A systematic review and meta-analysis of outcomes after elective surgery for ulcerative colitis

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Abstract

Aim Approximately 20%–30% of patients with ulcerative colitis (UC) will undergo surgery during their disease course, the vast majority being elective due to chronic refractory disease. The risks of elective surgery are reported variably. The aim of this systematic review and meta-analysis is to summarize the outcomes after elective surgery for UC.

Methods A systematic review was conducted that analysed studies reporting outcomes for elective surgery in the modern era (>2002). It was prospectively registered on the PROSPERO database (ref: CRD42018115513). Searches were performed of Embase and MEDLINE on 15 January 2019. Outcomes were split by operation performed. Primary outcome was quality of life; secondary outcomes were early, late and functional outcomes after surgery. Outcomes reported in five or more studies underwent a meta-analysis of incidence using random effects. Heterogeneity is reported with I^2, and publication bias was assessed using Doi plots and the Luis Furuya-Kanamori index.

Results A total of 34 studies were included (11 774 patients). Quality of life was reported in 12 studies, with variable and contrasting results. Thirteen outcomes (eight early surgical complications, five functional outcomes) were included in the formal meta-analysis, all of which were outcomes for ileal pouch–anal anastomosis (IPAA). A further 71 outcomes were reported (50 IPAA, 21 end ileostomy). Only 14 of 84 outcomes received formal definitions, with high inter-study variation of definitions.

Conclusion Outcomes after elective surgery for UC are variably defined. This systematic review and meta-analysis highlights the range of reported incidences and provides practical information that facilitates shared decision making in clinical practice.

Keywords ulcerative colitis, surgery, inflammatory bowel disease, outcomes research

Introduction

Ulcerative colitis (UC) is a chronic, relapsing–remitting condition of the colon and rectum [1]. It causes debilitating symptoms such as bleeding per rectum, frequency of defaecation, abdominal pain and tenesmus [2]. UC is managed primarily via a variety of anti-inflammatory and immunosuppressant medications such as aminosalicylates, corticosteroids, anti-tumour necrosis factor (anti-TNF) agents, vedolizumab, ustekinumab and tofacitinib [3–7]. Despite medical treatment, approximately 20%–30% of patients require surgery during their disease course [8]. Patients may undergo emergency surgery; however, the vast majority of patients undergo elective surgery due to chronic refractory disease [9].

The decision between elective surgery and continued medical therapy is said to be preference-sensitive, in that it depends on patient preferences due to clinical equipoise in the area [10]. The same can be said for the decision between reconstructive operations and remaining with a permanent stoma. The most common reconstructive operation – ileal pouch–anal anastomosis (IPAA) – avoids a permanent stoma; however, it is associated with complications such as pouchitis, increased stool frequency and faecal incontinence [11]. A permanent stoma offers more control over excretory functions but carries significant psychosocial consequences and complications such as parastomal hernia [12].

Shared decision making is a process whereby clinicians share the most up-to-date clinical information on

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the risks and benefits of a procedure to allow the patient to make a decision based on their preferences [13]. Operative options for UC, particularly reconstructive operations, remain low volume operations and complications from such operations are reported variably within the literature [11,14]. One previous systematic review reports outcomes after colectomy, but includes both emergency and elective procedures in data synthesis [11]. In order to fully counsel our patients, it is imperative to have accurate and up-to-date information on the safety and outcomes of elective surgery for UC.

The aim of this review is to summarize evidence of the most up-to-date clinical outcomes following elective surgery for UC, including both short- and long-term complications, functional outcomes and quality of life (QoL). This review forms part of a larger body of work in the creation of a decision aid for patients considering elective surgery or ongoing medical therapy.

Method

Methodological framework

The review was conducted with reference to the *Cochrane Handbook for Systematic Reviews* [15] and is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16]. The review protocol was prospectively registered on the PROSPERO database (ref: CRD42018115513) [17]. An electronic database search was undertaken on 15 January 2019 using a pre-defined search strategy (Table S1). The search strategy was kept deliberately broad to encompass as many studies as possible. The electronic databases searched were MEDLINE (via OvidSP) and Embase (via OvidSP). Titles and abstracts were screened for eligibility using the Rayyan web application [18] by two independent researchers (DMB, AMF), with conflicts resolved by a third researcher (MJL). Full texts were retrieved and screened against the eligibility criteria. All systematic reviews returned from the search were hand searched for papers which were reassessed at full text against the inclusion criteria.

Eligibility criteria

All studies in English including adult patients (> 18 years of age) reporting any outcome after elective surgery for UC performed during or after 2002 (post-biologic introduction) were eligible for inclusion. This approach has been adopted previously in the literature [11] as it ensures up-to-date surgical

outcomes are collected, primarily as biologic use reduced the need for surgical intervention but also due to universal biologic use affecting postoperative outcomes. Additionally, surgical practice has altered and it is imperative that outcomes are synthesized which reflect modern surgical practice. For studies performed over a number of years prior to and including 2002, the range was set at 5 years before 2002, i.e. 1997–2005. Surgical procedures included the following: total and subtotal colectomy with permanent end ileostomy or diverting ileostomy, IPAA and ileorectal anastomosis, with any performed as open, laparoscopic or robotic approaches, in one, two or three stages. Only studies of 20 patients or more, with a diagnosis of UC, were included. This was chosen as the threshold to capture low sample size QoL studies but exclude case series, case reports or studies with a very small sample which may bias pooling of results. Studies with a mixed population, e.g. UC and familial adenomatous polyposis, were only included if data for patients with UC could be separately identified. Case reports, conference abstracts or review articles were excluded.

Outcomes

The primary outcome was QoL, as previous work by this group illustrated this as the preferred patient informational preference preoperatively [19]. Secondary outcomes were early and late surgical complications as defined by the individual study (a method used previously in systematic reviews for UC [11]) as well as functional outcomes after surgery.

Data extraction

Data were extracted by one investigator (AMF) and verified by a second (DMB). All data were entered into Microsoft Excel® (Microsoft, Redmond, Washington, USA). Basic descriptive details for papers collected were first author, year of publication, journal of publication, country of origin, study period, sample size, surgical procedure(s) and study design. Data were also collected on any outcome (see above) reported within the paper, and the relevant incidence rate was recorded.

