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

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Abbreviations

RFU remote follow-up

CRC colorectal cancer

PROMs patient reported outcome measures

HRQoL Health related quality of life

NICE National Institute for Health and Care Excellence

FACS Follow up after colorectal surgery randomised controlled trial

EuroQol European Quality of Life Research Foundation

EORTC European Organisation for Research and Treatment of Cancer

EQ-5D-5L EuroQol Health Questionnaire- 5 Domain– 5 Level Version 1.0

QLQ-C30 EORTC C30 Questionnaire Version 1.0

QLQ-C29 EORTC C29 Questionnaire Version 1.0

NUH Nottingham University Hospitals Trust

APER Abdominoperineal resection

LARS Low anterior resection syndrome

Abstract

Background: 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.

Methods: 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:428 respondents (59.3%), mean age of 71years(SD 10.1) and a median RFU time of 2.6years (IQR: 1.6-4.8 years) were included. 26.6% of patients reported 'perfect health'. The median EQ-5D index score was 0.785 (IQR: 0.671-1) and QLQ-C30 Global HRQoL score was 75 (IQR: 58.3-83.3). Females had 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 that breached RFU protocol and were seen in adhoc colorectal clinics. However, there was no statistical difference in HRQoL between patients who adhered to or breached RFU protocols.

Conclusions: Overall HRQoL in patients in RFU is good, with no difference in those strictly followed up remotely. However, females, right-sided resections and patients with stomas may require additional clinical reviews.

What does this paper add to the existing 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 females, right-sided resections and patients with stomas may require additional clinical reviews.

Introduction

Colorectal cancer (CRC) is the 3rd most common malignancy in the UK; in excess of 41,000 new cases are diagnosed each year(1). With curative surgery as the mainstay of CRC treatment survivorship is increasing and age standardised five year survival rates are now 60.1%(2). The randomised Follow-up After Colorectal Surgery trial (FACS) found that CEA monitoring (initially 3 monthly for 2 years, then 6 monthly for 3 years) and CTCAP (6 monthly for 2 years, then annually for 3 years) resulted in improved detection of potentially curable recurrence(3). NICE thus advocates regular CTCAP, CEA level monitoring and colonoscopy to detect recurrence for 5 years after treatment completion(4). However no consensus exists as to how follow-up should be delivered(5) and significant variation in clinical practice exists on both a national and international level(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 and 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 appointment 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 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 results are abnormal. The potential drawback of RFU is that problems impacting on quality of life faced by survivors 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 non-validated 10 question patient satisfaction questionnaire and found high levels of satisfaction there is a deficit of research into standardised measures of HRQoL in this patient group patients. The most commonly used instruments for HRQoL are the EQ-5D developed by the European Quality of Life Research Foundation (EuroQoL) and the 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.

Methods

In 2011 Nottingham University Hospitals Trust (NUH) adopted a RFU approach for those who had undergone surgery for colorectal cancer. Patients are typically reviewed once in a post-operative 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 cancer specialist nursing team. Patient demographics and details regarding their diagnosis and treatment are entered prospectively into a RFU database (Microsoft Access™, Seattle, USA). A small number of patients at the start of the database were included with neuroendocrine tumours and polyps 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 full protocol). The team then orders the required tests, reviews the results, communicates the results to the patient and if abnormal the patient is referred to the clinician led multi-disciplinary team. **Figure 1** illustrates the typical journey of a patient and entry into the remote follow up programme. It is important to note that during RFU patients may request to be seen on an ad hoc basis in colorectal clinic if they have any troubling symptoms requiring further management.

We undertook a cross-sectional study of all patient in RFU using 3 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 5 point scale (ranging from ‘no problems’ to 'extreme problems’) to measures everyday function across the 5 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 respondent’s answers to the 5 domain questions standardised to the general UK population(17). The

index score can range between -0.594 and 1; 1 corresponds to perfect health and lower than 0 correspond to health states which are 'worse than dead'(18).

EORTC produces questionnaires to enable HRQoL assessment 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 4 point scale ranging from 'not at all' to 'very much'. For QLQ-C30 answers to several questions can be combined to provide overall score for items such as 'physical function' and 'emotional function'. QLQ-C30 also has 2 questions about overall health and quality of life with a 7 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 RFU enrolment. Utilising the RFU database 722 living patients were identified as having undergone surgical intervention for CRC between 1st March 2011 and 31st December 2016. A letter outlining the project rationale from the colorectal team and the 3 questionnaires were sent to the identified patients on 21st 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 response rate. On 21st December 2018 returned questionnaires were collated.

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 second checked by an external validator (A Gupta) against the physical forms and any discrepancies were amended.

For patients on the database demographics, year of RFU, site of cancer, operation type and recurrence details are collected prospectively. We undertook retrospective review of this

information for all questionnaire returners to ensure accuracy. Further data was collected including Duke's stage at operation, operative details, presence of stoma, whether neo-adjuvant and/or adjuvant treatment was received, site of cancer recurrence. Retrospective database review and additional data was 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 to 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, multi-disciplinary team outcome letters, discharge summaries, pathology results and follow-up imaging reports. Demographic data for non-responders was also collected for comparison. Questionnaire responses and clinical data were combined for subsequent analysis.

We categorised age into 3 groups based on their age at time of questionnaire completion (<65, 65-74, 75+). We also grouped patients by resection side to compare overall HRQoL and symptom experience in patients who underwent either right or left-sided resections. For the purposes of this analysis results from patient who underwent 'other colorectal resections' were excluded (appendix 2)

Patients with a stoma at 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 to 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 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 the QLQ-C30 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, non-parametric 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 patient who had right or left- sided resections. Tests of hypothesis included chi square testing for categorical variables, t-test for parametric variables Kruskal Wallis test for non-parametric variables. A p-value of less than 0.05 was used to determine statistical significance.

Outcomes in this study were presented in terms of EQ-5D index and QLQ-C30 global quality of life scores, 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 MacMillian Cancer Centre as part of our continual assessment of our cancer pathway.

Results

In total 722 patients were contacted and 463 (64.1%) responses were received (**Figure 2**. Questionnaires were not completed in 259 (35.9%). 3 patients died during the data collection period and 3 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 non-responders were compared to identify any heterogeneity between these groups (**Table 1**). 42.5% of responders were female compared with 44.8% of non-responders; 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; mean age of non-responders was 67.5 years (S.D. 10.2) versus 71.1 years (S.D 12.5) 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 .427 returned all 3 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 98.6% and for QLQ-C29 91.6%.

Demographics and cancer specific features: 57.8% of included patients were male, mean age was 71.3 years (S.D. 10.1) and median time in remote follow up was 2.6 years (IQR: 1.6-4.8 years). Details of cancer specific features are summarised in **Table 2**; in those with cancer recurrence median time from operation to recurrence was 1.4 years (IQR 0.9-2.7 years).

Details of surgical treatment and stoma: Specific operation types included in each category are detailed in appendix 2. 27.1% of patients had a stoma at time of questionnaire completion.

Demographics of patients who breached protocol: The number of responders who breached protocol by being seen in clinic after entry in to RFU was 126 (29.4%); 52 (12.2%) of which were seen within the year prior to questionnaire completion. For gender there was no significant difference

between those who were seen in clinic and those who were not (chi2 =1.51, p=0.22). However patient breaching protocol were significantly younger (chi2 =7.79, p=0.05) and were significantly more likely to have undergone a left sided resection or APER (chi2 =7.93, p=0.005). Further demographic details are outlined in **table 3**.

HRQoL overall: 2 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 non-parametric methods to test statistical significance. For QLQ-C30 global HRQoL the median score was 75.0 (IQR: 58.3 – 83.3). For 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 percentage of patients reporting 'no problems' versus 'problems' across EQ-5D functional domains. 26.6% reported no problems in any domain 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 patient 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 females (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 the 75+ group (IQR: 0.671-0.879). Similarly for QLQ-C30 median scores this pattern was seen. QLQ-C30 scores proved significantly lower in patient with a stoma (p=0.003). Gender across the age groups was homogenous (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 impacted EQ-5D scores negatively (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 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; lower scores were 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 resections. There was no difference between the gender distribution of these groups (chi^2=1.68, p=0.20); age was significantly lower in patients undergoing left-sided resections (Mean = 70.5 years, S.D= 9.5 years) compared to right-sided (Mean=73.9 years, S.D=9.8 years) (p=0.005). A significantly higher number of patients in the left group had stomas (chi2= 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 3rd year (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 (p=0.265) and QLQ-C30 scores (p=0. 8084) were stratified by year of RFU.

EQ-5D domain comparison (table 5): EQ-5D domain scores for pain, activity, mobility, self-care and anxiety were compared to published norms from a cohort of unselected members of the general UK population(21). Across all domain's 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 (p=0.001). 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: In total 41.9% reported feeling less attractive as a result of their disease or treatment. No sexual interest was reported in 29.5% of males and 65.1% of females. In males, age had a significant influence over sexual interest (chi^2=20.8, p<0.001) but for females this was not observed (chi^2 6.68, p=0.083). Erectile dysfunction was experienced by 74.6% of male responders and this was more prevalent as age group increased (chi^2=7.78, p=0.020). 106 female responders (80.3%) provided an answer to "Did you have pain or discomfort during intercourse?" 21.7% reported dyspareunia and 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 without (p=0.72, p=0.23). Trouble with stoma care was reported in 25%. Stoma presence was contributed negatively to body image with problems reported in 66.7% compared to 43.0% of patients without a stoma (chi^2=18.5940, p<0.001). No difference in sexual interest was noted between patient with and without a stoma. Erectile difficult 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 resections. 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. Left-sided resection patients reported feeling less masculine/feminine as a result of treatment (chi^2= 6.2267, p=0.012) and less attractive

301 (chi^2 =3.9232, p=0.048). No differences were observed across functional scales or symptoms scales

302 derived from responses to the QLQ-C30 questionnaire.

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Discussion

This study is the first to examine HRQoL in operatively managed CRC patients enrolled in a RFU programme. We have 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 resections. 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 relating to stoma presence or side of operation; however right-sided resection patients reported higher pain severity (p=0.0335). Body dissatisfaction and erectile dysfunction rates were high. Our results suggest that female patients, who are older with right sided resections 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 low number of missed answers. Possible limitations are that questionnaire responders were significantly older than non-responders and hence the results may not be reflective of the experience of younger patients. No baseline data was collected; we therefore only present a snapshot of HRQoL within a RFU population and in comparison to the subgroup of patients who breached protocol, other studies and population norms. Co-morbidity has been shown to negatively impact HRQoL in CRC patients(27); our study did not examine co-morbidity as it was felt that retrospective collection of this data would be unreliable due to inconsistency in local reporting. Similarly lower socio-economic status negatively influences HRQoL(28) and this demographic data was unavailable in our study population.

Comparative groups:

Younger patients, those with who underwent left sided resections 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.

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 to the general population. Pain was the most frequently reported problem; 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 surveyed. This data may partly explain why these patients breached protocol; clinician review being sought by those patients with ongoing problems.

Our findings reiterate previous UK based studies which have found stoma presence(25, 29) and cancer recurrence(25) negatively impact 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 females report lower HRQoL scores than their male counterparts(30). Finnish and Iranian studies focusing on CRC patients found no difference between male and female responses to EQ-5D and QLQ-C30 data(31, 32). We found significantly lower score in females which has been previously observed in 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 post diagnosis and our findings reflect this(29).

Downing et al (2015) reported 34.5% of CRC patients between 12-36 months post diagnosis stated that they had 'no problems' in any EQ-5D functional domain. Comparatively in our cohort 'no problems' were reported in 26.6% and 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 (2015). The percentage of patients <65 years was less in our study (27.3% vs 33.0%) and >75 years was greater (39.9% vs 31.1%).

Another UK study utilising QLQ-C30 scores in CRC patients >2 years post diagnosis reported no significant difference between median scores of colonic and rectal cancer patients(24). Similarly we found no significant difference between rectal and colonic cancer patients. Recent publications have primarily focused on HRQoL in anterior resection patients. An international study demonstrated that low HRQoL correlates with severity of LARS(34) and this impact has also been shown to persist over time(35).There is however a deficit of literature comparing outcomes between right and left-sided resection patients. One small case control study which reported no difference in EQ-5D scores stratified by resection side(38). Recently Buchli et al (2018) reported on HRQoL and LARS stratified by resection side(39). This study found that major LARS symptoms were more frequently experienced by right-sided resection patients and that major symptoms were an independent predictor of lower HRQoL scores. Our data corroborates this within our study population lower HRQoL scores were associated with right-sided resection. Our findings highlight that the long term HRQoL outcomes of right-sided resection patients should be of clinical concern. The outcomes in this patient group patients 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 contribute negatively 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 activity limitation. Right-sided resection patients 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 3rd year of follow-up as this was the post-operatively time point with the lowest overall HRQoL scores. Given the ongoing global challenges with the Covid-19 pandemic this will likely be delivered virtually.

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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.

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 firstly consented to participate.

Consent to publish

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

Data availability

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

Competing interests

The authors declare no competing interests.

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Table 1: Demographics of responders vs non-responders

	Responders	%	Non-responders	%	P values
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	71.7	-	67.5	-	<0.01*

