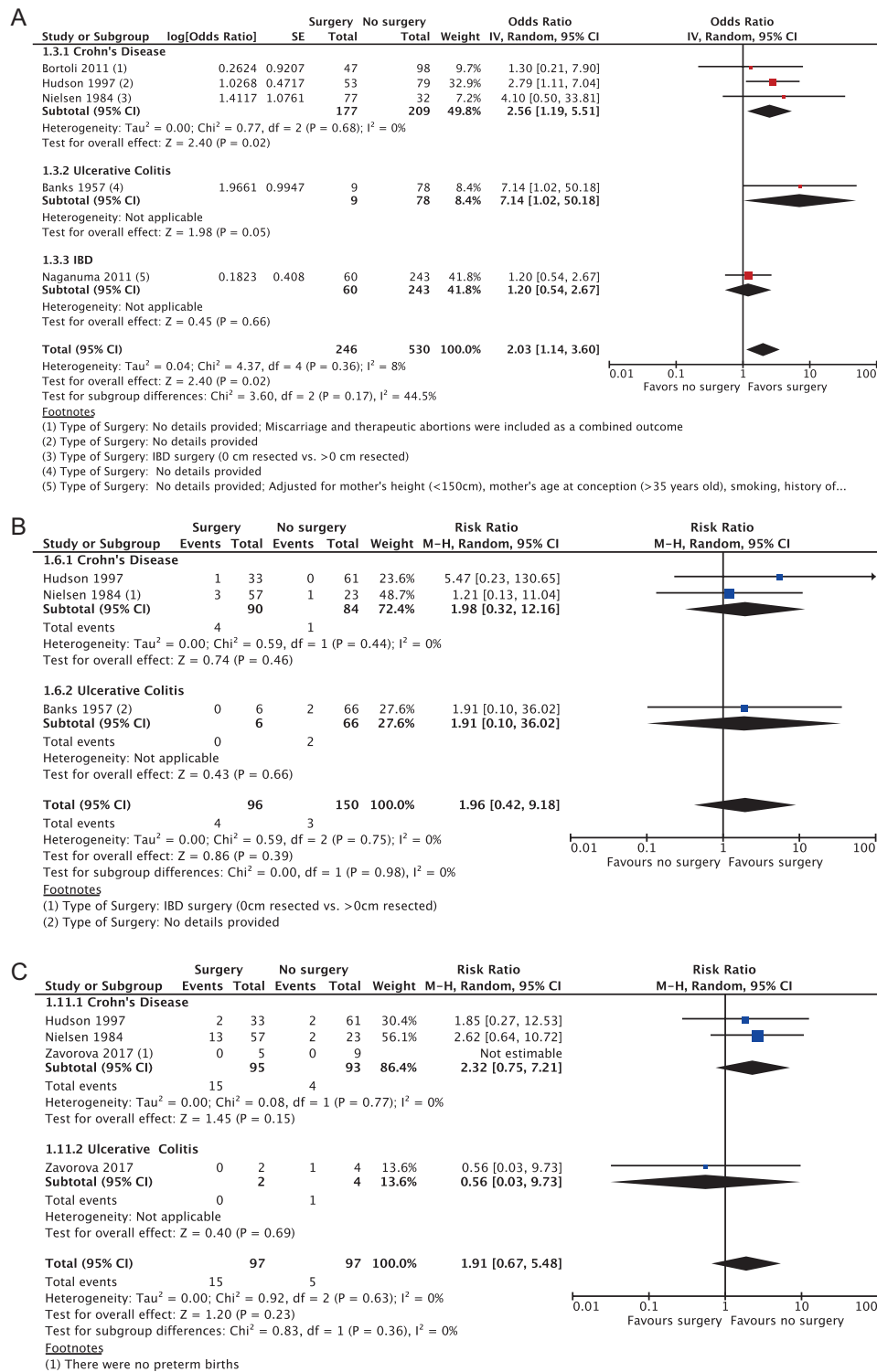
Three studies observed use of ART before and after surgery in female UC patients (Table 4). Results from these studies are not directly comparable because the types of patients considered 'at risk' for using ART differed between studies. In one study, 5.3% (5/95) of women attempting pregnancy used ART before surgery compared to 30.3% (20/66) after surgery (9). Among women who were infertile following 12 months of attempted pregnancy, 42.2% (19/45) used ART before surgery compared to 51.4% (36/70) after surgery (13). In the final study, 8.6% (6/70) of pregnancies before restorative proctocolectomy occurred in women using ART compared to 34.3% (11/32) of pregnancies occurring after surgery (14). The overall certainty of evidence was downgraded from low to very low due to high risk of bias.

