Long-term health-related quality of life following colorectal cancer surgery: patient-reported outcomes in a remote follow-up population

Francesca Ligori Malcolm1,2 | Alfred Adiamah1,2 | Ayan Banerjea1,2 | Denyse Whitehead1,2 | Alisha Gupta1,2 | Joe West1,2,3 | David J. Humes1,2

the Nottingham Colorectal Service

Abstract

Aim: Remote follow-up (RFU) after colorectal cancer (CRC) surgery allows delivery of surveillance tests without the need for regular outpatient clinical appointments. However, little is known about health-related quality of life (HRQoL) in RFU patients. The main aim of this study was to quantify HRQoL in our RFU population to identify particular patient groups that may benefit from a more personalised approach to follow-up, including access to a survivorship clinic.

Method: EQ-5D, QLQ-C30 and QLQ-C29 questionnaires were distributed to CRC patients enrolled in a RFU programme. The primary outcome of HRQoL scores was analysed by year of RFU, demographics, operation type, stoma and adherence to RFU protocols.

Results: A total of 428 respondents were included, with a mean age of 71 years (SD 10.1 years) and a median RFU time of 2.6 years [interquartile range (IQR) 1.6–4.8 years]. ‘Perfect health’ was reported by 26.6% of patients. The median EQ-5D index score was 0.785 (IQR 0.671–1) and the median QLQ-C30 Global HRQoL score was 75 (IQR 58.3–83.3). Women had a significantly lower EQ-5D median score of 0.767 (IQR 0.666–0.879, \( P = 0.0088 \)). Lower QLQ-C30 HRQoL scores were seen in stoma patients (median 66.6, IQR 58.3–83.3, \( P = 0.0029 \)). Erectile dysfunction (\( P = 0.0006 \)) and poor body image (\( P = 0.001 \)) were also reported more frequently in stoma patients. Patients undergoing right-sided resection reported a lower median EQ-5D score of 0.765 (IQR 0.666–0.879, \( P = 0.028 \)) and higher pain severity (\( P = 0.0367 \)) compared with left-sided resections. There were 128 (29.4%) patients who breached RFU protocol and were seen in ad hoc colorectal clinics. However, there was no statistical difference in HRQoL between patients who adhered to or breached RFU protocols.

Conclusion: Overall HRQoL in patients in RFU is good, with no difference in those strictly followed up remotely. However, women, patients with right-sided resection and patients with a stoma may require additional clinical reviews.

KEYWORDS
Long-term follow-up, colorectal cancer surgery, patient-reported outcomes
INTRODUCTION

Colorectal cancer (CRC) is the third most common malignancy in the UK, with over 41,000 new cases being diagnosed each year [1]. With curative surgery as the mainstay of CRC treatment, survivorship is increasing and age-standardised 5-year survival rates are now 60.1% [2]. The randomised Follow-up After Colorectal Surgery (FACS) trial found that carcinoembryonic antigen (CEA) monitoring (initially 3-monthly for 2 years, then 6-monthly for 3 years) and CT of the chest abdomen pelvis (CTCAP; 6-monthly for 2 years, then annually for 3 years) resulted in improved detection of potentially curable recurrence [3]. The National Institute of Health and Care Excellence (NICE) thus advocates regular CTCAP, CEA level monitoring and colonoscopy to detect recurrence for 5 years after completion of treatment [4]. However, no consensus exists as to how follow-up should be delivered [5] and there is significant variation in clinical practice at both national and international levels [6].

Clinical practice at both national and international levels [6]. Clinician-led follow-up requires patients to attend regular clinic appointments over 5 years [7]. This method is resource heavy and increasing survival rates can overwhelm outpatient services [8]. Timing of clinic visits may sometimes adversely affect follow-up schedules; more importantly, administrative errors around significant results or ‘lost to follow-up’ issues present a significant governance risk. Meta-analysis of randomised controlled trials has found no evidence that face-to-face follow-up is required for effective surveillance [9] and attendance at clinical appointments has been recognised to increase patient anxiety [10].