Statistical analysis

QoL data are predominantly reported narratively due to the wide range of methods used to report QoL data. Where possible, figurative data are used. Postoperative outcomes were split and pooled according to the

different operation(s) reported in each study. Outcomes that are reported in less than five studies are reported as ranges to allow quantification of the uncertainty around each event. For outcomes that were reported in five or more studies, a meta-analysis of the incidence of each outcome was undertaken using the double arcsine method, with the random-effects (DerSimonian–Laird) model. There is no recommended number of studies required for use of meta-analysis methods [20]; however, we opted for five studies to factor in studies of small sample size to allow more accurate pooling of results. The I^2 statistic was used as a measure of heterogeneity which was not due to chance alone. Heterogeneity was classified as low (< 25%), moderate (25%–75%) or high (> 75%). Publication bias was assessed using the Luis Furuya-Kanamori (LFK) index and by visually inspecting Doi plots. Doi plots and the LFK index were chosen as they have been shown to have a higher sensitivity when used on meta-analyses of this size [21]. An LFK index of −1 to 1 indicates no asymmetry in the plot, 1–2 or (−2 to −1) suggests minor asymmetry and > 2 (or < −2) indicates major asymmetry. Statistical analysis was undertaken using the MetaXL (www.epigear.com) plug-in for Microsoft Excel. A sensitivity analysis was planned to include studies with a sample size of 100 or greater. *Post hoc* analysis of patient demographic data was performed to identify the possibility of subgroup analyses.

Risk of bias

Risk of bias was assessed by one researcher (DMB) and verified by a second (MJL). Risk of bias was assessed using the validated Joanna Briggs Institute prevalence critical appraisal tool [22]. This assessment tool is a validated tool for use in systematic reviews of incidence and prevalence. It contains 10 objective questions (Table S6) to assess the quality of papers reporting incidence and prevalence. Quality of papers was only assessed at full text.

Deviation from the protocol

Appendicectomy was originally listed as included. However, after discussion it was excluded due to it not currently being routinely offered as a surgical option for UC patients in the UK. We also aimed to assess risk of bias using the ROBINS tool; this was found to be an inappropriate tool for assessing risk of bias in our study, however, and thus we changed to the prevalence tool mentioned above. The Cochrane Library was not searched for pragmatic reasons.

Results

Study selection

The study selection process is summarized in Fig. 1. The initial search strategy identified 5420 papers, of which 3777 remained following removal of duplicates. Following screening of abstracts, 277 articles were assessed at full text, of which 245 were excluded, leaving a total of 32 papers for inclusion in analysis. Eight systematic reviews were identified in the initial search which contained 156 papers. Twenty-two were assessed at full text, two of which met the inclusion criteria. This left a total of 34 papers to be included within the final analysis.

Study characteristics

Study characteristics of the 34 included studies are shown in Table 1. The demographics of patients included in each study are shown in Table 2.

In total, 11 774 patients with UC were enrolled across the 34 studies. Of these, 11 686 underwent elective surgery for UC and 88 remained on continued medical therapy. The patients on continued medical therapy were included because they were reported in two studies which were relevant to the outcomes of this review as they compared QoL of elective surgery with continued medical therapy [42,53] A variety of surgical procedures were performed by a laparoscopic, open or robotic approach in one, two or three stages, and included IPAA and subtotal colectomy with permanent end ileostomy. None of the 34 studies were randomized clinical trials. Of the 34 studies included, the most common country of origin was the USA ($n = 15$), whilst the remaining studies were conducted in 13 different countries including Japan ($n = 4$), the Netherlands ($n = 3$) and China ($n = 2$).

Quality of life

Twelve studies assessed QoL in a variety of different patient populations, using a range of different methods and questionnaires (Table S2). Six studies assessed QoL in postoperative IPAA cohorts alone [23,25,26, 30,33,48], two compared QoL before and after surgery for IPAA [28,54], two compared postoperative cohorts of IPAA to ileostomy [29,39] and two compared IPAA to continued medical therapy [42,53]. Due to the large variability in QoL questionnaires used, the variation in study populations and also inter-study variation of
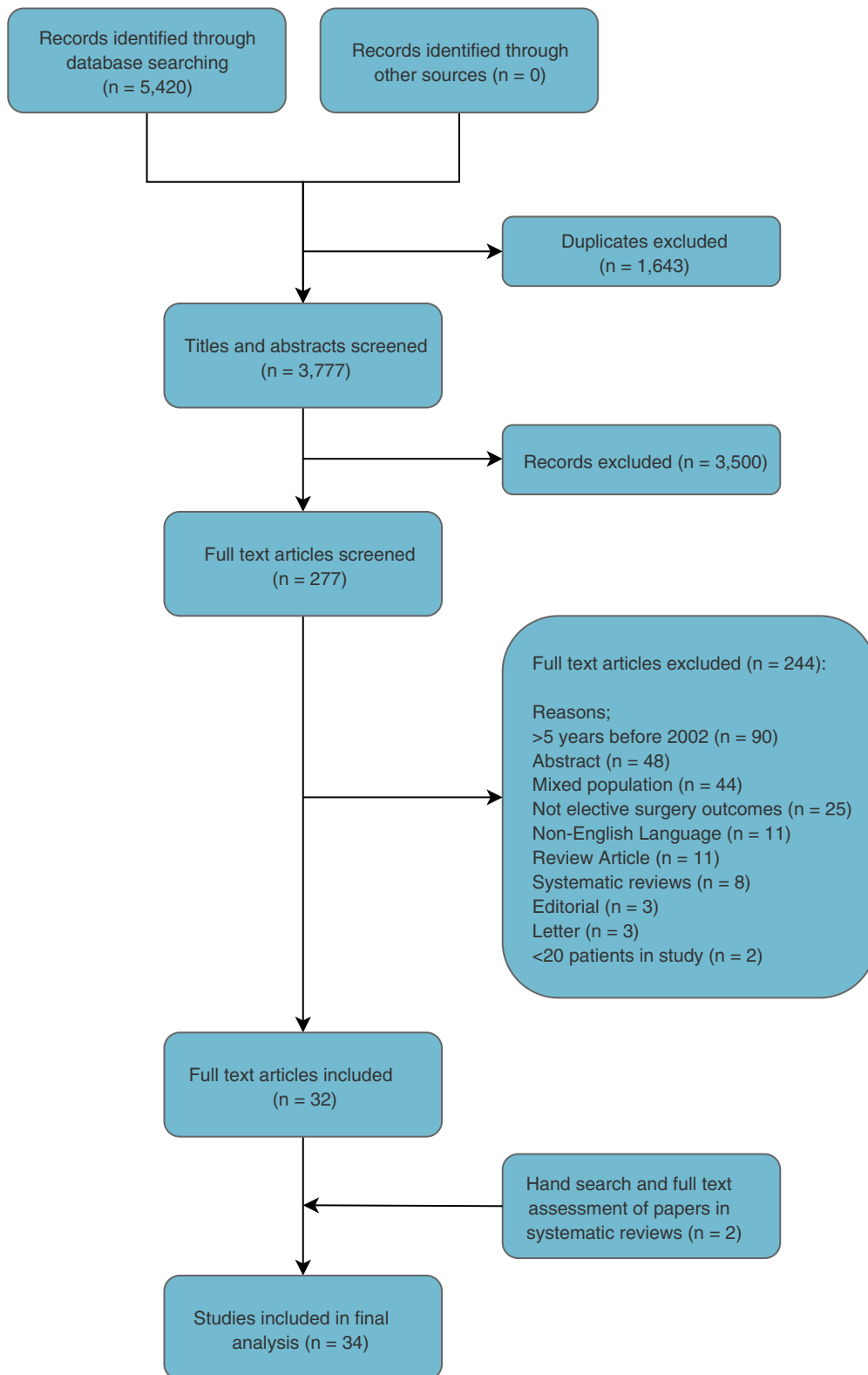
Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram summarising study selection process.