#### Caesarean Section

Two studies described delivery by caesarean section before and after surgery in females with UC; 11.0% (8/73) of infants were delivered via caesarean section before surgery compared to 48.0% (36/75) after surgery (Table 3). The overall certainty of evidence was downgraded from low to very low due to high risk of bias.

#### Gestational Diabetes and Preeclampsia

One study reported gestational diabetes and preeclampsia before and after surgery. Among female UC patients with pregnancies both before and after surgery, 8.1% (3/37)



**Figure 2.** Risk of (A) miscarriage, (B) stillbirth and (C) preterm birth (<37 weeks of completed gestation) in women with inflammatory bowel disease (IBD) who did and did not have previous IBD-related surgery.

developed gestational diabetes and 5.4% (2/37) had preeclampsia before surgery. None experienced either condition in pregnancies after surgery. The overall certainty of evidence for both outcomes was downgraded from low to very low due to high risk of bias.

*Time to Pregnancy*

Two studies observed time to pregnancy before and after surgery among women with UC (Table 5). One reported a median (range) time of 2 (1 to 3) months to pregnancy in five women before total colectomy with ileorectal anastomosis

**Table 2.** Infertility in female patients with ulcerative colitis before and after surgery

Type of surgery	Study	Before surgery		After surgery	
		Infertile, <i>n</i> (%)	Total, <i>n</i>	Infertile, <i>n</i> (%)	Total, <i>n</i>
Infertility at 12 months					
Restorative proctocolectomy with IPAA	Gorgun 2004 (13)	45 (38.5)	117	70 (58.3)	120
	Olsen 2002 (35)	18 (21.4)	84	122 (81.9)	149
IPAA	Johnson 2004 (9)	4 (4.2)	95	29 (43.9)	66
Total colectomy with ileorectal anastomosis	Mortier 2006 (15)	1 (20.0)	5	8 (53.3)	15
Restorative proctocolectomy	Tulchinsky 2013 (14)	0 (0.0)	26	10 (37.0)	27
	Total	68 (20.8)	327	239 (63.4)	377
Infertility at 6 months					
Total colectomy with ileorectal anastomosis	Mortier 2006 (15)	1 (20.0)	5	9 (60.0)	15
Infertility at 24 months					
Restorative proctocolectomy with IPAA	Olsen 2002 (35)	13 (15.5)	84	108 (72.5)	149
Total colectomy with ileorectal anastomosis	Mortier 2006 (15)	1 (20.0)	5	7 (46.7)	15
	Total	14 (15.7)	89	115 (70.1)	164

IPAA, Ileal pouch-anal anastomosis.