‘Remote’ follow-up (RFU) enables timely delivery of surveillance tests and negates the need for regular clinic attendance. This form of follow-up, also referred to as ‘personalised stratified follow up’, forms part of the National Health Service (NHS) Long Term Plan for Cancer [11]. Robust protocol-driven RFU schemes have been demonstrated to be safe, acceptable to patients and cost-effective [6,12]. Patients undergo tests at the scheduled interval, results administration can be protocolised and ‘well survivors’ need only return to clinic if their results are abnormal. The potential drawback of RFU is that problems affecting survivors’ quality of life may not be addressed. The National Cancer Survivorship Initiative emphasises the importance of quality of life assessment in patients living beyond a cancer diagnosis [13]. Siddika et al. (2015) surveyed 100 RFU patients with a nonvalidated 10-question patient satisfaction questionnaire and found high levels of satisfaction. There is a deficit of research into standardised measures of health-related quality of life (HRQoL) in this patient group. The most commonly used instruments for HRQoL are EQ-5D, developed by the European Quality of Life Research Foundation (EuroQoL), and QLQ-C30, created by the European Organisation for Research and Treatment of Cancer (EORTC).

Aims

Long-term HRQoL after CRC surgery in patients under RFU is of interest due to a lack of literature describing outcomes in this group. The primary aim of this study was to quantify HRQoL in our RFU population to identify particular patient groups that may benefit from a more personalised approach to follow-up, including access to a survivorship clinic.

What does this paper add to the literature?

Remote follow-up after colorectal cancer surgery allows safe delivery of surveillance tests and obviates the need for regular clinic appointments. However, there is a paucity of information on patient-reported quality of life within this set-up. This study found that women, patients with a right-sided resection and patients with a stoma may require additional clinical reviews.

METHOD

In 2011 Nottingham University Hospitals Trust (NUH) adopted a RFU approach for those who had undergone surgery for CRC. Patients are typically reviewed once in a postoperative clinic to address problems related to surgery and subsequent symptoms. If required at this time further adjuvant treatment is arranged and delivered by the oncology team. All patients are simultaneously enrolled into RFU, which begins at time of treatment completion. This service is coordinated and run by a specialist cancer nursing team. Patient demographics and details regarding their diagnosis and treatment are entered prospectively into a RFU database (Microsoft Access™, Seattle, Washington, USA). When the database started a small number of patients with neuroendocrine tumours and polyps were included, but we planned to exclude these from the analysis of CRC. This database is used to identify when patients require blood tests, CT scans and colonoscopy at appropriate time intervals (see Appendix 1 for the full protocol). The team then orders the required tests, reviews the results and communicates the results to the patient; if they are abnormal, the patient is referred to the clinician-led multidisciplinary team. Figure 1 illustrates the typical journey of a patient and entry into the RFU programme. It is important to note that during RFU patients may request to be seen on an ad hoc basis in a colorectal clinic if they have any troubling symptoms that require further management.

We undertook a cross-sectional study of all patients in RFU using three validated questionnaires to ensure coverage of a wide breadth of HRQoL domains. Prior to distribution, permission to use each questionnaire for the purposes of this study was granted by EuroQol for the EQ-5D-5L [14] and EORTC for QLQ-C30 [15] and QLQ-C29 [16]. The widely used EQ-5D-5L was selected to provide an insight into general HRQoL. This uses a five-point scale (ranging from ‘no problems’ to ‘extreme problems’) to measure everyday function across the five domains of mobility, self-care, usual activities, pain and anxiety. Responses can then be used to generate a single ‘index’ score which...
is a summary of respondents’ answers to the five domain questions standardised to the UK general population [17]. The index score can range between −0.594 and 1; 1 corresponds to perfect health and less than 0 corresponds to health states which are ‘worse than dead’ [18].

EORTC produces questionnaires to enable assessment of HRQoL specifically in cancer patients. We selected the general oncological QLQ-C30 and the complementary CRC-specific QLQ-C29 for use in this study. The answers to symptom-specific questions are recorded on a four-point scale ranging from ‘not at all’ to ‘very much’. For QLQ-C30, answers to several questions can be combined to provide an overall score for items such as ‘physical function’ and ‘emotional function’. QLQ-C30 also has two questions about overall health and quality of life with a seven-point scale ranging from ‘very poor’ to ‘excellent’. For these questions an overall quality of life score can be derived [19].