Table 1 Summary of included studies.

Study	Country	Study time period	Design	Sample size	Intervention(s)
Aghdaei *et al.* [23]	Iran	NR	Observational cross-sectional survey	68	IPAA
Baek *et al.* [24]	USA	1998–2004	Retrospective cohort	149	Open IPAA, L-IPAA
Barnes *et al.* [25]	USA	2011–2016	Prospective cohort	243	IPAA
Berndtsson *et al.* [26]	Sweden	NR	Prospective cohort	43	IPAA
Cohan *et al.* [27]	USA	2005–2012	Retrospective cohort	2493	1-stage and 2-stage IPAA
Cohan *et al.* [28]	USA	2006–2014	Prospective cohort	37	IPAA and end ileostomy
Exarchos *et al.* [29]	Greece	2010–2016	Prospective cohort	47	RPC with IPAA
Fasen *et al.* [30]	USA	1998–2008	Prospective cohort	73	2-stage and 3-stage IPAA
Fichera *et al.* [31]	USA	2002–2007	Prospective cohort	179	Open IPAA, L-IPAA
Hasegawa *et al.* [32]	Japan	2002–2006	Retrospective cohort	21	L-IPAA
Heikens *et al.* [33]	Netherlands	1998–2005	Prospective cohort	71	IPAA
Hicks *et al.* [34]	USA	2000–2011	Retrospective cohort	99	IPAA
Holubar *et al.* [35]	USA	2000–2007	Prospective cohort	44	Laparoscopic total proctocolectomy with end ileostomy
Ide *et al.* [36]	Japan	2001–2012	Retrospective cohort	234	RPC with IPAA
Ikeuchi *et al.* [37]	Japan	1999–2003	Prospective cohort	242	1-stage and 2-stage IPAA
Kawamura *et al.* [38]	Japan	2002–2010	Retrospective cohort	28	Laparoscopic RPC with IPAA
Kuruvilla *et al.* [39]	USA	2011	Cross-sectional survey	59	IPAA, subtotal colectomy with end ileostomy
Mark-Christensen *et al.* [40]	Denmark	2003–2014	Prospective cohort	251	Robotic-assisted IPAA, open IPAA
McKenna *et al.* [41]	USA	2002–2013	Retrospective cohort	909	Open, laparoscopic, 2-stage and 3-stage IPAA
Meijs *et al.* [42]	Netherlands	2013	Prospective cohort	58	IPAA
Mineccia *et al.* [43]	Italy	2005–2015	Retrospective cohort	78	L-IPAA, open IPAA
Moore *et al.* [44]	USA	2002–2008	Case–control	60	IPAA
Pandey *et al.* [45]	USA	2002–2008	Prospective cohort	118	2-stage and 3-stage IPAA
Patel *et al.* [46]	USA	2005–2010	Retrospective cohort	4664	Elective colectomy
Ryoo [47]	South Korea	1998–2013	Prospective cohort	72	IPAA
Salehimarzijarani *et al.* [48]	Iran	2006–2012	Cross-sectional survey	39	RPC with IPAA
Samples *et al.* [49]	USA	2003–2010	Retrospective cohort	248	2-stage IPAA
Tan *et al.* [50]	Singapore	1999–2011	Retrospective cohort	89	IPAA
Telem *et al.* [51]	USA	2002–2007	Retrospective cohort	90	Laparoscopic and open subtotal colectomy with end ileostomy
Tulchinsky *et al.* [52]	Israel	NR	Prospective cohort	44	RPC with IPAA
van Gennep *et al.* [53]	Netherlands and Belgium	2010–2015	Retrospective cohort	118	IPAA
Xu *et al.* [54]	China	2008–2016	Retrospective cohort	58	IPAA
Zhu and Xing [55]	China	2010–2013	Prospective cohort	40	L-IPAA and open IPAA
Zittan *et al.* [56]	Canada	2002–2013	Retrospective cohort	758	2-stage and 3-stage IPAA

IPAA, ileal pouch–anal anastomosis; L-IPAA, laparoscopic ileal pouch–anal anastomosis; NR, not reported; RPC, restorative proctocolectomy.

analysis of questionnaires, a formal synthesis of results was not possible. We narratively describe our results below.