546 **Table 2: Demographic and cancer specific details by site of tumour**

Site of cancer	Colonic	%	Rectal	%	Overall	%	P values
	288	67.3	140	32.7	428	100.0	
Gender							
Male	156	54.2	91	65.0	247	57.8	
Female	132	45.8	49	35.0	181	42.2	0.03*
Age							
<65	71	24.7	47	33.6	118	27.6	
65-74	89	30.9	50	35.7	139	32.5	
75+	128	44.4	43	30.7	171	39.9	0.02*
Mean age	72.4	-	69.1	-	71.3	-	
Year of remote follow-up							
Year 1	30	10.4	13	9.3	43	10.1	
Year 2	73	25.3	38	27.1	111	25.9	
Year 3	61	21.1	39	27.9	100	23.4	
Year 4+	124	43.1	50	35.7	174	40.6	0.35
Dukes stage at operation							
A	63	21.9	49	35.0	112	26.1	
B	120	41.7	39	27.9	159	37.2	
C	102	35.4	35	25.0	137	32.0	<0.01*
D	1	0.3	1	0.7	2	0.5	
Unknown/Not applicable*	2	0.7	16	11.4	18	4.2	
Treatment							
Neoadjuvant**	5	1.7	29	20.7	34	7.9	
Adjuvant	108	37.6	25	17.9	133	31.1	
Neoadjuvant + adjuvant	5	1.7	15	10.7	20	4.7	
Only surgical	170	59.0	71	50.7	241	56.3	<0.01*
Recurrence							
Local	7	1.6	3	2.1	10	2.3	
Distal	33	11.5	14	10.0	47	11.0	
Overall	40	13.1	17	12.1	57	13.3	
No recurrence	248	86.9	123	87.9	371	86.7	0.93

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548 *Dukes stage not recorded or not applicable due to complete response to neoadjuvant treatment

549 **long course chemoradiotherapy, short course radiotherapy, chemotherapy as part of FOXFROT

550 trial(22)

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554 **Table 3: Demographic and cancer specific details by adherence to RFU protocol.**

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Remote follow up adherence	Yes	%	No*	%	Overall	%	P values
	302	70.6	126	29.4	428	100.0	
Gender							
Male (n=247)	180	59.6	67	53.2	247	57.7	
Female (n=181)	122	40.4	59	46.8	181	42.3	0.220
Age							
<65 years (n=118)	72	23.8	46	36.5	118	27.5	
65-74 years (n=139)	101	33.5	38	30.2	139	32.5	
75+ years (n=171)	129	42.7	42	33.3	171	40.0	0.02*
Mean age	68.6	-	65.0	-	71.3	-	
Year of remote follow-up							
Year 1 (n=43)	37	12.3	6	4.8	43	10.1	
Year 2 (n=111)	72	23.8	39	31.0	111	25.9	
Year 3 (n=100)	72	23.8	28	22.2	100	23.4	
Year 4+ (n=174)	121	40.1	53	42.0	174	40.6	0.076
Tumour site							
Colonic (n=288)	216	71.5	72	57.1	288	67.3	
Rectal (n=140)	86	28.5	54	42.9	140	32.7	0.004
Resection site							
Right (n=143)	113	37.4	27	23.7	140	34.3	
Left (n=268)	181	59.9	87	76.3	268	65.7	0.005
Oncological treatment							
Surgery alone (n=241)	178	58.9	63	50.0	241	56.3	
Neoadjuvant +/- Adjuvant (n=187)	124	41.1	63	50.0	187	43.7	0.078
Recurrence							
No recurrence (n=371)	271	89.7	100	79.4	371	86.7	
Recurrence (n=57)	31	10.3	26	20.6	57	13.3	0.004

556 *patients who breached protocol by being seen in clinic following entry into RFU

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563 **Table 4: Quality of life measure results summarised by demographic, cancer related and operation**

564 **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	**0.009***	0.090
Age Group		
<65 years (n=118)	0.768 (IQR: 0.654-1)	75 (IQR: 50-91.6)
65-74 years (n=139)	0.837 (IQR: 0.698-1)	83.3 (IQR: 66.7-91.6)
75+ years (n=171)	0.767 (IQR: 0.671-0.879)	75 (IQR: 58.3-83.3)
p-value	**0.05***	**0.01***
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)	83.3 (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	**0.009***	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	**0.028***	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	**0.003***
Protocol adherence		
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)
p-value	0.0649	0.1105

565 **statistical significance demonstrated on Kruskal Wallis test*

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568 **Table 5: Our results for EQ-5D problem reporting overall, in comparison to the general population.**

	Problem domains and percentage of patients reporting problems				
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 5 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***
Protocol Adherence					
Yes, no clinic follow-up (n=296)	45.8	13.9	44.4	52.9	41.9
No, protocol breached and seen in clinic after entry to RFU (n=124)	49.2	19.1	55.2	63.2	43.2
Chi2, p value	0.520	0.176	0.043*	0.05*	0.804

569 *statistically significant results

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FIGURES

Figure 1: timeline illustrating typical journey of patients through diagnosis, treatment and RFU.

Figure 2: Flowchart to illustrate questionnaire response and subsequent details of included and excluded responders.

Figure 3: Bar Chat showing percentage of patients reporting problems vs no problems across EQ-5D functional scales

Figure 4: Box Plot summarising EQ-5D index scores by year of remote follow up