**Table 3.** Outcomes of pregnancy in female patients with ulcerative colitis before and after surgery

Type of surgery	Study	Before surgery		After surgery	
		Miscarriage, <i>n</i> (%)	Total, <i>n</i>	Miscarriage, <i>n</i> (%)	Total, <i>n</i>
Miscarriage					
IPAA	Hahnloser 2004 (31)	10 (27.0)	37	6 (16.2)	37
Restorative proctocolectomy	Ravid 2002 (36)	1 (6.3)	16	9 (13.8)	65
	Tulchinsky 2013 (14)	8 (11.4)	70	6 (18.8)	32
	Total	19 (15.4)	123	21 (15.7)	134
Stillbirth					
IPAA	Hahnloser 2004 (31)	2 (7.4)	27	2 (6.5)	31
Restorative proctocolectomy	Ravid 2002 (36)	0 (0)	11	1 (2.0)	49
	Total	2 (5.3)	38	3 (3.8)	80
Caesarean section					
IPAA	Ravid 2002 (36)	0 (0)	11	24 (49.0)	49 <sup>a</sup>
Restorative proctocolectomy	Tulchinsky 2013 (14)	8 (12.9)	62	12 (46.2)	26
	Total	8 (11.0)	73	36 (48.0)	75

IPAA, Ileal pouch-anal anastomosis.

<sup>a</sup>Includes a set of twins (one born vaginally and one born via caesarean section).

compared to 5 (2 to 36) months in 15 women attempting pregnancy after surgery (15). The second reported a mean (SD) of 5.0 (11.6) months to pregnancy before restorative proctocolectomy; pregnancy occurred immediately in 32/70 pregnancies (26 women) (14). After surgery, the mean time to pregnancy was 16.3 (25.1) months; 17 of 27 women successfully conceived a total of 32 times. The overall certainty of evidence was downgraded from low to very low due to high risk of bias.

## Discussion

Based on available data, it is uncertain if previous IBD-related surgery is associated with infertility and pregnancy outcomes in women with IBD, or if differences in infertility exist between women with UC who underwent laparoscopic and open IPAA. Our conclusions are based on very low-quality evidence due to the observational nature of the data, limited number of studies, small sample sizes and high risk of bias. Thus, our findings should be interpreted with caution.

**Table 4.** Use of assisted reproductive technology in female patients with ulcerative colitis before and after surgery

Type of surgery	Study	Before surgery		After surgery	
		Use of ART, n (%)	Total, n	Use of ART, n (%)	Total, n
IPAA	Johnson 2004 (9)	5 (5.3)	95 <sup>a</sup>	20 (30.3)	66 <sup>a</sup>
Restorative proctocolectomy with IPAA	Gorgun 2004 (13)	19 (42.2)	45 <sup>b</sup>	36 (51.4)	70 <sup>b</sup>
Restorative proctocolectomy	Tulchinsky 2013 (14)	6 (8.6)	70 <sup>c</sup>	11 (34.3)	32 <sup>c</sup>

ART, Assisted reproductive technology; IPAA, Ileal pouch-anal anastomosis.

<sup>a</sup>Number of women attempting pregnancy.

<sup>b</sup>Number of women infertile following 12 months of attempting pregnancy.

<sup>c</sup>Number of pregnancies in which women used ART.

**Table 5.** Time to pregnancy in female patients with ulcerative colitis before and after surgery, measured in months

Type of surgery	Study	Measure	Before surgery		After surgery	
			Time to pregnancy	Number of women attempting pregnancy	Time to pregnancy	Number of women attempting pregnancy
Total colectomy with ileorectal anastomosis	Mortier 2006 (15)	Median (range)	2 (1–3)	5	5 (2–36)	15
Restorative proctocolectomy	Tulchinsky 2013 (14)	Mean (SD)	5.0 (11.6)	26 (70 pregnancies <sup>a</sup> )	16.3 (25.1)	27 <sup>b</sup> (32 pregnancies)

SD, Standard deviation.

<sup>a</sup>Pregnancy occurred ‘immediately’ in 32 pregnancies.

<sup>b</sup>17/27 women successfully conceived.