A total of six studies report QoL in postoperative IPAA cohorts. Two studies reported general health to be comparable to that of the general population [23,33] following IPAA surgery, whilst physical and mental health were reportedly lower than the general population [23]. Additionally, one study [48] reported QoL to be average or good in 97.4% of the cohort following IPAA surgery. Sexual desire and sexual satisfaction were reported to increase post-surgery [26],

Table 2 Summary of patient demographics of included studies.

Study	Study subgroups	Age, years, mean (SD) [range]	Sex (% men)	Preoperative medication use (%)
Aghdaei et al. [23]	IPAA	39.3 (11.1)	56.9	NR
Baek et al. [24]	Open IPAA Lap IPAA	Open: 34.5 (10.3) Lap: 33.3 (11.3)	Open: 40.7 Lap: 41.4	NR
Barnes et al. [25]	No IPAA symptoms IPAA symptoms	IPAA no symptoms: 18–39 = 48%, 40–59 = 43%, > 60 = 9% IPAA symptoms: 19–39 = 55%, 40–59 = 37%, > 60 = 8%	IPAA no symptoms: 39 IPAA symptoms: 29	NR
Berndtsson et al. [26]	IPAA	35 [22–53]	58.1	NR
Cohan et al. [27]	Age < 50 Age 51–60 Age > 60	Age < 50: n = 1831 Age 51–60: n = 408 Age > 60: n = 254	Age < 50: 55.8 Age 51–60: 65.7 Age > 60: 63	NR
Cohan et al. [28]	Male patient Female patient Male partner Female partner	Male patient: 41 [26–76] Female patient: 34 [25–76] Male partner: 33 [26–69] Female partner: 42 [26–80]	Male patient: n = 25 Female patient: n = 12 Male partner: n = 12 Female partner: n = 25	NR
Exarchos et al. [29]	RPC with IPAA	< 50 = 70.2%	63.8	NR
Fasen et al. [30]	IPAA	38.1 (11.2)	67	NR
Fichera et al. [31]	Open IPAA Lap IPAA	Open: 36.9 Lap: 36.3	Open: 57.8 Lap: 50.7	Steroids: 99 Anti-TNF: 25
Hasegawa et al. [32]	IPAA	29 [16–64]	76.2	NR
Heikens et al. [33]	IPAA	35.1 [29.3–40.3]	40.8	NR
Hicks et al. [34]	IPAA	32.6 (1.4)	55.6	Steroids: 66.7 Anti-TNF: 26.3 Other: 43.4
Holubar et al. [35]	HALS RPC + end ileostomy Lap RPC + end ileostomy Incision-less RPC + end ileostomy	HALS: 63 [30–79] Lap: 70 [50–83] Incision-less: 69 [51–86]	HALS: 70 Lap: 38 Incision-less: 38	NR
Ide et al. [36]	Pelvic sepsis IPAA Non-pelvic sepsis IPAA	Pelvic sepsis: 33.2 (15.2) Non-pelvic sepsis: 26.1 (15.5)	Pelvic sepsis: 31 Non-pelvic sepsis: 54.1	NR
Ikeuchi et al. [37]	1-stage IPAA 2-stage IPAA	1 stage: 30 [15–69] 2 stage: 35.5 [16–68]	1 stage: 48 2 stage: 51	NR
Kawamura et al. [38]	IPAA in severe UC IPAA in mild-mod UC	Severe: 34 [16–64] Mild-mod: 35 [16–66]	Severe: 57 Mild-mod: 62	Other severe: 57 Other mild-mod: 43
Kuruvilla et al. [39]	IPAA Permanent ileostomy	IPAA: 50.7 (14.5) Ileostomy: 54.8 (15.6)	IPAA: 65.7 Ileostomy: 69.6	NR
Mark-Christensen et al. [40]	Open IPAA Robot assisted IPAA	Open: 36.5 (12.7) Robot: 35.4 (13.6)	Open: 56 Robot: 52	NR
McKenna et al. [41]	IPAA in obese patients IPAA in non-obese patient	Obese: 42.5 Non-obese: 37.1	Obese: 57.8 Non-obese: 59.7	Steroids obese: 44.2 Steroids non-obese: 37.2 Anti-TNF obese: 19 Anti-TNF non-obese: 21.3 Other obese: 21.4 Other non-obese: 21.9

Table 2 (Continued).

Study	Study subgroups	Age, years, mean (SD) [range]	Sex (% men)	Preoperative medication use (%)
Meijs et al. [42]	IPAA Continued anti-TNF	IPAA: 42 [22–67] Anti-TNF: 45 [19–68]	IPAA: 51.7 Anti-TNF: 35	NR
Mineccia et al. [43]	Open IPAA Lap IPAA	Open: 45 Lap: 37	Open: 72.9 Lap: 56.6	Steroids open: 97.9 Steroids lap: 100 Anti-TNF open: 4.2 Anti-TNF lap: 16.7 Other open: 47.9 Other lap: 86.6
Moore et al. [44]	African American IPAA patients Caucasian patients	African American: 39.7 Caucasian: 45.8	African American: 41.7 Caucasian: 56.3	NR
Pandey et al. [45]	2-stage IPAA 3-stage IPAA	2 stage: 37.5 (12.5) 3 stage: 35 (10.9)	2 stage: 50 3 stage: 60	Steroids 2 stage: 67 Steroids 3 stage: 96 Anti-TNF 2 stage: 16 Anti-TNF 3 stage: 43
Patel et al. [46]	Elective colectomy	43.95	56.7	Steroids: 39.9
Ryoo [47]	IPAA	< 40 = 34.7%	38.9	NR
Salehimarzijarani et al. [48]	RPC with IPAA	37 [18–63]	51.3	NR
Samples et al. [49]	Classic 2-stage Variant 2-stage	Classic: 38 [28–54] Variant: 38 [26–52]	Classic: 51.8 Variant: 54.1	Steroids classic: 73.4 Steroids variant: 83.5 Anti-TNF classic: 20.1 Anti-TNF variant: 32.1 Other classic: 44.6 Other variant: 31.2
Tan et al. [50]	IPAA	46 [28–54]	61.8	NR
Telem et al. [51]	Open IPAA Lap IPAA	Open: 42.6 (4.48) Lap: 39.8 (5.62)	Open: 61 Lap: 45	Steroids open: 95 Steroids lap: 90 Other open: 89 Other lap: 83
Tulchinsky et al. [52]	RPC with IPAA pregnancy outcomes	30 (8.0)	0	NR
van Gennep et al. [53]	IPAA Anti-TNF	IPAA: 45.8 (12.4) Anti-TNF: 40.9 (14.8)	IPAA: 45.8 Anti-TNF: 57.6	NR
Xu et al. [54]	IPAA	37.5 [27.8–52]	32.8	Steroids: 51.7 Other: 12.1
Zhu and Xing [55]	Open IPAA HALS IPAA	Open: 43[22–65] HALS: 39 [23–74]	Open: 45 HALS: 40	NR
Zittan et al. [56]	IPAA	37.1 (12.1)	57.6	Steroids: 50.9 Anti-TNF: 57.6 Other: 18.8