Data collection

All patients gave permission to be contacted when they initially consented to enrolment in RFU. Utilising the RFU database, 722 living patients were identified as having undergone surgical intervention for CRC between 1 March 2011 and 31 December 2016. A letter outlining the project rationale from the colorectal team and the three questionnaires were sent to the identified patients on 21 August 2018. A prepaid envelope was provided to encourage participation and a window of 4 months was allocated for patients to return the questionnaires to maximize the response rate. Returned questionnaires were collated on 21 December 2018.

Questionnaires were produced in a computer-readable format. Returned questionnaires were scanned and transformed into an electronic database using Teleform Scan Station, Teleform Reader and Teleform Verifier software produced by OpenText™ [20]. At the time of scanning, all software output was manually checked against the physical questionnaires to ensure accurate transfer of information and corrected accordingly. Ambiguous responses and questions left blank were treated as missing data. The electronic output was re-checked by an external validator (AG) against the physical forms and any discrepancies were amended.

For patients on the database, information on demographics, year of RFU, site of cancer, operation type and recurrence details was collected prospectively. We undertook retrospective review of this information for all questionnaire returners to ensure accuracy. Further data were collected including Dukes stage at operation, operative details, presence of stoma, whether neoadjuvant and/or adjuvant treatment was received and site of cancer recurrence. Retrospective database review and additional data were obtained from electronic hospital records. Patients who were seen by a colorectal surgeon after entry into RFU were identified as having ‘breached protocol’ and these patients provided a comparative group with those who were purely followed up remotely. Details of any clinic attendance within the year prior to questionnaire completion were also recorded. Operation was categorised into ‘right-sided resection’, ‘left-sided resection’ or ‘other colorectal resection’ (Appendix 2). This involved review of clinic letters, multidisciplinary team outcome letters, discharge summaries, pathology results and follow-up imaging reports. Demographic data for nonresponders were also collected for comparison. Questionnaire responses and clinical data were combined for subsequent analysis.

We categorised age into three groups based on age at the time of questionnaire completion (<65, 65–74, 75+ years). We also grouped patients by resection side to compare overall HRQoL and symptom experience in patients who underwent either right- or left-sided resection. For the purposes of this analysis, results from patients who underwent ‘other colorectal resections’ were excluded (Appendix 2).

Patients with a stoma at the time of questionnaire completion were identified from the answer to Question 48 ‘Do you have a stoma bag (colostomy/ileostomy)?’ on the QLQ-C30. Time elapsed since each patient’s operation was used to stratify year of remote follow-up into Year 1, Year 2, Year 3 and Year 4+.

Comparative groups

Results for EQ-5D domains were compared with published norms for the general UK population [21]. Overall HRQoL scores and EQ-5D domains were also analysed between patients who breached protocol and those who did not. Further comparisons were made for patients who were seen in the year prior to questionnaire completion to determine whether recent breaches of protocol had any influence on HRQoL.

Data analysis

All statistical analysis was performed using Stata 12.0 [22]. EQ-5D index scores were calculated using the Crosswalk Index Value
Calculator [17], which is the method advocated by NICE [23]. For QLQ-C30 the symptom, function and overall global quality of life scores were calculated using the linear transformation method described in the EORTC manual [19].

Descriptive statistics were used to report demographics, operation-specific factors and cancer-specific features. Parametric variables were reported by mean and standard deviation, nonparametric variables were reported using the median and interquartile range. Key areas of interest were overall HRQoL scores, HRQoL at different stages of RFU, HRQoL in patients who breached protocol, symptomatology and if reported experience differed in patients who had right- or left-sided resection. Tests of hypothesis included chi-square testing for categorical variables, t-test for parametric variables and Kruskal–Wallis test for nonparametric variables. A $P$-value of less than 0.05 was used to determine statistical significance.

Outcomes in this study are presented in terms of EQ-5D index and QLQ-C30 global quality of life scores, the percentage reporting problems for each functional domain on EQ-5D, results of symptom scales for QLQ-C30 and individual symptom questions on QLQ-C29. This service evaluation was conducted in association with the Macmillan Cancer Centre as part of our continual assessment of our cancer pathway.