Notably, our findings differed from two systematic reviews that concluded infertility was more common in women with IPAA than those without (2,3). Our conclusions likely differed from these reviews due to different methodology—we only included studies that rigorously defined infertility (i.e., an inability to become pregnant within a prespecified amount of time without using birth control). This ensured equal follow-up time among all women regardless of surgical history and was not distorted by differing rates of voluntary infertility or other characteristics among women with and without previous surgery (e.g., disease severity). Infertility estimates can vary drastically when using different definitions, resulting in different conclusions when comparing rates between groups (16). Secondly, we did not meta-analyze studies assessing infertility in women before and after IPAA construction due to concerns about the statistical validity of not accounting for repeated observations and residual confounding by age. In a comparison of age-specific infertility estimates before and after IPAA, no differences in infertility were observed among women undergoing surgery before 30 while infertility rates were higher when IPAA occurred after 30 (13)—an age after which fertility begins to decline more rapidly than at previous

ages (17). Consequently, we cannot be certain if there is a true association between IPAA and infertility or if the finding is observed due to the uncontrolled effect of age. Increased infertility observed among women with familial adenomatous polyposis following IPAA (18) may have resulted from the same biases identified in studies of women with IBD.

We originally intended to evaluate the impact of specific surgical interventions on infertility and pregnancy-related outcomes. However, no two studies provided sufficient details of the types of surgery women required or evaluated the same surgical procedure. Further, many studies grouped multiple procedures (i.e., compared any previous IBD-related surgery to those without surgery) and no studies compared women with and without a stoma. Consequently, we are unable to evaluate procedure-specific conclusions about the impact of surgery on infertility. Since variation across surgery types is likely, the applicability of our findings for women considering IBD-related intestinal resection is limited. For example, IPAA construction is more likely to result in fallopian tube damage compared to limited small bowel resection (19,20). Tubal factors contribute to infertility more often among women with an IPAA (21). Other procedures may be less likely to have a similar impact on



fallopian tubes. Further, variations may exist across pouch types (e.g., J, S or Kock pouches) and surgical techniques. One small study reported a numeric increase in adhesions among women who underwent three-stage versus two-stage IPAA construction, which may subsequently impact infertility (22), while another reported numeric increases in infertility among those with a stapled anastomosis compared to those with a hand-sewn anastomosis (23).

Prior studies have suggested sexual dysfunction is more common in women with IBD than in the general population and may be further increased in women who have had previous IBD surgery, although findings have been inconsistent (24, 25). Impaired sexual function may also contribute to involuntary infertility and studies evaluating infertility in women with IBD must consider the relative contributions of voluntary and involuntary infertility.

Very-low-quality evidence suggests caesarean section may be more likely in women with prior IBD-related surgery compared to women without. However, insufficient information was available to determine if this association reflected physician and patient preference or obstetric indications. A survey of Canadian gastroenterologists reported very little consensus regarding the impact of mode of delivery among women with IPAA (26). Recently published clinical practice guidelines recommend caesarean section for women with IPAA due to concerns about pouch function and sphincter injury after vaginal delivery (27), but were based on limited evidence. The guidelines also recommend women with active perianal disease deliver by caesarean section. For all other women with IBD, regardless of surgical history, vaginal delivery is recommended unless there are obstetric reasons for caesarean section (27). Increasing evidence points to the safety of vaginal delivery for women without IPAA or active perianal disease, despite earlier concerns that vaginal delivery might increase the risk of perianal disease (28).

In conclusion, there is limited information about the impact of IBD-related surgery on the risk of female infertility. Although there were associations between IBD-related surgery and some secondary outcomes (miscarriage, use of ART, caesarean section and low birth weight), these findings were based on very-low-quality evidence from studies with small sample sizes that did not account for other disease-related factors (e.g., disease activity). To better evaluate how surgery impacts female infertility and pregnancy outcomes, well-designed, large, prospective cohort studies with detailed information on IBD disease activity and phenotype, medical and surgical treatment and attempted pregnancies and outcomes are needed. Health care providers should counsel women that the risk of infertility after intra-abdominal surgery may be increased; additionally, patients should be aware that the existing research is of poor quality and limited quantity.

## Supplementary Data

Supplementary data are available at *Journal of the Canadian Association of Gastroenterology* online.

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