HALS, hand assisted laparoscopic surgery; IPAA, ileal pouch–anal anastomosis; NR, not reported; RPC, restorative proctocolectomy; Anti-TNF, anti-tumour necrosis factor.

despite a different study reporting that there was no change in the quality of relationships after surgery [30]. Barnes et al. [25] report 82% of the patients in their cohort to experience pouch-related symptoms – with an impact on QoL through pain interference, depression, decreased social function and increased levels of fatigue.

Two studies reported QoL both before and after surgery for IPAA to allow for a comparison of QoL parameters. Cohan et al. [28] report a significant increase in the median score for both men and women in physical function (men 60–91/100, women 49–85/100) and mental function (men 62–83/100, women 57–80/100) after IPAA surgery when using the Short Form 36 (SF-36) questionnaire. They also report a significant increase in sexual function in both sexes. Xu et al. [54] describe 54% of the patients in their cohort

having over a 50% improvement in their Cleveland Global Quality of Life (CGQL) score following IPAA surgery.

Two studies compared IPAA patients to ileostomy patients. One of these studies used questionnaires on a patient population before and 8 weeks after closure of their defunctioning ileostomy [29]. This study reported a significant increase in both the Inflammatory Bowel Disease Questionnaire (153.3–178/250, $P < 0.05$) and CGQL (17.4–23.4/30, $P < 0.001$) scores following closure of the ileostomy. This is in keeping with the study by Kuruvilla et al. [39] who also describe a significantly increased CGQL in IPAA patients compared to ileostomy cohorts (0.9 vs 0.8 respectively, $P < 0.05$). Contrary to this, Kuruvilla et al. also utilize the Inflammatory Bowel Disease Questionnaire and EQ-5D-3L questionnaires and found no significant difference in global QoL when comparing IPAA and ileostomy, despite ileostomy patients reporting decreased social and sexual functioning. Notably, no studies commented on the need for medication after surgery or return to work following surgery.

Two studies compared IPAA to continued medical therapy and were contradictory in their conclusion, despite both using the SF-36 for global QoL assessment. Meijs et al. [42] describe no significant difference in global QoL between the cohorts, whereas van Gennep et al. [53] describe a significantly improved global QoL when undergoing IPAA. Both studies also used the Colorectal Functional Outcome Questionnaire which yielded similar results, reporting IPAA to significantly increase stool frequency and the need for anti-diarrhoeal medication.

Ileal pouch–anal anastomosis outcomes

A full list of early and late outcomes for IPAA is provided in Table 3. A total of 35 early surgical complications were reported following IPAA reconstructive surgery across 21 studies, but only seven studies defined short-term complications as within 30 days of surgery. Eleven studies reported eight late postoperative outcomes with only four studies specifying the length of follow-up, although this was variable between studies.

Eight of the early surgical complications were reported in five or more studies and underwent formal meta-analysis. A summary of the incidence and 95% confidence intervals is provided in Fig. 2; forest plots for each meta-analysis are provided in Figs S1–S8. The incidence of small bowel obstruction (11.3%, 95% CI 6.6%–17.1%, I^2 93%) was reported in 11 studies, whilst wound infection (13.4%, 95% CI 9.5%–17.8%, I^2 91%) was reported in 10 studies. Ileus (11.7%, 95% CI 6.3%–

18.4%, I^2 89%) and anastomotic leak (6.1%, 95% CI 2.5%–11.1%, I^2 88%) were both reported in eight studies. Deep vein thrombosis (4.7%, 95% CI 3.3%–6.3%, I^2 66%) was reported in six studies. Urinary tract infections (4.1%, 95% CI 0.94%–7.1%, I^2 94%), pneumonia (2.3%, 95% CI 0.94%–4.2%, I^2 75%) and intraabdominal collection (5.3%, 95% CI 2.1%–9.6%, I^2 68%) were all reported in five studies. Doi plots (Figs S9–S16) and LFK indices indicated high levels of heterogeneity with six of the eight complications showing major asymmetry within the Doi plots.

IPAA pouch complications and functional outcomes

Sixteen studies reported 20 long-term pouch complications and functional outcomes (Table 4) with five reporting follow-up time, four as a minimum of 1 year and the other as 3–6 months. Pouch outcomes were reported variably, e.g. most studies calculated mean stool frequency; however, others opted to categorize stool frequency as 1–6 or > 6.

Five of the pouch outcomes were reported in five or more studies and underwent formal meta-analysis. A summary of the incidence and 95% confidence intervals is provided in Fig. 3; forest plots for each meta-analysis are provided in Figs S17–S21. Chronic pouchitis (23.0%, 95% CI 16.5%–30.2%, I^2 91%) was the most frequently reported pouch outcome ($n = 14$). Anal stricture was reported in eight studies (10.8%, 95% CI 6.7%–15.6%, I^2 85%), pouch failure (5.5%, 95% CI 1.9%–10.6%, I^2 85%) in seven studies and both pouch fistula (6.6%, 95% CI 3.2%–11%, I^2 72%) and faecal incontinence (18.6%, 95% CI 5.8%–35.8%, I^2 95%) were reported in five studies. Doi plots (Figs S22–S26) and LFK indices suggested publication bias in three of the outcomes, moderate bias in one and no bias in one.

Subtotal colectomy with ileostomy outcomes

A total of 18 early surgical complications were reported in three studies [35,46,51] (Table 5). One study [39] reported three late complications of an end ileostomy with a sample size of 24 patients. The complications reported were peristomal skin irritation (13%), parastomal hernia (39.1%) and stoma leak (17.4%).