**RESULTS**

A total of 722 patients were contacted and 463 (64.1%) responses were received (Figure 2). Questionnaires were not completed in 259 (35.9%). Three patients died during the data collection period and three declined to participate. The remaining 253 patients had not returned the form at 4 months and were hence assumed to have declined to participate.

Demographics of responders and nonresponders were compared to identify any heterogeneity between these groups (Table 1). Of the responders, 42.5% were female compared with 44.8% of nonresponders; chi-square demonstrated no significant difference ($\chi^2 = 0.34, P = 0.56$). There was, however, a significant difference in mean age between the groups: the mean age of nonresponders was 67.5 years (SD 10.2 years) versus 71.1 years (SD 12.5 years) in responders ($t(720) = 4.1, P < 0.0001$).

**Missing questionnaire data**

Of the 428 patients included in the data analysis, 35 responders were excluded as they had undergone polypectomy alone. A total of 427 returned all three questionnaires. One patient returned...
the completed EQ-5D and QLQ-C30 but did not return the QLQ-C29. The majority of questionnaires were filled out completely; for EQ-5D answers were complete in 98.4%, for QLQ-C30 in 98.6% and for QLQ-C29 in 91.6%.

Demographics and cancer-specific features

Men made up 57.8% of included patients. Mean age was 71.3 years (SD 10.1 years) and median time in remote follow-up was 2.6 years [interquartile range (IQR) 1.6–4.8 years]. Details of cancer-specific features are summarised in Table 2; in those with cancer recurrence the median time from operation to recurrence was 1.4 years (IQR 0.9–2.7 years).

Details of surgical treatment and stoma

The specific operation types included in each category are detailed in Appendix 2. At the time of questionnaire completion 27.1% of patients had a stoma.

Demographics of patients who breached protocol

The number of responders who breached protocol by being seen in clinic after entry into RFU was 126 (29.4%); 52 (12.2%) of these were seen within the year prior to questionnaire completion. Regarding gender, there was no significant difference between those who were seen in clinic and those who were not ($\chi^2 = 1.51$, $P = 0.22$). However, patients breaching protocol were significantly younger ($\chi^2 = 7.79$, $P = 0.05$) and were significantly more likely to have undergone a left-sided resection or Abdomino Perineal Excision of Rectum ($\chi^2 = 7.93$, $P = 0.005$). Further demographic details are outlined in Table 3.

Overall HRQoL

Two overall measures of quality of life were utilised: the index score from EQ-5D and the global quality of life score from QLQ-C30. The distribution of results for each score was negatively skewed, hence we used nonparametric methods to test statistical significance. For QLQ-C30 global HRQoL the median score was 75.0 (IQR 58.3–83.3). For the EQ-5D index score the median was 0.785 (IQR 0.671–1), which corresponds to a health state with no problems with mobility, self-care or depression, moderate problems in usual activities and slight problems with pain. Figure 3 summarises the percentage of patients reporting ‘no problems’ versus ‘problems’ across EQ-5D functional domains. No problems in any domain were reported in 26.6% and 10.7% reported problems in every domain.

HRQoL scores by demographics, cancer-specific features, stoma and adherence to protocol

Table 4 presents median quality of life scores across the proposed subgroups. No statistically significant differences were found for each HRQoL measure for site of tumour or those who had neoadjuvant and/or adjuvant treatment versus surgery alone. No significant differences between patients who adhered strictly to RFU protocol and those who breached protocol were identified on overall HRQoL scores. Furthermore, there was no significant difference in patients who breached protocol in the year prior to questionnaire completion. EQ-5D index scores were found to be significantly lower in women ($P = 0.009$) and in patients with cancer recurrence ($P = 0.0092$). QLQ-C30 scores and EQ-5D index values demonstrated a significant variation across age groups on analysis. 5D-5L index values by age group peaked at 65–74 years (median 0.837, IQR 0.698–1). Lower median scores of 0.768 for those <65 years (IQR 0.623–1) and those aged 75+ (IQR 0.671–0.879). QLQ-C30 scores proved significantly lower in patients with a stoma ($P = 0.003$), gender across the age groups was homogeneous ($\chi^2 = 0.59$, $P = 0.74$) and there was no statistically significant difference in stoma presence ($\chi^2 = 5.68$, $P = 0.058$). Recurrence of cancer had a negative impact on EQ-5D scores ($P = 0.009$) and higher rates of recurrence were seen in patients <65 years and over 75 ($\chi^2 = 10.75$, $P = 0.005$). There were, however, no differences between age groups and stage at the time of operation ($\chi^2 = 4.36$, $P = 0.59$).

