Living with Ulcerative Colitis Study (LUCY) in England: a retrospective study evaluating healthcare resource utilisation and direct healthcare costs of postoperative care in ulcerative colitis

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ABSTRACT
Objective Ulcerative colitis (UC) is a lifelong, relapsing–remitting disease. Patients non-responsive to pharmacological treatment may require a colectomy. We estimated pre-colectomy and post-colectomy healthcare resource utilisation (HCRU) and costs in England.

Design/Method A retrospective, longitudinal cohort study indexing adult patients with UC undergoing colectomy (2009–2015), using linked Clinical Practice Research Datalink/Hospital Episode Statistics data, was conducted. HCRU, healthcare costs and pharmacological treatments were evaluated during 12 months prior to and including colectomy (baseline) and 24 months post-colectomy (follow-up; F–U), comparing baseline/F–U, emergency/elective colectomy and subtotal/full colectomy using descriptive statistics and paired/unpaired tests.

Results 249 patients from 26 165 identified were analysed including 145 (58%) elective and 184 (74%) full colectomies. Number/cost of general practitioner consultations increased post-colectomy (p<0.001), and then decreased at 13–24 months (p<0.05). From baseline to F–U, the number of outpatient visits, number/cost of hospitalisations and total direct healthcare costs decreased (all p<0.01). Postoperative HCRU was similar between elective and emergency colectomies, except for the costs of colectomy-related hospitalisations and medication, which were lower in the elective group (p<0.05). Postoperative costs were higher for subtotal versus full colectomies (p<0.001). At 1–12 month F–U, 30%, 19% and 5% of patients received aminosalicylates, steroids and immunosuppressants, respectively.

Conclusion HCRU/costs increased for primary care in the first year post-colectomy but decreased for secondary care, and varied according to the colectomy type. Ongoing and potentially unnecessary pharmacological therapy was seen in up to 30% of patients. These findings can inform patients and decision-makers of potential benefits and burdens of colectomy in UC.

INTRODUCTION
Ulcerative colitis (UC) is a relapsing–remitting inflammatory bowel disease. Patients usually present with bloody diarrhoea, abdominal pain, urgency and tenesmus. Globally, UC prevalence ranges from 2.4 to 505 cases/100 000 people, with an estimated annual incidence of 10/100 000 people, and a prevalence of approximately 240/100 000 (around 146 000 cases) in the UK.

Various pharmacological UC treatments exist, including aminosalicylates (5-ASAs), corticosteroids, immunosuppressants, biologics...
and tofacitinib. European guidelines recommend sustained steroid-free remission as the treatment goal. 7-9 Despite these options, some patients with UC require a colectomy. 10

The highest colectomy rates are seen during the first few years after diagnosis. 11 Patients usually undergo colectomy due to acute severe UC (10%-60% of patients). 12-14 A retrospective analysis reported that 56% of patients with UC who were non-responders to infliximab underwent colectomy. 15 International studies reported colectomies in 7%-10% of patients with UC, with decreasing colectomy rates over recent years. 16-18

Active UC is associated with reduced health-related quality of life (HRQoL) and productivity, 19-24 frequent visits to accident and emergency departments (A&E), hospital stays and healthcare costs, 24-26 with greater costs with increasing frequency of relapse. 27 Although colectomy may be life-saving, it was recommended not to be considered a cure for UC. 28 Patients undergoing colectomy can still experience poor HRQoL, 28-31 anxiety and depression, problems with body image and sexual function, and decreased productivity. 32 Approximately one-third of patients having UC-related surgery experience some form of postoperative complications 33; and these can result in substantial humanistic and economic burden. 34

Although studies report high costs associated with UC-related surgery, there are limited data on healthcare resource utilisation (HCRU) in postoperative settings. 35,36 Surgery in UC may be an emergency or elective procedure 37; costs associated with emergency versus elective procedures were reported to be higher. 38

We aimed to estimate preoperative and postoperative HCRU and direct healthcare costs among patients with UC undergoing a colectomy, and to examine preoperative and postoperative patterns of concomitant medication use, postoperative complications and the association of colectomy type with HCRU, direct healthcare costs and postoperative medication use.