Outcome definitions

Of the 35 studies in this review, five did not provide outcome definitions as either (i) they reported mortality only or (ii) they reported QoL only. Of the remaining studies, 18 of the 30 did not report any definition of

Table 3 Early and late IPAA complications.

Outcome	Number of studies reporting outcome	Reported incidence* (%)	Reference of studies reporting outcome
Early complications			
Small bowel obstruction	11	11.3 (6.6–17.1)	31, 32, 37, 38, 40, 41, 43, 45, 53, 54, 56
Intestinal perforation	1	4.8	31
DVT	6	4.7 (3.3–6.3)	29, 31, 34, 41, 47, 56
Wound infection	10	13.4 (9.5–17.8)	27, 38, 41, 45, 47, 49, 50, 54, 55, 56
Anastomotic leak	8	6.1 (2.5–11.1)	31, 34, 38, 40, 43, 53, 54, 56
UTI	5	4.1 (0.94–9.1)	37, 41, 45, 50, 56
Ileus	8	11.7 (6.3–18.4)	29, 31, 34, 41, 45, 47, 50, 55
Haemorrhage (postoperative)	2	3.2–8.3	40, 47
Pelvic abscess	3	1.7–17.8	30, 53, 56
30-day readmission	2	28.3–30.2	34, 40
Cardiac arrest	1	0.12	27
Pneumonia	5	2.3 (0.94–4.2)	27, 47, 50, 55, 56
Wound dehiscence	1	1.04	27
Sepsis	3	1.3–7.9	27, 43, 55
PE	1	1.04	27
30-day mortality	2	0.24–0.55	27, 31
30-day reoperation	2	6.5–7.5	27, 55
Intraabdominal collection	5	5.3 (2.1–9.6)	29, 40, 45, 50, 55
Tubo-ovarian abscess	1	2.1	29
Acute pouchitis	3	0.44–17	29, 41, 53
Pelvic sepsis	4	8.9–18.9	33, 34, 36, 41
Major complication (Clavien–Dindo > 4)	1	17.9	38
Anal stricture dilation	1	22.3	31
Pouch leak	2	6.6–11.1	37, 45
Portal vein thrombosis	1	11.9	45
Any pulmonary complication	1	3.4	45
Perianal abscess	1	0.8	40
Pouch fistula	1	1.2	40
Abdominal wall haematoma	1	0.8	40
Anastomotic stenosis	1	2.8	40
Parastomal hernia	1	0.4	40
Pneumothorax	1	0.4	40
Any infectious complication	1	13.7	37
Length of stay	3	4–72 days	32, 45, 55
Operative time	1	359–560 min	32
Late complications			
Impotence	3	4.2–40.5	22, 25, 33
Small bowel obstruction	4	1.7–19.5	23, 34, 38, 53
Pelvic abscess	1	8.1	23
Sexual dysfunction	2	11.3–33.1	23, 41
Infertility	1	37	52
Incisional hernia	3	2.7–5.2	34, 47, 54
Perianal abscess	1	7	38
Ileus	1	13.8	47

DVT, deep vein thrombosis; IPAA, ileal pouch–anal anastomosis; PE, pulmonary embolism; UTI, urinary tract infection.
*Reported as pooled incidence with 95% confidence interval for outcomes reported in five or more studies. For outcomes reported in less than five studies they are reported as a range.
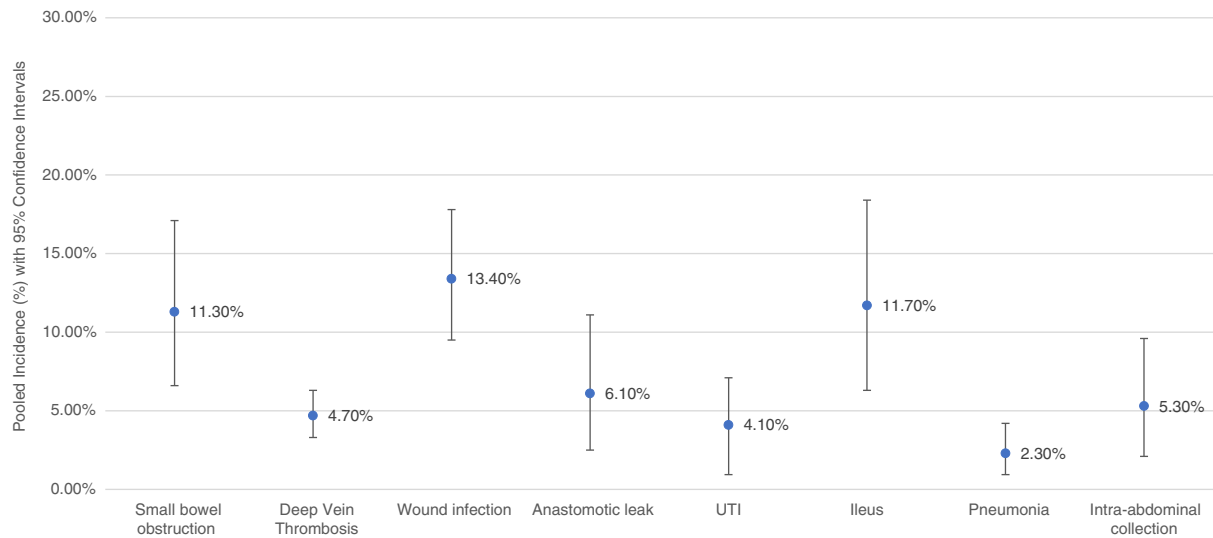
Figure 2 Summary of meta-analysis of early complications following ileal pouch–anal anastomosis.