Right- and left-sided resection

No significant difference was demonstrated between right or left resection groups in terms of QLQ-C30 score. However, a statistically significant difference between EQ-5D index scores was noted, with lower scores being reported by patients who underwent right colonic operations ($P = 0.028$). A perfect health score of 1 was reported by at least 25% of patients in the left group; this ceiling effect was only seen in 10% of the patients who underwent right-sided resection. There was no difference between the gender distribution of these groups ($\chi^2 = 1.68$, $P = 0.20$) but age was significantly lower in patients undergoing left-sided resection (mean = 70.5 years,

**TABLE 1** Demographics of responders versus nonresponders

|                  | Responders | Nonresponders | $P$-value |
|------------------|------------|---------------|-----------|
| Overall          | 463 (64.1%)| 259 (35.9%)   | –         |
| Male             | 266 (57.5%)| 143 (55.2%)   | –         |
| Female           | 197 (42.5%)| 116 (44.8%)   | 0.56      |
| Mean age (years) | 71.7       | 67.5          | <0.01*    |

* indicates statistically significant difference.
SD = 9.5 years) compared with right-sided (mean = 73.9 years, SD = 9.8 years, \( P = 0.005 \)). A significantly higher number of patients in the left group had a stoma (\( \chi^2 = 57.9, P < 0.001 \)).

**HRQoL score by year of RFU**

Overall, the trend of QLQ-C30 score by year of follow-up was stable. Index scores by year were highest at Year 1 (median 0.837, IQR 0.723–1) and lowest in the Year 3 (median 0.750, IQR 0.592–1); Figure 4 illustrates the overall trend of index score by year. No significant difference was found when EQ-5D index scores stratified by year of RFU were compared with published norms from a cohort of unselected members of the general UK population [21] (Table 5). Across all domains patients within RFU reported significantly more pain (\( P < 0.001 \)) and anxiety (\( P < 0.001 \)) and higher levels of anxiety (\( P < 0.001 \)), mobility problems (\( P < 0.001 \)) and difficulty with self-care

**EQ-5D domain comparison**

EQ-5D domain scores for pain, activity, mobility, self-care and anxiety were compared with published norms from a cohort of unselected members of the general UK population [21] (Table 5). Across all domains patients within RFU reported significantly more pain (\( P < 0.001 \)) and anxiety (\( P < 0.001 \)) and higher levels of anxiety (\( P < 0.001 \)), mobility problems (\( P < 0.001 \)) and difficulty with self-care.
Domains were compared between patients adhering to RFU protocol and those who breached protocol. Statistically significant differences noted were higher rates of pain \((P = 0.05)\) and more limitation to activity \((P = 0.043)\) in the group that breached protocol.

**Symptom reporting**

Abdominal symptoms such as pain were reported in 28.5% and bloating in 41.0%. Constipation affected 34.7% of responders and 33.9% reported diarrhoea. Blood in the stool was noted by 4.8% and stool containing mucus was experienced by 12.7%.

**Sexual function overall**

A total of 41.9% reported feeling less attractive as a result of their disease or treatment. No sexual interest was reported in 29.5% of men and 65.1% of women. In men, age had a significant influence on sexual interest \((\chi^2 = 20.8, P < 0.001)\) but this was not observed for women \((\chi^2 = 6.68, P = 0.083)\). Erectile dysfunction was experienced by 74.6% of male responders and this was more prevalent with increasing age \((\chi^2 = 7.78, P = 0.020)\). One hundred and six female respondents (80.3%) provided an answer to ‘Did you have pain or discomfort during intercourse?’ and 21.7% reported dyspareunia; this was significantly higher in the youngest age group \((\chi^2 = 20.01, P < 0.001)\).