**Materials and Methods**

**Study design**

This study used linked Clinical Practice Research Datalink (CPRD), GOLD and Hospital Episode Statistics (HES) data (this study is based in part on data from the Clinical Practice Research Datalink obtained under licence from the UK Medicines and Healthcare products Regulatory Agency. The data are provided by patients and collected by the NHS as part of their care and support. The interpretation and conclusions contained in this study are those of the author/s alone; copyright 2017, reused with the permission of the Health and Social Care Information Centre. All rights reserved; the OPCS Classification of Interventions and Procedures, codes, terms and text is Crown copyright (2016) published by the Health and Social Care Information Centre, also known as NHS Digital, and licensed under the Open Government Licence available at http://www.nationalarchives.gov.uk/doc/open-government-licence/version/3/). CPRD captures anonymised data related to all primary care patient interactions at participating general practitioner (GP) practices in the UK. 39 HES captures details on all secondary care patient interactions at NHS hospitals in England, with limited data on treatments prescribed; only high-cost drugs are observed and specific treatments can rarely be identified. 40

A retrospective, longitudinal cohort study was conducted (online supplementary figure 1). The study cohort comprised of adult patients (aged 18 or over) undergoing a colectomy between 1 January 2009 and 31 December 2015 (indexing period), with a prior UC diagnosis, and continuously registered with the GP practice for the 12-month period prior to (ie, baseline) and 24-month period following (ie, follow-up; F-U) colectomy. The first/earliest colectomy observed determined the index date. Patients with a colectomy recorded in the 12 months prior to the index event were excluded, as were patients with a diagnosis of Crohn’s disease and/or cancer (due to overlap in high-cost drug coding for UC and cancer treatments) recorded within the study period (1 January 2008–31 December 2017). Code lists for study cohort identification are detailed in online supplementary table S1.

Patients undergoing elective and emergency colectomies (defined according to type of hospital admission), and subtotal and full colectomies, were considered. As the latter could not be ascertained from the procedural coding system used, the index colectomy was classified as subtotal if an additional colectomy-related procedure was recorded during F-U.

**Outcomes**

Outcomes measured included baseline demographics and clinical characteristics, HCRU/costs and postoperative complications.

Direct healthcare costs were calculated at baseline and F-U by imputing unit costs to a range of healthcare resources. Costs of prescriptions (primary care only) for
5-ASAs, steroids and immunosuppressants were calculated using net ingredient costs from Prescription Cost Analysis 2017 tables.\(^4\) GP consultation costs were calculated by applying unit costs from the Personal Social Services Research Unit.\(^4\) Costs of hospital interactions were calculated by deriving Healthcare Resource Groups (HRGs) for each visit/stay and subsequently applying national tariffs (2018/2019) for each HRG.\(^4\) Costs pertaining to A&E visits resulting in hospitalisation and additional procedures/surgeries are incorporated into HRGs derived for each visit/stay; therefore, specific costs relating to these resources cannot be identified. Costs of stoma care were not included due to data limitations.

Costs associated with the index colectomy (and the inpatient spell during which the index colectomy was performed) were attributed to the baseline period as the hospital admission date will have occurred prior to the index date, that is, date of colectomy, by definition.

Postoperative complications were assessed (online supplementary table S2) via the presence of diagnostic codes recorded following index colectomy, with gastrointestinal (GI) complications assessed throughout F-U and all other complications in the first 30 days of F-U only (widened to 60 days in a sensitivity analysis).

Due to coding limitations for high-cost drugs in HES data, specific biologic therapies prescribed/administered could not be identified; therefore, use of biologic therapies could not be assessed in this study.

Analysis
All outcomes were analysed descriptively and reported using frequencies and percentages for categorical, and counts, means, medians and SD for continuous variables.

Significance testing between baseline and F-U was conducted using paired t-tests for numeric and McNemar’s test for dichotomous outcomes. Significance testing between patient subgroups was conducted using t-tests for numeric and \(\chi^2\) or Fisher’s exact tests (if any expected cell count was \(\leq 5\) ) for dichotomous outcomes.

All statistical analyses were performed using Stata V.15.1 or later.\(^4\)

Ethics
The study was approved by an Independent Scientific Advisory Committee (Protocol No.: 18_263).

RESULTS
Eligible patients
In total, 26,165 patients were indexed; 249 patients had a prior UC diagnosis and satisfied selection criteria. Numbers of patients indexed decreased from 48 (2009) to 10 (2015). Reasons for patient exclusion are in online supplementary figure 2.

Demographics and disease characteristics
Demographic and clinical characteristics are shown in table 1.
Although outpatient visits decreased following surgery, mean number of visits to the colorectal surgery department increased from 0.9 at baseline to 2.1 at 1–12 month F-U (p<0.001), and then decreased to 1.2 at 13–24 month F-U (p<0.001). The mean length of individual hospital stay decreased from 12.6 days at baseline to 3.4 days at 1–12 month F-U (p<0.001) and 2.4 days at 13–24 month F-U (p<0.05 vs 1–12 month F-U; p<0.001 vs baseline).

Mean total direct healthcare costs at baseline, 1–12 month and 13–24 month F-U were £10366, £4433 and £3333, respectively, with higher costs at baseline driven by costs of the inpatient spell needed for index colectomy. Costs were lower at 1–12 month F-U versus baseline (p<0.001; figure 2A).

GP consultation costs increased post-colectomy from baseline to 1–12 month F-U (p<0.001). Hospital stay costs related to colectomy and medication decreased from baseline to 1–12 month F-U (p<0.001), while costs of outpatient visits and hospital stays unrelated to colectomy were similar at baseline and 1–12 month F-U (figure 2A).

Costs of GP consultations, outpatient visits, hospital stays unrelated to colectomy and medication (5-ASA, steroid and immunosuppressant therapies only) decreased at 13–24 month vs 1–12 month F-U, with changes statistically significant except for costs of medication (p<0.01; figure 2A). Costs of hospital stays related to colectomy remained similar at 13–24 month and 1–12 month F-U (figure 2A). Costs of GP consultations were comparable between baseline and 13–24 month F-U. All other costs were lower at 13–24 month F-U versus baseline (all p<0.01).

HCRU and costs by emergency/elective colectomy

At baseline, numbers of hospitalisations and outpatient visits were higher and admissions via A&E were lower in the elective versus emergency cohort (p<0.05). The length of hospital stay from admission to colectomy and from colectomy to discharge was lower in elective versus emergency colectomy patients (p<0.01). Otherwise, there were limited differences in HCRU during F-U.

Mean total direct healthcare costs in emergency and elective colectomy patients were comparable at baseline (£10133 and £10533, respectively) and numerically higher for emergency colectomy patients at 24-month F-U (£8595 and £7171, respectively). At baseline, costs of outpatient visits and medication were higher in elective versus emergency colectomy patients (p<0.001). F-U costs of hospital stays related to colectomy and medication were lower in elective versus emergency colectomy patients (p<0.05). All other costs were comparable at baseline and F-U between elective versus emergency colectomy patients.

HCRU and costs by subtotal/full colectomy

At baseline, number of outpatient visits was higher in subtotal versus full colectomy patients (p<0.05), but otherwise there were limited differences in HCRU. During F-U,
GP consultations were comparable between subtotal and full colectomy patients; however, the number of outpatient visits, and number and length of hospital stays, were greater in subtotal versus full colectomy patients (p<0.0001), as was the proportion of patients prescribed 5-ASAs (p<0.05).

There were no differences in direct costs in full versus subtotal colectomy patients at baseline (figure 2B). During F-U, total direct costs were higher in subtotal versus full colectomy patients (p<0.0001; figure 2B). Direct costs of GP consultations, hospital stays (both colectomy-related and non-colectomy-related) and outpatient visits were higher in subtotal versus full colectomy patients (p<0.05; figure 2B).

**Pharmacological treatment**

Although proportions of patients receiving 5-ASAs, steroids and immunosuppressants were lower at 1–12 month F-U versus baseline (p<0.001), a substantial proportion of patients received treatment with 5-ASAs (30%), steroids (19%) and/or immunosuppressants (5%) in 12 months following index colectomy. Proportions of patients receiving 5-ASAs and steroids decreased from 1 to 12 month to 13–24 month F-U (p<0.01), while immunosuppressant use remained stable across two F-U periods (figure 3A). The most commonly prescribed medications in each class during both baseline and F-U were mesalazine (5-ASA), prednisolone and azathioprine.

The proportion of patients receiving 5-ASAs, steroids and immunosuppressants at baseline was numerically higher in elective versus emergency colectomy patients (p<0.001 for immunosuppressants). Conversely, the proportion of patients receiving 5-ASAs and steroids post-colectomy was numerically lower in elective versus emergency colectomy patients (p<0.05 for 5-ASAs).

A higher proportion of subtotal versus full colectomy patients received 5-ASA (77% vs 61%, respectively; p<0.05) and steroid treatment (69% vs 53%, respectively; p<0.05) at baseline, while immunosuppressant use...
was numerically higher in subtotal versus full colectomy patients (45% vs 54%, respectively). At 1–12 month F-U after the initial colectomy, a higher proportion of subtotal versus full colectomy patients received 5-ASA treatment (59% vs 20%, respectively; p<0.001), while a numerically higher proportion of subtotal versus full colectomy patients received steroid treatment (26% vs 16%, respectively), and administration of immunosuppressants was comparable in subtotal and full colectomy patients.

Use of 5-ASAs decreased in the first 10 months following colectomy and then stabilised, while steroid use decreased after the first 2 months of F-U to a constant level (figure 3B). The proportion of patients receiving immunosuppressants remained stable from immediately after the index date until end of F-U at 24 months (figure 3B).

**Postoperative complications**

During F-U, 39% of patients experienced postoperative GI complications, with 21% of these suspected of experiencing chitinous (ICD-10: K91.8—Other postprocedural disorders of digestive system, not elsewhere classified). Steroid use at baseline was not associated with postoperative GI complications, which were experienced by 38% of patients with no steroid use and 40% of patients with steroids (p=0.795).

Fewer than 10% of patients reported any other type of complication during the 30-day postoperative period; widening the observation period to 60 days in a sensitivity analysis did not impact findings.

The proportion of patients experiencing postoperative complications was similar in patients having emergency and elective surgery.

**DISCUSSION**

This analysis of primary and secondary care data from the UK explored HCRU, healthcare costs and medication use in patients with UC prior to and following colectomy, and the potential influence of emergency versus elective and subtotal versus full colectomy on postoperative HCRU, costs and medication. We found a lower annual colectomy rate between January 2009 and December 2015 than that reported in another HES data study between April 1997 and March 2012. \(^\text{45}\) However, this could be explained by the decrease in colectomy rates over time. \(^\text{16,46,47}\)

Visits to the colorectal surgery department and GP consultations increased during F-U, probably reflecting increased patient monitoring after surgery; however, use of most secondary care resources decreased following colectomy. Although direct healthcare costs decreased from baseline (mean cost/patient >£10 000), they remained substantial 12 months later (mean cost/patient >£4000). \(^\text{35}\) Mean total costs associated with UC-related surgery over 6 months in a UK study were reported to be approximately £15 000, \(^\text{35}\) while in the US, colectomy and 6 months follow-up costs were $90 445. \(^\text{36}\)

Despite the total direct healthcare costs at baseline being similar, regardless of whether colectomy was elective or emergency, the mean total direct healthcare costs during F-U were 17% lower in patients undergoing elective colectomy, yet statistical significance was not observed—likely a result of the limited sample size studied. Previous studies have shown higher cost differences but in different healthcare systems. A Canadian study reported a two-thirds higher cost in emergency versus elective colectomies. \(^\text{38}\) A US National Inpatient Sample also suggested that costs and outcomes of emergency colectomies depended on whether the surgery occurred within the first 24 hours, with greater complications and costs if colectomies were delayed until >24 hours after admission. \(^\text{46}\) In our analysis, the mean time from admission to colectomy was 1.3 days in elective vs 10.5 days in emergency colectomies.

We showed that although use of 5-ASAs, steroids and immunosuppressants decreased following surgery, around one-third and one-fifth of patients, respectively, received 5-ASAs and steroids even after surgery, with these increasing to three-fifths and one-third, respectively, when subtotal colectomy patients were considered. This supports the view that colectomy is not a cure for UC and even patients undergoing full colectomy can require further medical or surgical care. \(^\text{28,35}\) However, it should be noted that the indication of prescribed medications is not captured in these data, but despite this, a substantial proportion of patients still appear to receive 5-ASA, immunosuppressant and steroid treatment following full colectomy. Further research is required to fully understand this.

Almost 40% of patients experienced GI complications at 24 month F-U, but the incidence of other postoperative complications was very low. No differences were seen in our analysis between elective and emergency surgery in rates of any postoperative complications, which is similar to a US tertiary care study which reported complications in 47% of patients undergoing colectomy. \(^\text{48}\) By contrast, a Canadian study reported postoperative complications in only 27% of patients, with a significantly higher risk of post-colectomy complications in emergency surgery patients. \(^\text{50}\) A systematic review identified a high level of variability in rates of postoperative complications; those up to 30 days postoperatively occurring in 9%–65% of patients and those after 30 days postoperatively occurring in 17%–55% of patients. \(^\text{35}\) However, it should be noted that due to coding limitations within HES, it was not possible to explicitly identify complications due to colectomy. Instead, the presence of diagnostic codes indicative of complications typically related to colectomy were used. This study had limitations. Linkage of the CPRD to HES reduced the sample from the UK to English patients, and patients receiving private medical care, in prisons, some residential homes or homeless were not represented. Identifying patients with UC via ICD-10 and Read diagnosis codes might have led to inappropriate patients’ inclusion/exclusion. Overestimation of HCRU/
In conclusion, although HCRU and healthcare costs in patients with UC decreased post-colectomy, there was still a substantial HCRU and economic burden postoperatively. Patients undergoing colectomy still require medical attention and use healthcare resources, which should be considered in their follow-up.

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Patient consent for publication Not required.

Ethics approval This was a retrospective analysis of data, involving no decisions regarding patient interventions or the omission of interventions, and all patient-level data in the data sources were anonymised. Hence, institutional review board/ethics approval and patient informed consent were not needed. Use of linked CPRD-HES data required Independent Scientific Advisory Committee approval; an abridged version of the protocol was supplied to the committee and approval was granted (Protocol No.: 18_263).

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Data availability statement Data may be obtained from a third party and are not publicly available. The deidentified patient data accessed and analysed for the purposes of this study are available from the Clinical Practice Research Datalink (email: enquiries@cpdrc.org) and access to these data are permissible on approval of a written study protocol by the Independent Scientific Advisory Committee.

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