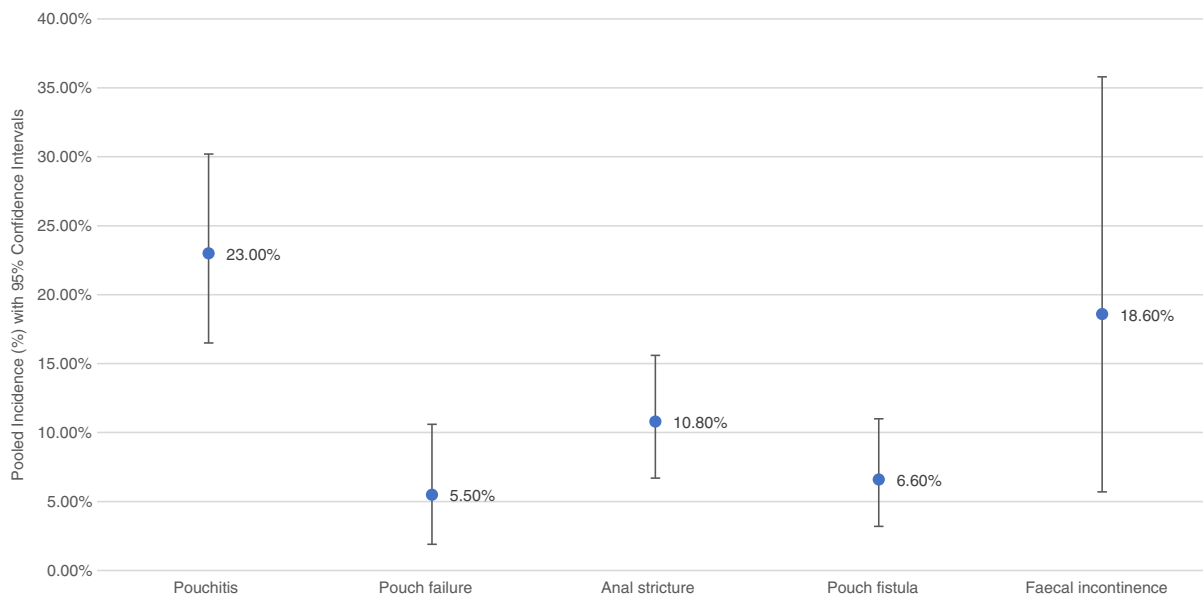**Table 4** IPAA pouch complications and functional outcomes.

Outcome	Number of studies reporting outcome	Reported incidence* (%)	Reference of studies reporting outcome
IPAA complications			
De novo Crohn's of the pouch	1	25	44
Chronic pouchitis	14	23.0 (16.5–30.2)	22, 23, 30, 33, 34, 38, 39, 41, 43, 44, 47, 49, 53, 54
Pouch failure	7	5.5 (1.9–10.6)	33, 34, 43, 44, 47, 54, 56
Pouch fistula	5	6.6 (3.2–11.0)	33, 34, 47, 54, 56
Faecal incontinence	5	18.6 (5.8–35.8)	22, 30, 39, 41, 54
Night defaecation	1	14	22
Anal pain	1	11.4	22
Pouch leakage	2	8.1–10.1	22, 49
Frequency	1	10.1	22
Anal stricture	8	10.8 (6.7–15.6)	23, 31, 33, 34, 49, 53, 54, 56
Pouch excision	1	3.4	23
Stool frequency 1–6	1	57.3	23
Stool frequency > 6	1	42.8	23
Night stools 1–2	1	75.2	23
Night stools > 2	1	23.4	23
Stool frequency (mean)	4	6–6.8 stool/day	30, 31, 39, 41
Stool frequency by night (mean)	3	1.9–2 stools/night	30, 39, 41
Use of anti-diarrhoeals	2	36.6–57.5	30, 33
'Very well' functioning pouch	1	44.9	43
'Adequate' functioning pouch	1	49	43

IPAA, ileal pouch–anal anastomosis.

*Reported as pooled incidence with 95% confidence interval for outcomes reported in five or more studies. For outcomes reported in less than five studies they are reported as a range.

the outcome measures used in their study. In the remaining 12 studies, 14 of the 84 outcomes received formal definitions (Table S3). Chronic pouchitis (*n* = 5, three variations of definition) was the most frequently defined, followed by pouch failure (*n* = 3, no variations) and small bowel obstruction (*n* = 2, two variations). The remaining outcomes were only defined once so could not yield variable definitions.

Figure 3 Summary of meta-analysis of pouch long term and functional outcomes.

Table 5 Subtotal colectomy with ileostomy outcomes.

Outcome	Number of studies reporting outcome	Reported incidence* (%)	Reference of studies reporting outcome
Early complications			
Small bowel obstruction	2	2.2–9.1	35, 51
Deep vein thrombosis	2	2.2–2.4	35, 46
Wound infection	3	6.8–14	35, 46, 51
Urinary retention	1	6.8	35
Urinary tract infection	2	4.4–4.5	35, 46
Ileus	2	2.2–12	35, 51
Pelvic abscess	1	2.2	35
30-day readmission	2	12–13.6	35, 51
Cardiac arrest	1	0.19	46
Pneumonia	1	1.8	46
Wound dehiscence	1	3.3	51
Sepsis	1	7.9	46
Pulmonary embolism	1	0.79	46
30-day mortality	1	0.67	46
30-day reoperative rate	1	7.4	46
Major complications (Clavien–Dindo > 3)	1	9.9	35
Acute renal failure	1	0.33	46
Length of stay	2	3–72 days	35, 46

*Reported as range of incidence reported across studies.

Sensitivity analysis

A sensitivity analysis was performed on studies with a cohort of patients which was greater than 100 to compare results of the meta-analysis with only larger cohort studies (Table S4). Compared to overall rates, generally there was not a large difference in pooled incidence when using large cohorts only. Urinary tract infections (4.1% *vs* 2.6%), ileus (11.7% *vs* 8.9%) and pouch failure (5.5% *vs* 2.5%) had the largest reduction in incidence,

whereas intraabdominal collection (5.3% *vs* 6.7%) and chronic pouchitis (23% *vs* 23.6%) had a minor rise in incidence for larger cohorts. Heterogeneity using the I^2 statistic increased for all meta-analysis outcomes when using larger cohort studies only.

Quality (risk of bias) assessment
Risk of bias was variable across the studies included within our final analysis (Table S5); however, one of the included studies used qualitative methodology and thus could not be formally assessed. Generally, included studies recruited participants appropriately and performed appropriate statistical analyses. Twenty-four of the included studies did not have an adequate sample size and 23 did not use objective criteria for the measurement of their outcomes. Studies were poor at commenting on the coverage of data within their sample – in particular reporting how they dealt with missing or incomplete data and the impact on reported incidence rates. Lastly, only nine of the studies assessed provided clear information on the effect of confounding factors on the data reported.