**Symptoms in stoma patients**

Rates of abdominal pain and bloating were not significantly different between those with a stoma and those without \((P = 0.72, P = 0.23)\). Trouble with stoma care was reported in 25%. Presence of a stoma contributed negatively to body image, with problems reported in 66.7% compared with 43.0% of patients without a stoma.
No difference in sexual interest was noted between patients with and without a stoma. Erectile difficulty was significantly higher in stoma patients ($\chi^2 = 7.5689$, $P = 0.006$).

**Symptoms by right and left resection**

Comparisons were made between patients who had right- or left-sided resection. Reported experience of abdominal pain (32.8% right, 25.8% left) and bloating (46.7% right, 38.5% left) was similar in these groups ($P = 0.131$ for pain and $P = 0.106$ for bloating). Pain severity was, however, higher in the group who had right colonic surgery ($P = 0.0335$). For constipation and diarrhoea no significant difference was observed in symptom reporting or severity. No differences were observed for sexual interest or function. Patients with a left-sided resection reported feeling less masculine/feminine as a result of treatment ($\chi^2 = 6.2267$, $P = 0.012$) and less attractive ($\chi^2 = 3.9232$, $P = 0.048$). No differences were observed across functional scales or symptom scales derived from responses to the QLQ-C30 questionnaire.

**DISCUSSION**

This study is the first to examine HRQoL in operatively managed CRC patients enrolled in a RFU programme. We used validated questionnaires to quantify HRQoL and to understand the symptoms experienced by patients in RFU. Reassuringly, HRQoL scores were demonstrated to be consistently high and similar regardless of time since operation, treatment and cancer site. Lower scores were associated with being female, cancer recurrence, stoma presence and right-sided resection. Frequently reported symptoms included abdominal pain (28.5%), bloating (41.0%), constipation (34.7%) and diarrhoea (33.9%). No difference in these symptoms was observed in relation to stoma presence or side of operation; however, patients with right-sided resection reported higher pain severity ($P = 0.0335$). Rates of body dissatisfaction and erectile dysfunction were high. Our results suggest that female patients who are older with right-sided resection may require additional clinical reviews rather than just remote follow-up. Additionally, support should be offered regarding sexual dysfunction to those patients in RFU programmes.

Strengths of this study include the response rate of 64.1%, which is higher than that of similar studies in long-term CRC survivors [24–26], and the small number of missed answers. Possible limitations are that questionnaire responders were significantly older than nonresponders and hence the results may not be reflective of the experience of younger patients. No baseline data were collected; we therefore only present a snapshot of HRQoL within a RFU population and in comparison with the subgroup of patients who breached protocol, other studies and population norms. Comorbidity has been shown to have a negative impact on HRQoL in CRC patients [27]; our study did not examine comorbidity as it was felt that retrospective collection of these data would be unreliable due to inconsistency in local reporting. Similarly, lower socio-economic status has a negative influence on HRQoL [28] and these demographic data were unavailable in our study population.

**Comparative groups**

Younger patients, those with who underwent left-sided resection and those with recurrent cancer were more likely to breach protocol and be seen in clinic. No overall differences were found in the subgroup of patients who breached protocol by being seen in clinic following entry into RFU. This suggests that the extra support required by these patients was provided appropriately through an ad hoc clinic visit.
TABLE 4 Quality of life measure results summarised by demographic, cancer-related and operation-specific details

| Health-related quality of life measure | EQ-5D index score | QLQ-C30 quality of life score |
|---------------------------------------|-------------------|------------------------------|
| Overall for study population (n = 428) | 0.785 (IQR 0.671-1) | 75 (IQR 58.3-83.3) |
| Gender | | |
| Male (n = 247) | 0.836 (IQR 0.679-1) | 83.3 (IQR 66.7-91.7) |
| Female (n = 181) | 0.767 (IQR 0.666-0.879) | 75 (IQR 54.1-83.3) |
| P-value | 0.009a | 0.090 |
| Age (years) | | |
| <65 (n = 118) | 0.768 (IQR 0.654-1) | 75 (IQR 50-91.6) |
| 65–74 (n = 139) | 0.837 (IQR 0.698-1) | 83.3 (IQR 66.7-91.6) |
| 75+ (n = 171) | 0.767 (IQR 0.671-0.879) | 75 (IQR 58.3-83.3) |
| P-value | 0.05a | 0.01a |
| Year of remote follow-up | | |
| Year 1 (n = 43) | 0.837 (IQR 0.723-1) | 83.3 (IQR 58.3-83.3) |
| Year 2 (n = 111) | 0.7955 (IQR 0.683-1) | 83.3 (IQR 66.7-83.3) |
| Year 3 (n = 100) | 0.750 (IQR 0.592-1) | 75 (IQR 58.3-83.3) |
| Year 4+ (n = 174) | 0.790 (IQR 0.671-0.879) | 75 (IQR 58.3-91.7) |
| P-value | 0.26 | 0.80 |
| Tumour site | | |
| Colonic (n = 288) | 0.768 (IQR 0.671-0.906) | 75 (IQR 58.3-83.3) |
| Rectal (n = 140) | 0.795 (IQR 0.671-1) | 79.1 (IQR 58.3-83.3) |
| P-value | 0.22 | 0.78 |
| Oncological treatment | | |
| Surgery alone (n = 241) | 0.795 (IQR 0.679-1) | 75 (IQR 66.7-83.3) |
| Neoadjuvant ± adjuvant(n = 187) | 0.778 (IQR 0.647-1) | 75 (IQR 58.3-83.3) |
| P-value | 0.52 | 0.98 |
| Recurrence | | |
| No recurrence (n = 371) | 0.795 (IQR 0.683-1) | 83.3 (IQR 66.7-83.3) |
| Recurrence (n = 57) | 0.762 (IQR 0.498-0.848) | 75 (IQR 50-87.5) |
| P-value | 0.009a | 0.41 |
| Resection side | | |
| Right-sided resection (n = 140) | 0.765 (IQR 0.666-0.879) | 75 (IQR 58.3-83.3) |
| Left-sided resection (n = 268) | 0.813 (IQR 0.679-1) | 83.3 (IQR 66.7-91.7) |
| P-value | 0.028a | 0.19 |
| Stoma at time of questionnaire completion | | |
| No stoma (n = 312) | 0.795 (IQR 0.681-1) | 83.3 (IQR 62.5-91.7) |
| Stoma(n = 116) | 0.778 (IQR 0.629-0.906) | 66.6 (IQR 58.3-83.3) |
| P-value | 0.19 | 0.003a |

(Continues)
EQ-5D results in a sample reflective of the English population also provides a useful comparison [21]. As expected, our population had a statistically significantly higher rate of problems across all domains compared with the general population. Pain was the most frequently reported problem, with 56.0% reporting at least ‘slight problems’ with pain. Domain differences were compared based on protocol adherence. Across all domains problem reporting was higher in patients who breached protocol; yet pain and activity limitation were the only domains to reach statistical significance. A significant difference may be seen for every domain if a larger sample size were to be surveyed. These data may partly explain why these patients breached protocol, namely clinician review being sought by those patients with ongoing problems.

### TABLE 4 (Continued)

| Health-related quality of life measure | EQ-5D index score | QLQ-C30 quality of life score |
|---------------------------------------|-------------------|-----------------------------|
| Yes, no clinic appointments within the RFU (n = 296) | 0.8025 (IQR 0.6865-1) | 83.3 (IQR 58.3-83.3) |
| No, ad hoc clinic appointment within RFU (n = 124) | 0.74 (IQR 0.642-0.879) | 75 (IQR 58.3-83.3) |

*Statistical significance demonstrated on Kruskal–Wallis test.

### FIGURE 4
Box plot summarising EQ-5D index scores by year of remote follow-up

### TABLE 5
Our results for EQ-5D problem reporting overall, in comparison with the general population

| Study population | Mobility (%) | Self-care (%) | Activity (%) | Pain (%) | Anxiety (%) |
|------------------|--------------|---------------|--------------|----------|-------------|
| Our study: English CRC patients under remote follow-up (n = 428) | 46.9 | 15.5 | 47.7 | 56.0 | 42.3 |
| English population reporting problems using five-level EQ-5D (n = 996) [21] | 26.0 | 9.2 | 23.7 | 41.6 | 24.0 |
| P-value | P < 0.001* | P < 0.001* | P < 0.001* | P < 0.001* | P < 0.001* |

*Statistically significant results.
Our findings reiterate previous UK-based studies which have found that stoma presence [25,29] and cancer recurrence [25] have a negative impact on HRQoL in CRC patients. There is variation in the reported influence of gender on HRQoL depending on the population studied. In general population terms it is well recognised that women report lower HRQoL scores than men [30]. Finnish and Iranian studies focusing on CRC patients found no difference between male and female responses to EQ-5D and QLQ-C30 [31,32]. We found significantly lower scores in women, which has been previously observed in the UK and Japanese cohorts [25,33]. Within our RFU patients high rates of abdominal symptoms and sexual dysfunction were found, and both of these sequelae have been widely reported in CRC survivors [26,34–37]. Persistence of abdominal symptoms over time was reported in CRC patients at 1 and 3 years postdiagnosis, and our findings reflect this [29].

Downing et al. [25] reported that 34.5% of CRC patients between 12 and 36 months postdiagnosis stated that they had ‘no problems’ in any EQ-5D functional domain. In our cohort, ‘no problems’ were reported in 26.6% and there were higher rates of problem reporting across each domain apart from self-care. These results can perhaps be attributed to demographic differences between study populations: in particular, within our cohort 42.2% were female versus the 37.2% in Downing et al.’s study. The percentage of patients <65 years was lower in our study (27.3% vs. 33.0%) and that >75 years was higher (39.9% vs. 31.1%).

Another UK study utilising QLQ-C30 scores in CRC patients >2 years postdiagnosis reported no significant difference between median scores of colonic and rectal cancer patients [24]. We also found no significant difference between rectal and colonic cancer patients. Recent publications have primarily focused on HRQoL after anterior resection. An international study demonstrated that low HRQoL correlates with severity of low anterior resection syndrome (LARS) [34] and this impact has also been shown to persist over time [35]. There is, however, a deficit of literature comparing outcomes between patients with right- and left-sided resection. One small case–control study which reported no difference in EQ-5D scores was stratified by resection side [38]. Recently, Buchli et al. reported on HRQoL and LARS stratified by resection side [39]. That study found that major LARS symptoms were more frequently experienced by patients with right-sided resection and that major symptoms were an independent predictor of lower HRQoL scores. Our data corroborate this: within our study population lower HRQoL scores were associated with right-sided resection. Our findings highlight that the long-term HRQoL outcomes of patients with right-sided resection should be of clinical concern. The outcomes in this patient group have perhaps been overshadowed by the current focus on LARS.

CONCLUSION

Our findings provide us with confidence that patients enrolled in our RFU programme experience high HRQoL which remains stable. We have identified factors which make a negative contribution to HRQoL; this information will be a useful tool in future service planning and patient counselling. Patients who breached protocol did not differ on overall HRQoL score but were more likely to experience pain and limitation of activity. Patients with right-sided resection reported significantly worse HRQoL, and we therefore highlight this patient group as a focus for further investigation. Overall, these findings suggest that even within a RFU setting, targeted clinics dedicated to addressing these specific problems and patient groups could mitigate deterioration in HRQoL after CRC surgery. A targeted clinic for these patients is being planned for those in the third year of follow-up as this was the postoperative time point with the lowest overall HRQoL scores. Given the ongoing global challenges with the COVID-19 pandemic this is likely to be delivered virtually.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Following assessment with the UK Health Research Authority (HRA) decision tool, it was ruled that no formal ethics approval was required for this particular study. Patients returned the quality of life questionnaire packs if they first consented to participate.

CONSENT TO PUBLISH

Not applicable. No individual-level data are included in this paper.

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CONFLICT OF INTEREST

None of the authors have any conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

FLM, AA, AB, JW and DJH participated in the study concept and design, data collection, data analysis, reviewed the paper and approved.
the final paper for submission. DW and AG participated in the study design, data collection, reviewed the paper and approved the final paper for submission.

DATA AVAILABILITY STATEMENT
The data in this publication are confidential. Any data requests should be made to the corresponding author.

ORCID
Francesca Ligori Malcolm @ https://orcid.org/0000-0002-4114-126X
Alfred Adiamah @ https://orcid.org/0000-0002-0624-6197
Ayan Banerjea @ https://orcid.org/0000-0002-3094-2870

TWITTER
Alfred Adiamah @AdiamahAlfred

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SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section.

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