Discussion

This systematic review and meta-analysis reports outcomes after elective surgery for UC. Importantly, in order to be able to counsel those considering elective surgery for UC, and in contrast to previous reviews, only patients undergoing elective surgery have been included. In addition, the cohorts were restricted to patients who underwent surgery during or after 2002. This method has been adopted previously in the literature as this is when routine biologic agents became universally available in clinical practice [11]. In this review, 34 studies were identified with a total of 11 774 patients enrolled across the studies.

QoL was reported using a variety of different tools and was measured both in isolated IPAA operative cohorts and in comparator studies to ileostomy patients or medical therapy patients. Generally, QoL was reported to be increased for patients undergoing IPAA, despite a significant number of patients experiencing pouch-related symptoms [25]. Studies comparing continued medical therapy to elective surgery contrasted in that QoL was reported to be superior in elective surgery in one study [53] but comparable in another [42], despite utilization of the same QoL questionnaire. This is probably due to heterogeneity in the study population but may also represent differential analysis utilized within each study. The variability observed in studies reporting QoL further reiterates the equipoise in this decision, and that the decision should be based on patient preferences.

Identified studies reporting outcomes following elective surgery for UC predominantly focus on IPAA – the most common reconstructive operation in the time period studied. In our review, only 14 of the 84 outcomes reported received a formal definition within the original study, and importantly definitions of the same outcome were often variable between studies. This is further illustrated in our risk of bias assessment where only 10 studies used objective, standard criteria for measurement of a condition, although the majority of these studies used validated QoL questionnaires. Recent systematic reviews in colorectal surgery have highlighted the range of definitions used within studies for the same outcome [57,58]. The results of our review highlight not only the need for a core outcome set when reporting elective surgery for UC but also the need to provide formal definitions of outcome measures *a priori*.

There are some limitations to our study. There was a high degree of heterogeneity within our meta-analysis. It is likely that the heterogeneity within our study is due to the lack of definition of outcome measures, variability in definitions of those that were defined and also variation in the length of follow-up time between studies. Intervention factors may also contribute to the observed heterogeneity, particularly the number of stages over which an IPAA was carried out. Whilst the *Cochrane Handbook* does not advocate meta-analysis in settings of high heterogeneity, we have made a conscious decision to perform this here for two reasons. First, without the pooling of data there is a wide range of incidences that could be quoted to patients which could lead to overestimation or underestimation of outcomes, which may directly influence patient decision making. Second, quantifying the levels of uncertainty around an event – or in this case high levels of heterogeneity – is noted to be an essential component to shared decision making in clinical practice [59]. By providing clinicians with a single incidence rate of common outcomes, with the levels of uncertainty around these outcomes, we provide the materials to clinicians to facilitate shared decision making in clinical practice in the context of elective surgery for UC. We recognize that we did not search the Cochrane Library for pragmatic reasons and it may yield additional studies; however, our combination of MEDLINE and Embase has been proved not to affect the significance of results of meta-analyses in the vast majority of cases [60].

We did not perform a subgroup analysis as *post hoc* visualization of the included patient demographics demonstrated a gross variation in reporting of demographics that made identification of subgroups not possible. The most pertinent subgroup which we could not

identify is those on preoperative biologics: however, there are several publications within the literature that note either no or a very small increased impact of the use of biologics on postoperative outcomes in UC patients [61,62].

Outcomes were split by early and late complications as defined by the individual study, although many studies did not provide formal definitions of these time periods. We still opted to compile the results in this way as this method has been previously adopted in the literature by Peyrin-Biroulet *et al.* [11]. In our review we opted not to meta-analyse QoL data for a variety of reasons: primarily a large number of different questionnaires were used, but also questionnaires were analysed differently depending on the individual study methodology; thus formal synthesis was not possible or comparable. It is therefore recommended that when counselling patients on QoL after surgery, clinicians summarize the general QoL findings reported in this study but also the uncertainty in QoL post-surgery – noting that the literature around QoL is contrasting. Finally, we restricted the sample size of included studies to 20 or more patients. Small sample sizes may introduce bias into the observed incidence in a particular study; however, as we aimed to review all outcomes as well as QoL, it was necessary to maintain a low threshold for inclusion. A sensitivity analysis was performed to examine the effect of sample size on observed incidence. The exclusion of smaller studies (< 100 participants) led to minor alterations in observed incidence in all outcomes that were meta-analysed. Heterogeneity increased in all outcomes following the removal of smaller studies which further supports the need for inclusion of smaller studies in our meta-analysis.

In summary, both short- and long-term complications following surgery for UC are common and variably reported. QoL studies produce variable results and it is clear that there are contrasting results in QoL before and after elective surgery for UC, as well as between the different reconstructive surgical options. It is therefore essential that clinicians adopt a shared decision making model in clinical practice to allow patients to consider the risks and benefits of all options to ultimately make a decision based on their preferences. The results of this systematic review and meta-analysis provide an up-to-date quantification of the clinical outcomes following elective surgery for UC, and the different reconstructive surgical operations, in the era of routine biologic use. It is anticipated that the results of this study will guide clinicians in their reporting of risks to patients, as well as provide information on the levels of uncertainty around such events. The significant limitations of this meta-analysis can only be resolved if future studies include (i) a core outcome set for studies reporting elective surgery for UC (including a standardized measure of QoL) and (ii) high-quality prospective data collection.

Conflicts of interest

Alan Lobo is a consultant, advisory board member or received lecture fees for MSD, Janssen, Pfizer, Takeda Pharma, AbbVie, Dr Falk, Shield Pharmaceuticals and Vifor Pharma. The other authors have no conflicts of interest to declare.

Author contributions

All authors provided intellectual input into the study design and methodology. DMB, AMF and MJL screened texts, performed data extraction and risks of bias assessment. DMB and MJL drafted the manuscript. All authors provided comments and edited the manuscript to become the final version for submission. All authors approved the final version of the manuscript.

Data availability statement

There is no primary data within this manuscript to share.

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Supporting Information

Additional Supporting Information may be found in the online version of this article: