Food-related quality of life is impaired in inflammatory bowel disease and associated with reduced intake of key nutrients

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Abbreviations:

BMI	Body mass index
CD	Crohn's disease
CRP	C-reactive protein
EPIC-FFQ	European Prospective Investigation into Cancer - Food Frequency Questionnaire
FR-QoL	Food-related quality of life
FR-QoL-29	Food-related quality of life-29 questionnaire

IBD	Inflammatory bowel disease
IBD-DS	Inflammatory bowel disease distress scale
IBD-F	Inflammatory bowel disease fatigue scale
IBD-FI	Inflammatory bowel disease fatigue – severity subscale
IBD-FII	Inflammatory bowel disease fatigue – impact subscale
IBDQ	Inflammatory bowel disease quality of life scale
HADS	Hospital anxiety and depression scale
HADS-A	Hospital anxiety and depression – anxiety subscale
HADS-D	Hospital anxiety and depression – depression subscale
HBI	Harvey Bradshaw Index
MUST	Malnutrition Universal Screening Tool
NHS	National Health Service
QoL	Quality of life
SCCAI	Simple Clinical Colitis Activity Index
SD	Standard deviation
UC	Ulcerative colitis
UK	United Kingdom

Abstract

Background: Inflammatory bowel disease (IBD) may impact the extent to which food, eating and drinking bring satisfaction and enjoyment to peoples' lives and this may impact dietary intake. The prevalence of impaired food-related quality of life (FR-QoL), its associated factors and impact on diet have not been explored.

Objective: To measure the prevalence and nature of the burden of FR-QoL in people with IBD, the factors associated with these and its association with nutrient intake.

Design: 1576 outpatients with IBD (≥16 years old) were recruited in person from seven IBD centers across the United Kingdom. Patients completed validated questionnaires to measure FR-QoL (FR-QoL-29), quality of life, distress, fatigue, anxiety and depression. Dietary intake was recorded using the EPIC food frequency questionnaire. A health professional recorded disease activity, Montreal classification, blood results, BMI and malnutrition risk. FR-QoL was regressed onto explanatory variables using univariable and multivariable analysis.

Results: Data from 1221 patients were available (77.4% response) (Crohn's disease 65%, ulcerative colitis 35%). FR-QoL mean score was 80.8 (SD 26.9) with wide ranges (minimum 29, maximum 145). Following multivariable regression, the strongest associations with FR-QoL were the number of recent disease flares (five flares β= -12.7, $p<0.001$), IBD-specific quality of life (β= 0.33, $p<0.001$) and IBD-related distress (β= -0.26, $p<0.001$). Patients with poorer FR-QoL had lower intakes of fiber (non-starch polysaccharide) (Q1 to Q5 difference= 2.1 g/d, 95% CI 0.4, 3.8, p=0.048), calcium (192.6 mg/d, 95% CI 112.5, 272.6, $p<0.001$), phosphorus (167 mg/d, 95% CI 58, 276, p=0.041) and magnesium (34.4 mg/d, 95% CI 9.3, 59.4, p=0.041).

Conclusions: Impaired FR-QoL is prevalent in IBD, and associated with recurrent disease flares, reduced IBD-specific quality of life and greater IBD-related distress. Poorer FR-QoL was associated with lower intakes of key nutrients of importance to IBD, including those relating to gut health and bone mineralization.

Keywords: Inflammatory bowel disease, Crohn's disease, ulcerative colitis, food-related issues, food-related quality of life, nutritional status

Introduction

Inflammatory bowel disease (IBD) is a chronic, relapsing-remitting inflammatory disorder of the gastrointestinal tract affecting in excess of 0.3% of the world's population (1) with 40% being diagnosed as teenagers or young adults (16-29 years of age) (2). Crohn's disease (CD) and ulcerative colitis (UC) are the two main forms of IBD and gastrointestinal symptoms of diarrhea, urgency and abdominal pain can have extra-intestinal consequences including anorexia, weight loss (3-5) and fatigue (6, 7), as well as considerable psychosocial impacts of impaired quality of life (QoL) (8, 9), anxiety, depression (10, 11) and distress (12, 13).

IBD can have a profound impact on nutrient metabolism and requirements, with reports of low body mass index (BMI) and lean body mass (14), undernutrition or obesity (15) and hypermetabolism (16). Dietary interventions can be used to treat CD, such as exclusive enteral nutrition (17) and more recently partial enteral nutrition with exclusion of certain dietary carbohydrates, food additives, and gluten (18). People with IBD frequently report specific foods can impact their symptoms, although the responsible foods are highly individual to each patient (19-22), and restriction of fermentable carbohydrates may be beneficial in managing non-inflammatory symptoms in IBD (23).

Nutrients perform a host of essential biological functions, but food, eating and drinking also fulfil important social and psychological roles, including being a source of pleasure, a coping mechanism, communicating belonging to social or cultural groups, and are a focus around how people interact, entertain and celebrate with family, friends and colleagues (24). The extent to which these psychosocial roles of food, eating and drinking bring enjoyment to peoples' lives is termed food-related quality of life (FR-QoL) (21).

The impact of IBD on FR-QoL has been explored in qualitative interviews that report exclusion from social interactions involving food (e.g. religious, family, celebrations) and

uncertainty regarding the impact of eating and drinking on bowel function together with reduced autonomy, all of which can result in stress and anxiety (21, 25). People with IBD use different food-related strategies to control symptoms, such as identifying trigger foods, following restrictive diets, controlling portion size and eating more or less frequently, that may potentially have consequences on nutrient intake. These adaptive behaviors combined with limited knowledge about diet in IBD can adversely affect their FR-QoL and result in social isolation (21, 25). A questionnaire that measures FR-QoL has been developed and validated (26) and only one small study has measured this in IBD (27).

The complex nutritional issues, dietary treatments, food restrictions and perceived food triggers that occur in IBD may impact FR-QoL. However, studies measuring the magnitude of the problem FR-QoL, its contributing factors and its impact on nutrient intake have not been performed in large representative populations of people with IBD. This study aimed to measure the prevalence and nature of the burden of FR-QoL in people with IBD, the factors associated with these and their association with nutrient intake.

Subjects and methods

Population and recruitment

People with IBD were recruited from gastroenterology out-patient clinics at seven different National Health Service (NHS) Trusts across the United Kingdom (UK). The recruitment approach aimed to achieve a nationally representative patient population covering various geographical areas of the UK, urban and sub-urban locations and both specialist IBD and general clinics. Recruitment was performed between March 2017 and May 2018.

Inclusion criteria were a confirmed diagnosis of either CD or UC for at least 6 months, aged at least 16 years, consuming food as oral diet (intravenous nutrition, enteral nutrition, oral

nutritional support were acceptable as long as food constituted >50% of energy intake), non-institutionalized free-living, and sufficient command of written and spoken English to understand the study documentation and procedures. Exclusion criteria were a diagnosis of indeterminate colitis (due to low overall prevalence preventing meaningful statistical comparison), comorbidities that may also impact upon diet (e.g. diabetes, celiac disease, food allergies), and inability to give informed consent.

This study did not test an *a priori* hypothesis, due to lack of available preliminary data at the time of study design upon which to base such a hypothesis. Therefore, a precision-based sample size calculation was performed to measure FR-QoL-29 scores with a 2.5% level of precision (e=0.025) with 95% confidence (Z =1.96) among the total population of IBD in the UK (N=261,000) (1). Using a formula for finite populations ($n= (Z^2p(1-p)/e^2)/(1+(Z^2p(1-p)/e^2N))$ and assuming p=0.5, a sample size of 1,528 was required.

Patients attending out-patient clinics were screened against eligibility criteria by a researcher and, if eligible, were provided with questionnaires for completion either at the clinic appointment or at home (depending on their preference, for ethical reasons). Those completing questionnaires at home were provided with a pre-paid stamped addressed envelope and a reminder letter was sent to non-responders after four weeks.

The questionnaires were contained in a single booklet, the first section completed by the patient and the second section completed by the health professional researcher with access to the patients' medical records. The booklet was piloted for acceptability with a patient and public involvement group, completion time ranged from 15–45 mins (average 30 mins) which the group perceived as acceptable.

The questionnaire collected sociodemographic data (age, sex, marital status, ethnicity, smoking history, education level, employment status, living arrangements) and clinical data

(duration of diagnosis, number of disease flares in the previous two years, number of IBD-related surgeries, current stoma, IBD-related medications [name and dose]), which were completed through self-report by participants. Ethnicity was self-reported by participants using standard questions (28) and categorized into the five official categories recommended by the UK Government based upon ethnicity, race and nationality (Asian/Asian British; Black/African/Caribbean/Black British; Mixed/Multiple ethnic group; White; Other ethnic group)(29). These questionnaires were followed by those recording food-related quality of life, nutrient intake and nutritional risk, IBD-related psychosocial factors (completed by participants), and disease activity, disease classification and clinical data (completed by health professional researcher).

Food-related quality of life

The primary outcome was FR-QoL measured using the FR-QoL-29, which contains 29-items, each scored on 5-point Likert scale (1 strongly agree, 2 agree, 3 neither agree nor disagree, 4 disagree, 5 strongly disagree), with four questions reversed for scoring (Q8, Q9, Q24, Q25). Scores are summed with a total possible score ranging from 29 to 145, with higher scores reflecting greater FR-QoL. The FR-QoL-29 was developed based upon qualitative interviews within the IBD population (21), with good validity and reliability across a range of characteristics, including psychosocial aspects of eating and drinking in IBD (26).

Nutrient intake and nutritional risk

Nutrient intake was measured using the European Prospective Investigation into Cancer Food Frequency Questionnaire (EPIC-FFQ) (30), consisting of 130 food items with common portions or household measures and nine frequency categories. Data from the EPIC-FFQ were entered into the FETA software to calculate energy and nutrient intakes (31). Under- and over-reporters were excluded if the ratio of energy intake to basal metabolic rate

(calculated using sex and age-specific Schofield equations using measured body weight) was below or above the 2.5% and 97.5% percentiles respectively. Nutrient intake from supplements were not included as the goal was to analyze associations with intakes from diet.

Nutritional risk was measured using the Malnutrition Universal Screening Tool (MUST) consisting of scores for BMI, unplanned weight loss and acute disease effect (32). Scores were summed and categorized into low (score 0), medium (score 1) and high (score ≥2) risk of malnutrition. MUST is a valid measure of nutritional risk (32) and has been used in out-patients with IBD (33).

IBD-related psychosocial factors

Disease-specific quality of life was measured using the UK version of the IBD quality of life questionnaire (IBDQ) (34, 35), which measures overall physical, mental and social well-being in both CD and UC. The UK IBDQ consists of 30 items, scored using a four-point Likert scale, with scores summed to provide a total possible score ranging from 30 to 120, with a high score reflecting greater quality of life. IBD-specific fatigue was measured using the validated IBD-Fatigue scale (IBD-F) with five items rating severity of fatigue (IBD-FI subscale) and 30 items rating impact of fatigue (IBD-FII subscale), with higher sum scores reflecting worse fatigue (36). IBD-specific distress was measured using the IBD distress scale (IBD-DS), consisting of 28-items scored as a single domain with total scores ranging from 0 to 168, with higher scores indicating higher level of IBD-specific distress (12). Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS) consisting of seven items relating to anxiety (HADS-A subscale, score 0-21) and seven items relating to depression (HADS-D subscale, score 0-21). Higher scores indicate greater anxiety or depression (37).

Diagnosis, disease activity, disease classification and clinical data

The diagnosis of CD or UC was confirmed by review of patients' previous investigations from their medical notes. Patients were diagnosed with CD or UC by a gastroenterologist based upon endoscopic, radiological and histological assessment in accordance with British and European guidelines (38, 39). Disease activity was measured using the Harvey Bradshaw Index (HBI) for CD (40) and the Simple Clinical Colitis Activity Index (SCCAI) for UC (41), a higher score reflecting greater disease activity with a score of ≥5 representing active disease (42). Disease location and extent were recorded using the Montreal classification for both CD and UC (43).

Hemoglobin, serum albumin, C-reactive protein (CRP), platelet count, ferritin, folate and Vitamin B_{12}, together with fecal calprotectin were recorded when measured for clinical purposes that day (or within a one-month window).

All disease activity, classification and clinical data were recorded by the health professional researcher based upon participant interview, review of medical records and clinical biochemistry.

Ethical considerations

All procedures followed were in accordance with ethical standards and approved by the Yorkshire & The Humber – Sheffield Research Ethics Committee (17/YH/0044). Eligible patients were provided with a patient information sheet explaining the aims and nature of the study and had the opportunity to ask questions and seek clarification before deciding upon participation. Participants signed a consent form and were allocated a unique study code enabling anonymized inclusion of survey data. No participant identifiable data were collected. Participants had the right to withdraw from the study at any time, without having to give a reason for doing so and without their right and access to treatment being compromised.

Statistical analysis

A total of 150 questionnaires were double entered to check data entry accuracy. Missing data was replaced through multiple imputation (MI) adopting the multiple imputation using chained equations method (44). A total of 40 imputed datasets were created using Plumpton et al's (45) approach, with the multiple imputation fraction of missing data criterion being met (46). The FRQoL-29 total score and all explanatory variables were included in the imputation model for missing data, except for frequency of consumption of individual food items from the EPIC questionnaire. Missing data on the EPIC questionnaire were not assumed to be zero as this may under-estimate intake (47) and were not imputed as the optimal imputation method is uncertain (48). Instead, FFQs with 10 or more missing values for the 130 food items were excluded as per recommendations (31), with 53 of 1,183 (4.5%) FFQs excluded for this reason.

Descriptive statistics are presented for the original sample (categorical variables as frequencies and percentages; continuous variables as means and SD) along with summary statistics of FR-QoL-29 by each explanatory categorical variable (mean, SD) and Pearson's correlation coefficient between FR-QoL-29 and each continuous variable.

Prior to modelling, some explanatory variables were dichotomized (0 no; 1 yes) as follows: educational level (university degree-level education), relationship status (has a partner), current accommodation (homeowner), current employment status (in work or education), active disease (HBI $\geq$ 5 or SCCA $\geq$ 5). Univariable and multivariable regression were undertaken for all participants with IBD, as well as for CD and UC separately, with significance levels adjusted using a Bonferroni correction to account for multiple testing of three groups. All independent variables were entered into the multivariable model. The categorical variables included in the models are shown in **Table 1** and the continuous

variables are shown in **Table 2** (antibiotics, bile salt sequestrant, rectal 5ASA, vitamin supplements were excluded from the model because of low frequencies). Disease-specific extent variables were added separately for the CD (*ileal-colonic-ileocolonic*, upper GI) and UC models (*proctitis-distal-pancolitis*). Models were fitted to each dataset and the results presented as β estimates (95% confidence intervals) and p values. The β estimates for categorical variables represents the difference between the selected and reference categories. Collinearity was assessed using the variance inflation factor and normality by graphical inspection of the model residuals. Possible departure from a linear relationship between the psychosocial factors and FR-QoL-29 was assessed by adding a quadratic (squared) term for each variable to the model.

Nutrient intakes were estimated for each quintile of FR-QoL-29. Testing for statistical differences in nutrient intake across FR-QoL-29 quintiles was computed using a general linear model adjusting for sex, age, ethnicity, current disease activity (active/remission) together with all variables that were significantly associated with FR-QoL-29 in the multivariable regression model for IBD, CD alone or UC alone.

All statistical analysis was conducted using Stata version 16. The Stata ICE procedure was used to impute the 40 datasets and the MI procedure to fit the regression models and compute the F-tests. A p value of <0.05 was considered statistically significant.

Results

In total 1,576 participants consented of whom 1,221 (77.4%) returned a questionnaire containing complete analyzable data (**Supplementary Figure 1**). Demographic and clinical characteristics are shown in **Table 1** (categorical variables) and **Table 2** (continuous variables). Mean (SD) age was 39.8 (15.1), with even numbers of females (51%) and males (49%). Almost two-thirds (65%) had CD and one third (35%) had UC, with a mean disease

duration of 12.5 y (SD 10.4 y) and previous disease flare occurred on average, 1.9 y (SD 3.4 y) ago, with 32% having currently active disease.

The total score on the FR-QoL-29, calculated from summing the scores of the 29 individual items was mean 80.8 (SD 26.9) with values ranging from 29 (the lowest possible score) to 145 (the highest possible score)(**Figure 1**).

Table 3 shows the range of responses to each item of the FR-QoL-29. The four items most frequently rated as problematic (respondents agreed/strongly agreed) were: Q7 *'I have avoided food and drink I know does not agree with my IBD'* (71%); Q21 *'I have had to be more aware of what I am eating due to my IBD'* (70%); Q5 *'Certain foods have triggered symptoms of my IBD'* (69%); and Q2 *'My enjoyment of a particular food or drink has been affected by the knowledge that it might trigger my IBD symptoms'* (67%). The four items most infrequently rated as being problematic were: Q29 '*My IBD has meant that I have had to work hard to fit my eating habits in around my activities during the day'* (34%); Q15 '*The way I have had to eat for my IBD has restricted my lifestyle'* (35%); Q10 '*I have struggled to eat the way that is best for my IBD because of other commitments during the day'* (40%); and Q18 '*My IBD has prevented me from getting full pleasure from the food and drink I have had'* (42%).

Factors associated with FR-QoL in IBD (overall model)

The mean (SD) FR-QoL-29 total score for each categorical variable are shown in **Table 1** and the correlation between FR-QoL-29 total score and each continuous variable are shown in **Table 2**. These were entered separately into the univariable regression analysis for IBD and most variables were significantly associated with FR-QoL (**Supplementary Table 1**). The exceptions were having a partner, not currently in work or education, diagnosis (CD vs UC), previous IBD surgery, previous non-IBD gut surgery, duration of IBD diagnosis and C-

reactive protein concentrations. In the univariable analysis, the variables most strongly negatively associated with FR-QoL were number of disease flares in the previous two years (five flares β = -35.3, 95% CI -42.8, -27.7), severity of symptoms during previous disease flare (severe β = -23.4, 95% CI -32.5, -14.4), current active disease (β = -20.1, 95% CI -23.9, -16.4), receiving some artificial nutrition (β = -15.1, 95% CI -23.2, -7.0), steroid prescription (β = -11.8, 95% CI -17.6, -6.1), female sex (β = -11.1, 95% CI -14.7, -7.5) and risk of malnutrition (high risk β = -9.3, 95% CI -17.2, -1.3)(**Supplementary Table 1)**. All psychosocial factors were associated with FR-QoL with Pearson's r ranging from -0.52 (anxiety and depression) to -0.69 (distress) (**Table 2**).

All explanatory variables were entered into the multivariable model, which resulted in fewer statistically significant associations (**Table 4**, **Supplementary Table 1**). The variables with the strongest association with FR-QoL were the number of disease flares in the previous two years (five flares β = -12.7), IBD-related distress (β = -0.26) and IBD quality of life (β = 0.33). In relation to the latter, a patient on the 75th centile for IBD quality of life (IBDQ total score = 112) would have a FR-QoL-29 total score nine points higher than a patient on the 25th centile for IBDQ (IBDQ total score = 86). The only other variable associated with FR-QoL in the multivariable model was university degree level education (β = 3.1)(Table 4). People with CD had lower FR-QoL than those with UC, although this difference was relatively small and not statistically significant (β = -2.90, 95% CI -6.22, 0.43, p=0.11)(**Supplementary Table 1**).

Factors associated with FR-QoL in Crohn's disease and ulcerative colitis alone

In only those participants with CD, the majority of variables (21 out of 34) were significantly associated with FR-QoL on univariable analysis (**Supplementary Table 2**), with the most strongly negatively associated being the number of disease flares in the previous two years (five flares β = -34.3, 95% CI -43.6, -25.0), the severity of symptoms during last disease flare

(severe β = -20.3, 95% CI -31.6, -9.0), currently active disease (β = -19.3, 95% CI -24.0, -14.7), steroid prescription (β = -13.8, 95% CI -21.5, -6.1), receiving some artificial nutrition (β = -13.5, 95% CI -22.3, -4.8), female sex (β = -11.9, 95% CI -16.3, -7.5) and risk of malnutrition (high risk β = -9.3, 95% CI -18.6, 0.08) (**Supplementary Table 2**). Following multivariable regression in CD, only three explanatory variables were statistically significantly associated with FR-QoL: the number of disease flares in the previous two years (five flares β = -12.6); IBD quality of life (β = 0.41); and IBD-related distress (β = -0.26) (**Table 4**, **Supplementary Table 2**).

In only those participants with UC the majority of variables (19 out of 32) were significantly associated with FR-QoL in the univariable analysis (**Supplementary Table 3**), with the most strongly negatively associated being the number of disease flares in the previous two years (five flares β = -40.5, 95% CI -53.4, -27.6), severity of symptoms during previous disease flare (severe symptoms β = -28.9, 95% CI (-44.0, -13.8), currently active disease (β = -21.5, 95% CI -27.9, -15.1), receiving some artificial nutrition (β = -19.9, 95% CI -40.8, 1.0), risk of malnutrition (medium risk β = -12.6, 95% CI -25.2, 0.01) and female sex (β = -9.8, 95% CI -16.0, -3.5) (**Supplementary Table 3**). Following multivariable regression in UC, only IBD-related distress (β = -0.26) was statistically significantly associated with FR-QoL (**Table 4**, **Supplementary Table 3**).

In all models the variance inflation factor for each independent variable was less than 7. The highest variance inflation factors were for severity of disease. Residuals conformed well to a normal distribution. None of the psychosocial variables had statistically significant quadratic effects in any of the models.

FR-QoL and nutrient intake

Energy, nutrient and alcohol intake were compared between quintiles for FR-QoL-29. In the unadjusted model there were significant differences in intakes across quintiles of FR-QoL-29 for: fat (p=0.05); saturated fat (p=0.017); lactose (p=0.001); fiber (non-starch polysaccharide) (p=0.011); alcohol (p<0.001); folate (p=0.028); thiamine (p=0.022); riboflavin (p=0.001); vitamin C (p=0.039); potassium (p=0.024); phosphorus (p=0.005); calcium (p<0.001); magnesium (p=0.001); iron (p<0.001); and zinc (p=0.003), in each case intakes being lower in those with poorer FR-QoL (**Supplementary Table 4**).

The analysis was then adjusted for all variables that were significantly associated with FR-QoL-29 in the multivariable regression model for IBD, CD alone or UC alone, together with sex, age, ethnicity and current disease activity (active/remission) due to its association with nutrient intake in previously published studies. In the adjusted model there were significant differences in intakes across quintiles of FR-QoL-29 for: saturated fat (p=0.045); lactose (p<0.001); fiber (non-starch polysaccharide) (p=0.048); vitamin C (p=0.046); calcium (p<0.001); phosphorus (p=0.041); and magnesium (p=0.041) and in each case intakes being lower in those with poorer FR-QoL (**Table 5**).

Discussion

This is the first adequately powered study exploring the nature and burden of FR-QoL in any clinical disorder. The large sample has enabled a comprehensive analysis of the full range of demographic, clinical and psychosocial factors associated with reduced FR-QoL in IBD. In what is one of the largest dietary analysis in people with IBD, we demonstrate that poorer FR-QoL was associated with lower intakes of nutrients of key importance.

The mean score for FR-QoL (80.8, SD 26.9) is very similar to a previous report in 95 people with IBD in the United States (mean 82.0, SD 26.6) (27), and considerably lower than

previously reported in a non-gastrointestinal chronic disease such as asthma (125.4, SD 24.1) or in healthy volunteers (123.0, SD 16.5) (26).

The burden of FR-QoL was prevalent in patients with IBD. The items most commonly affecting patients (up to 71%) related to eating and its impact on symptom control (e.g. 'avoided food and drink I know does not agree with my IBD') and the consequence of this on the awareness and enjoyment of eating (e.g. 'being more aware of what I am eating due to my IBD'). Even the least frequently reported items were still experienced by over a third of patients and related to how modified eating behaviors impacted their daily activities (e.g. 'the way I have had to eat for my IBD has restricted my lifestyle').

These findings concur with our previous qualitative study that identified some people with IBD experiment with, and alter, their diet to manage symptoms (21). Identifying trigger foods through elimination and reintroduction or by trial and error, and manipulating the frequency and quantity of eating were common behaviors (21). The findings of the current study show these experiences are prevalent in IBD and commonly impact daily activities and life.

On multivariable analysis, the strongest association with poorer FR-QoL were a greater number of disease flares in the previous two years. Many experiences of eating and drinking will change during relapse: the foods that exacerbate symptoms can vary between relapse and remission; the resulting uncertainty of what to eat to reduce symptoms during relapse; and attempts to use diet to treat active disease (21). Interestingly, current active disease was significantly and strongly associated with FR-QoL on univariable analysis, but not on multivariable analysis. Taken together, these data suggest that regular fluctuations in experiences of eating and drinking in those with more frequent relapses may have a greater impact on FR-QoL than an isolated episode of active disease when a patient might anticipate

and accept altered eating experiences. These findings indicate a need for optimal chronic disease management and improved long-term symptom control in order to optimize FR-QoL.

Psychosocial factors were also associated with lower FR-QoL including higher level of IBD-related distress and reduced IBD quality of life, the latter confirming previous observations in a smaller cohort (27). Experiences of poor general QoL may therefore permeate into the psychosocial aspects of eating and drinking and specifically impair FR-QoL.

Crohn's disease has specific nutritional, physiological and clinical issues that might suggest a greater negative impact on FR-QoL, including: a greater impairment of nutritional status; previous experience of exclusive enteral nutrition that involves abstinence from eating all normal food (17); and non-inflammatory symptoms (e.g. bloating, abdominal pain) commonly associated with food intake being more common in CD (49). Despite this, CD was not associated with poorer FR-QoL compared with UC and therefore people with UC should be considered at similar risk of having impaired FR-QoL.

The burden of FR-QoL in IBD was not merely an impact on the psychosocial aspects of food, eating and drinking. People with poor FR-QoL also had marked differences in intake of key nutrients, including many indicatives of a healthful diet. For example, people with poorer FR-QoL had lower intakes of fiber (non-starch polysaccharide) (quintile 1 to quintile 5 mean difference = 2.1 g/d, 95% CI 0.4, 3.8). Such fibers are important as their fermentation results in the production of short-chain fatty acids (50), important for colonocyte integrity, and there is some evidence of low fiber intakes being associated with more frequent relapse in CD (51). Lower fiber intakes, in conjunction with lower vitamin C (17.4 mg/d, 95% CI 1.7, 33.2) and lower potassium (350 mg/d, 95% CI 77, 622) intakes in those with poorer FR-QoL may relate to avoidance of unrefined wholegrain cereals and intact plant foods such as legumes, beans,

fruits and vegetables, many of which are commonly avoided by people with IBD for fear of symptom induction or relapse (52-54).

There were also lower intakes of calcium (quintile 1 to quintile 5 mean difference = 192.6 mg/d, 95% CI 112.5, 272.6); phosphorus (167 mg/d, 95% CI 58, 276); and magnesium (34.4 mg/d, 95% CI 9.3, 59.4); and in those with poorer FR-QoL, all nutrients important in bone mineralization. This is of particular concern given lower bone mineral density and increased risk of bone fracture in IBD (55). Lower intakes of calcium and phosphorus in those with poorer FR-QoL may be the result of avoidance of dairy foods, which concurs with lower lactose intakes in poorer FR-QoL (5.6 g/d, 95% CI 3.2, 7.7) found here and with previous reports of dairy food avoidance in IBD (52-54). Dairy foods are prevalent in the food chain and frequently added to home-cooked and restaurant-cooked dishes and contained within ready meals, and avoidance of which may considerably impact food-related behaviors.

Understanding the relationship between IBD and FR-QoL may improve communication between health professionals and people with IBD regarding its impact on their lives. FR-QoL can be measured using the same questionnaire from this study for both clinical and research purposes. The modifiable factors described here should be addressed where possible, and any related impact of FR-QoL on nutrient intake should be addressed. Future studies should investigate how FR-QoL can be improved.

Strengths and limitations

The strengths of the study are its sample size, the largest ever analysis of FR-QoL in any clinical condition, and the nationwide recruitment of participants with almost 50:50 split in sex and wide age range, making the sample representative of the theoretical population of patients with IBD. There was a high response rate and high proportion of fully completed questionnaires thus considerably reducing response bias. Many of the studied parameters (e.g.

MUST and disease type, classification, severity), were measured or recorded from medical notes by the treating clinician or nurse to increase accuracy.

The study also has several limitations. The cross-sectional design prevents causality of the different factors on FR-QoL being inferred, hence, only associations can be described. Approximately two thirds of participants had CD and only one third UC and therefore does not reflect disease distribution in the UK and is the result of recruitment from secondary care where CD is more commonly managed than UC. The recruited population were 86.2% white reflecting national figures in the UK (86.0%), however, future studies should specifically investigate FR-QoL in minority ethnic groups. Although we included IBD centers in England and Scotland, we failed to recruit from centers in Wales and Northern Ireland. We aimed to record many blood results and fecal calprotectin from routine clinical testing, however, the widespread absence of such testing meant these values could not be fully utilized in data analysis. The compromise of our large sampling frame resulted in not performing these tests specifically for the purposes of this study, as doing so may have reduced recruitment and been financially unviable.

Conclusion

In this first, large cross-sectional survey of its kind, the burden of FR-QoL was shown to be prevalent in IBD, and associated with numerous factors including recurrent disease flares, reduced IBD quality of life and greater IBD-related distress, although higher educational level had positive associations with FR-QoL. Poorer FR-QoL was associated with lower intakes of numerous nutrients indicative of a less healthful diet.

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Conflict of interest

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TM: None

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Author contributions

KW, JOL, MCL, MM designed the research; WCD, JOL, MCL, FC, CS, AT, SS, AL, conducted research; KW supervised the research; TM and KW analyzed data; KW, TM, WCD wrote paper; KW had primary responsibility for final content; all authors read and approved the final manuscript.

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Table 1. Categorical demographic and clinical data and mean (SD) FR-QoL-29 total score for each category in patients with inflammatory bowel disease

Variable	Grouping	Frequency, n (%)	FR-QoL-29 score, mean (SD)
Sex (n=1,218)	Female	625 (51.3%)	75.4 (25.4)
	Male	593 (48.7%)	86.5 (27.3)
Ethnicity (n=1,215)[1]	Asian / Asian British	103 (8.5%)	72.4 (25.2)
	Black / African / Caribbean / Black British	28 (2.3%)	86.5 (25.7)
	Mixed/Multiple ethnic groups	23 (1.9%)	85.4 (28.7)
	White	1,047 (86.2%)	81.6 (27.0)
	Other ethnic group	14 (1.2%)	68.1 (20.0)
Education (n=1,194)	No formal qualifications	98 (8.2%)	79.5 (24.4)
	Vocational qualifications	55 (4.6%)	69.8 (22.2)
	School qualifications (16 y)	291 (24.4%)	76.0 (24.2)
	Advanced school qualification (18y)	229 (19.2%)	82.9 (28.9)
	University degree (e.g. Bachelors)	379 (31.7%)	83.6 (26.7)
	Postgraduate degree (e.g. MSc, PhD)	142 (11.9%)	86.8 (29.6)
Relationship status (n=1,218)	Married / Civil partnership	522 (42.9%)	82.0 (27.6)
	Living with a partner	220 (18.1%)	81.8 (25.8)
	Widowed	30 (2.5%)	77.4 (23.5)
	Divorced/Separated	51 (4.2%)	74.2 (22.4)
	Single	395 (32.4%)	79.7 (27.2)
Accommodation (n=1,215)	Homeowner	662 (54.5%)	83.6 (27.4)
	Renting	365 (30.0%)	77.8 (26.3)
	Living with family	188 (15.5%)	76.9 (25.3)
Employment (n=1,212)	Employed full time	647 (53.4%)	83.6 (27.0)
	Employed part time	186 (15.3%)	75.7 (25.8)
	Education full or part time	69 (5.7%)	83.3 (24.8)
	Domestic responsibilities full time	37 (3.1%)	72.2 (24.9)
	Retired	137 (11.3%)	87.3 (26.6)
	Unemployed	136 (11.2%)	69.4 (25.5)
Smoking behavior (n=1,212)	Current smoker	104 (8.6%)	72.8 (24.7)
	Previous smoker	385 (31.8%)	79.4 (26.8)
	Non-Smoker	723 (59.7%)	82.5 (27.0)

IBD diagnosis (n=1,221)	Crohn's disease	789 (64.6%)	79.7 (26.5)
	Ulcerative colitis	432 (35.4%)	82.7 (27.5)
Montreal classification, CD			
Location (n=766)	Ileal (L1)	193 (25.2%)	77.8 (25.1)
	Colonic (L2)	206 (26.9%)	83.8 (27.5)
	Ileocolonic (L3)	367 (47.9%)	78.2 (26.0)
Upper GI (n=789)	No upper GI involvement (L4)	734 (93.0%)	80.1 (26.5)
	Upper GI involvement (L4)	55 (7.0%)	74.3 (25.3)
Behavior (n=732)	Non-stricturing, non-penetrating (B1)	395 (54.0%)	80.2 (26.6)
	Stricturing (B2)	212 (29.0%)	77.2 (26.0)
	Penetrating (B3)	125 (17.1%)	81.2 (27.7)
Peri-anal (n=789)	No perianal disease	618 (78.3%)	79.4 (26.9)
	Perianal disease (p)	171 (21.7%)	80.7 (24.9)
Montreal classification, UC			
Extent (n=415)	Proctitis (E1)	77 (18.9%)	85.4 (27.8)
	Distal (E2)	154 (37.1%)	81.8 (26.8)
	Pancolitis (E3)	184 (44.3%)	82.2 (27.6)
Severity (n=418)	Clinical remission (S0)	210 (50.2%)	91.5 (27.6)
	Mild (S1)	124 (29.7%	77.7 (25.5)
	Moderate (S2)	74 (17.7%)	70.6 (22.1)
	Severe (S3)	10 (2.4%)	69.7 (29.8)
Disease activity			
Current activity	Remission	793 (68.3%)	87.2 (26.7)
(HBI/SCCAI) (n=1,161)	Active	368 (31.7%)	67.4 (22.1)
Disease flares in	None	275 (23.1%)	99.4 (25.9)
previous 2 y (n=1,191)	One	244 (20.5%)	85.0 (27.4)
	Two	179 (15.0%)	76.6 (23.1)
	Three	98 (8.2%)	80.3 (22.4)
	Four	83 (7.0%)	76.1 (21.5)
	Five	74 (6.2%)	64.2 (17.7)
	Ongoing activity without remission	238 (20.0%)	65.6 (21.8)
Self-reported symptom	None	54 (4.6%)	100.1 (28.7%)
severity during last flare	Mild	193 (16.4%)	87.9 (27.1%)
(n=1,174)	Moderate	476 (40.5%)	80.4 (25.1)
	Severe	451 (38.4%)	75.4 (27.0)
Surgery			

IBD surgery	No previous IBD surgery	811 (66.9%)	81.8 (27.3)
(n=1,212)	Previous IBD surgery	401 (33.1%)	78.8 (26.0)
Non-IBD GI surgery	No previous non-IBD GI surgery	1092 (92.1%)	81.2 (26.9)
(n=1,185)	Previous non-IBD GI surgery	93 (7.8%)	78.7 (26.5)
Current medications (n=1,221)			
Oral 5ASA	Not prescribed	883 (72.4%)	79.2 (26.5)
	Prescribed	338 (27.7%)	84.7 (27.4)
Biologics	Not prescribed	559 (45.8%)	83.9 (27.7)
	Prescribed	662 (54.2%)	78.1 (25.8)
Immune suppressant	Not prescribed	626 (51.3%)	78.8 (26.8)
	Prescribed	595 (48.7%)	82.8 (26.7)
Rectal 5ASA	Not prescribed	1210 (99.1%)	80.8 (26.9)
	Prescribed	11 (0.9%)	73.3 (24.2)
Steroids	Not prescribed	1080 (88.5%)	82.1 (26.6)
	Prescribed	141 (11.5%)	70.6 (26.5)
Antibiotics	Not prescribed	1219 (99.8%)	80.8 (26.9)
	Prescribed	2 (0.2%)	69.0 (17.0)
Bile salt sequestrant	Not prescribed	1212 (99.3%)	80.9 (26.9)
	Prescribed	9 (0.7%)	63.7 (15.0)
Nutrition			
Artificial nutrition	None	1113 (94.2%)	81.5 (26.9)
(n=1,182)	Yes (ONS 65, enteral 3, both 1)	69 (5.8%)	66.4 (20.6)
Malnutrition risk	Low	926 (84.4%)	82.4 (26.8)
(MUST) (n=1,097)	Medium	104 (9.5%)	74.6 (25.5)
	High	67 (6.1%)	72.5 (26.6)
Vitamin supplement	Not prescribed	1210 (99.1%)	80.8 (26.9)
(n=1,221)	Prescribed	11 (0.9%)	74.9 (25.4)

[1] Ethnicity was self-reported using standard questions and categorized into the five official categories recommended by the UK Government based upon ethnicity, race and nationality (Asian/Asian British; Black/African/Caribbean/Black British; Mixed/Multiple ethnic group; White; Other ethnic group).

Table 2. Continuous demographic and clinical data and their correlation with FR-QoL-29 total score (Pearson's correlation co-efficient) in patients with inflammatory bowel disease

		Correlation with FRQoL-29 score	
	Descriptives, mean (SD)	**Pearson's correlation coefficient, r**	**P value**
Age, years (n=1,102)	39.8 (15.1)	0.06	0.044
Duration of diagnosis, years (n=1,170)	12.5 (10.4)	0.05	0.076
Disease activity			
Crohn's disease (HBI) (n=746)	3.7 (4.4)	-0.38	<0.001
Ulcerative colitis (SCCAI) (n=426)	3.5 (2.8)	-0.40	<0.001
Fecal calprotectin, mg/l (n=134)	526.8 (981.2)	-0.08	0.35
Previous disease flare, years (n=858)	1.9 (3.4)	0.26	<0.001
Blood results			
Hemoglobin, g/dL (n=962)	135.8 (15.3)	0.17	<0.001
Ferritin, µg/L (n=202)	76.5 (106.7)	0.12	0.099
Serum albumin, g/dL (n=920)	42.6 (5.6)	0.08	0.015
C-reactive protein, mg/L (n=892)	7.5 (22.1)	-0.07	0.032
Platelet count, µL (n=954)	281.2 (86.8)	-0.12	<0.001
Vitamin B_{12}, ng/mL (n=159)	382.2 (331.7)	0.01	0.90
Folate, ng/mL (n=137)	18.5 (72.7)	0.03	0.74
IBD-related psychosocial variables			
Quality of life (UK IBDQ) (n=1,211)	99.2 (15.4)	0.63	<0.001
Fatigue severity (IBD-FI) (n=1,208)	9.5 (5.3)	-0.53	<0.001
Fatigue impact (IBD-FII) (n=1,209)	33.0 (27.7)	-0.57	<0.001
Distress score (IBD-DS) (n=1,214)	75.4 (44.5)	-0.69	<0.001
Anxiety (HADS-A) (n=1,215)	7.8 (4.9)	-0.52	<0.001
Depression (HADS-D) (n=1,213)	5.0 (4.1)	-0.52	<0.001

Table 3 Responses to each item of the FRQoL-29 representing the prevalence of issues with food-related quality of life in inflammatory bowel disease

FRQoL-29 item (n of respondents)	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
1. I have regretted eating and drinking things which have made my IBD symptoms worse (1,209)	333 (27.5%)	407 (33.7%)	172 (14.2%)	152 (12.6%)	145 (12.0%)
2. My enjoyment of a particular food or drink has been affected by the knowledge that it might trigger my IBD symptoms (1,212)	366 (30.2%)	452 (37.3%)	122 (10.1%)	152 (12.5%)	120 (9.9%)
3. My IBD has meant that I have had to leave the table while I am eating to go to the toilet (1,212)	323 (26.7%)	362 (29.9%)	94 (7.8%)	239 (19.7%)	194 (16.0%)
4. I have not been able to predict how long it will take for my body to respond to something I have had to eat or drink due to my IBD (1,210)	239 (19.8%)	453 (37.4%)	212 (17.5%)	194 (16.0%)	112 (9.3%)
5. Certain foods have triggered symptoms of my IBD (1,212)	402 (33.2%)	437 (36.1%)	154 (12.7%)	124 (10.2%)	95 (7.8%)
6. My IBD has meant that I have been nervous that if I eat something I will need to go to the toilet straight away (1,212)	289 (23.8%)	318 (26.2%)	162 (13.4%)	263 (21.7%)	180 (14.9%)
7. I have avoided having food and drink I know does not agree with my IBD (1,213)	463 (38.2%)	401 (33.1%)	117 (9.6%)	132 (10.9%)	100 (8.2%)
8. I have felt relaxed about what I can eat and drink despite my IBD (1,212)	162 (13.4%)	357 (29.5%)	213 (17.6%)	332 (27.4%)	148 (12.2%)
9. I have felt in control of what I eat and drink in relation to my IBD (1,213)	202 (16.7%)	501 (41.3%)	238 (19.6%)	212 (17.5%)	60 (4.9%)
10. I have struggled to eat the way that is best for my IBD because of other commitments during the day (1,212)	123 (10.1%)	364 (30.0%)	254 (21.0%)	332 (27.4%)	139 (11.5%)
11. I have been frustrated about not knowing how food and drink will react with my IBD (1,211)	205 (16.9%)	372 (30.7%)	240 (19.8%)	273 (22.5%)	121 (10.0%)
12. I have had to concentrate on what I have been eating and drinking because of my IBD (1,212)	219 (18.1%)	447 (36.9%)	207 (17.1%)	233 (19.2%)	106 (8.7%)
13. I have been worried that if I eat I will get symptoms of my IBD (1,214)	243 (20.0%)	370 (30.5%)	189 (15.6%)	264 (21.7%)	148 (12.2%)
14. I have felt the way that I eat and drink for my IBD has affected my day to day life (1,215)	255 (21.0%)	331 (27.2%)	193 (15.9%)	286 (23.5%)	150 (12.3%)
15. The way I have had to eat for my IBD has restricted my lifestyle (1,203)	151 (12.6%)	272 (22.6%)	195 (16.2%)	398 (33.1%)	187 (15.5%)
16. I have had to concentrate on what food I buy because of my IBD (1,207)	194 (16.1%)	424 (35.1%)	163 (13.5%)	285 (23.6%)	141 (11.7%)

17. It has been on my mind how my IBD will be affected by what I eat and drink (1,207)	215 (17.8%)	482 (39.9%)	170 (14.1%)	220 (18.2%)	120 (9.9%)
18. My IBD has prevented me from getting full pleasure from the food and drink I have had (1,212)	229 (18.9%)	279 (23.0%)	174 (14.4%)	364 (30.0%)	166 (13.7%)
19. I have felt that I need to know what is in the food I am eating due to my IBD (1,211)	188 (15.5%)	367 (30.3%)	211 (17.4%)	296 (24.4%)	149 (12.3%)
20. I have felt that I have had to be careful about when I have eaten because of my IBD (1,208)	202 (16.7%)	479 (39.7%)	146 (12.1%)	260 (21.5%)	121 (10.0%)
21. I have had to be more aware of what I am eating due to my IBD (1,210)	277 (22.9%)	574 (47.4%)	104 (8.6%)	166 (13.7%)	89 (7.4%)
22. I have missed being able to eat or drink whatever I want because of my IBD (1,210)	298 (24.6%)	286 (23.6%)	161 (13.3%)	319 (26.4%)	146 (12.1%)
23. I have felt that I would like to be able to eat and drink like everyone else (1,208)	363 (30.0%)	312 (25.8%)	214 (17.7%)	200 (16.6%)	119 (9.9%)
24. I have been happy to eat and drink around people I do not know despite my IBD (1,209)	300 (24.8%)	564 (46.7%)	147 (12.2%)	143 (11.8%)	55 (4.5%)
25. I have felt that I have been eating and drinking normally despite my IBD (1,207)	198 (16.4%)	413 (34.2%)	192 (15.9%)	290 (24.0%)	114 (9.4%)
26. I have found it hard not knowing if a certain food will trigger IBD symptoms (1,211)	162 (13.4%)	428 (35.3%)	259 (21.4%)	261 (21.6%)	101 (8.3%)
27. My IBD has meant I have had to make an effort to get all the nutrients my body needs (1,210)	182 (15.0%)	459 (37.9%)	239 (19.8%)	240 (19.8%)	90 (7.4%)
28. I have felt that I have not known how my IBD will react to food or drink (1,212)	144 (11.9%)	481 (39.7%)	257 (21.2%)	239 (19.7%)	91 (7.5%)
29. My IBD has meant that I have had to work hard to fit my eating habits in around my activities during the day (1,211)	133 (11.0%)	273 (22.5%)	262 (21.6%)	406 (33.5%)	137 (11.3%)

Q8, Q9, Q24 and Q25 are reversed for scoring.

Table 4 Variables that were significantly associated with FR-QoL-29 total score in multivariable regression models in the inflammatory bowel disease population, or in Crohn's disease or ulcerative colitis groups only

	IBD (all patients, n=1221)			Crohn's (n=789)			Ulcerative Colitis (n=432)		
Variables	**β**	**(95% CI)**	**p**	**β**	**(95% CI)**	**p**	**β**	**(95% CI)**	**p**
University degree level education									
No	Ref			-	-	-	-	-	-
Yes	3.1	(0.3, 5.9)	0.025	-	-	-	-	-	-
Disease flares in previous 2 years	$F_{(6,1161.9)}$ = 4.3, p <0.001			$F_{(6,730.0)}$ = 3.1, p = 0.015					
None	Ref			Ref					
One	-4.5	(-9.1, 0.1)	0.060	-4.4	(-10.0, 1.2)	0.17	-	-	-
Two	-7.5	(-12.7, -2.4)	0.002	-7.9	(-14.5, -1.3)	0.015	-	-	-
Three	-8.0	(-14.0, -2.0)	0.005	-7.5	(-15.7, 0.8)	0.087	-	-	-
Four	-7.5	(-14.00, -1.1)	0.016	-6.2	(-14.2, 1.8)	0.18	-	-	-
Five	-12.7	(-19.6, -5.8)	<0.001	-12.6	(-21.3, -4.0)	0.003	-	-	-
Ongoing disease activity	-8.2	(-13.6, -2.8)	0.001	-9.8	(-16.4, -3.2)	<0.001	-	-	-
Quality of life (IBDQ)	0.33	(0.17, 0.48)	<0.001	0.41	(0.21, 0.61)	<0.001	-	-	-
Distress score (IBD-DS)	-0.26	(-0.31, -0.20)	<0.001	-0.26	(-0.33, -0.19)	<0.001	-0.26	(-0.34, -0.17)	<0.001

Ref, reference group; - no statistical significance in the multivariable regression model; N/A not applicable

Table 5 Adjusted energy, nutrient and alcohol intakes from food and drinks across quintiles of food-related quality of life in 1,074 patients with inflammatory bowel disease

	Intakes in each quintile of FR-QoL-29 score, estimated marginal mean (95% CI)[1]					
	Q1 (29-56)	**Q2 (57-70)**	**Q3 (71-86)**	**Q4 (87-105)**	**Q5 (106-145)**	**p value[2]**
Energy (kcal/d)	1722 (1621, 1824)	1774 (1689, 1858)	1879 (1795, 1963)	1792 (1707, 1878)	1857 (1759, 1954)	0.096
Protein (g/d)	75.3 (70.5, 80.2)	80.0 (75.9, 84.0)	80.0 (76.0, 84.1)	79.7 (75.6, 83.8)	80.8 (76.2, 85.4)	0.54
Fat (g/d)	71.1 (66.0, 76.2)	71.2 (67.0, 75.4)	76.8 (72.6, 81.0)	71.2 (66.9, 75.5)	76.1 (71.2, 81.0)	0.18
Saturated (g/d)	26.5 (24.4, 28.7)	26.6 (24.8, 28.3)	29.6 (27.8, 31.4)	27.3 (25.5, 29.1)	29.8 (27.8, 31.9)	**0.045**
Monounsaturated (g/d)	26.6 (24.6, 28.6)	26.4 (24.8, 28.1)	28.2 (26.6, 29.8)	26.5 (24.8, 28.2)	28.0 (26.1, 29.9)	0.40
Polyunsaturated (g/d)	11.8 (10.9, 12.8)	12.1 (11.3, 12.8)	12.4 (11.6, 13.1)	11.3 (10.6, 12.1)	11.7 (10.9, 12.6)	0.41
Carbohydrate (g/d)	202.2 (188.7, 215.6)	209.7 (198.6, 220.9)	221.5 (210.5, 232.6)	212.2 (200.9, 223.6)	214.7 (201.8, 227.5)	0.31
Total sugars (g/d)	95.5 (87.2, 103.8)	100.6 (93.7, 107.6)	105.8 (98.9, 112.7)	104.4 (97.4, 111.5)	107.5 (99.5, 115.5)	0.40
Glucose (g/d)	17.4 (15.6, 19.2)	18.4 (16.9, 19.9)	18.2 (16.8, 19.7)	18.6 (17.1, 20.1)	18.8 (17.1, 20.5)	0.88
Fructose (g/d)	17.0 (15.0, 19.1)	19.1 (17.3, 20.8)	18.5 (16.8, 20.3)	19.4 (17.7, 21.2)	20.0 (18.1, 22.0)	0.40
Galactose (g/d)	0.35 (0.23, 0.47)	0.36 (0.26, 0.46)	0.51 (0.41, 0.61)	0.52 (0.42, 0.62)	0.53 (0.42, 0.65)	0.11
Sucrose (g/d)	44.7 (39.9, 49.4)	45.4 (41.4, 49.3)	47.7 (43.8, 51.6)	45.8 (41.8, 49.9)	46.0 (41.5, 50.5)	0.90
Lactose (g/d)	11.6 (10.1, 13.1)	12.9 (11.7, 14.2)	15.1 (13.8, 16.3)	15.2 (13.9, 16.5)	17.2 (15.8, 18.6)	**<0.001**
Maltose (g/d)	2.6 (2.3, 3.0)	2.6 (2.3, 2.9)	2.9 (2.6, 3.2)	2.6 (2.3, 2.9)	2.7 (2.3, 3.0)	0.70
Starch (g/d)	103.9 (96.6, 111.2)	105.8 (99.8, 111.9)	112.4 (106.4, 118.4)	104.6 (98.4, 110.7)	104.1 (97.1, 111.0)	0.25
Fiber (NSP, g/d)	12.0 (11.0, 13.1)	13.8 (12.9, 14.7)	13.7 (12.8, 14.6)	13.3 (12.3, 14.2)	14.2 (13.1, 15.2)	**0.048**
Alcohol (g/d)	3.5 (2.0, 4.9)	4.0 (2.8, 5.2)	5.5 (4.3, 6.7)	5.5 (4.2, 6.7)	6.4 (5.0, 7.8)	0.077
Vitamin A (RAE, µg/d)	1100 (953, 1248)	1063 (940, 1185)	1016 (894, 1138)	999 (874, 1125)	987 (845, 1129)	0.88
Thiamin (mg/d)	1.24 (1.16, 1.32)	1.34 (1.27, 1.41)	1.34 (1.27, 1.40)	1.27 (1.21, 1.34)	1.34 (1.26, 1.42)	0.16
Riboflavin (mg/d)	1.57 (1.46, 1.68)	1.65 (1.56, 1.74)	1.73 (1.64, 1.82)	1.69 (1.59, 1.78)	1.80 (1.69, 1.90)	0.096
Niacin (mg/d)	20.4 (19.0, 21.8)	21.6 (20.4, 22.8)	21.0 (19.9, 22.2)	21.0 (19.8, 22.2)	21.1 (19.7, 22.4)	0.74
Pyridoxine (mg/d)	1.95 (1.83, 2.06)	2.07 (1.97, 2.16)	2.05 (1.96, 2.15)	2.02 (1.92, 2.11)	2.05 (1.93, 2.16)	0.50
Folate (µg/d)	234.6 (218.0, 251.2)	251.5 (237.7, 265.3)	248.5 (234.8, 262.2)	239.6 (225.5, 253.7)	250.7 (234.7, 266.7)	0.37
Vitamin B_{12} (µg/d)	6.4 (5.6, 7.1)	6.3 (5.7, 6.9)	6.2 (5.6, 6.8)	6.3 (5.7, 6.9)	6.0 (5.3, 6.6)	0.94
Vitamin C (mg/d)	80.5 (70.5, 90.5)	98.6 (90.3, 106.9)	91.5 (83.3, 99.7)	93.7 (85.3, 102.1)	97.9 (88.4, 107.5)	**0.046**
Vitamin D (µg)	3.16 (2.82, 3.49)	3.03 (2.75, 3.31)	3.05 (2.77, 3.33)	2.93 (2.65, 3.22)	2.72 (2.39, 3.04)	0.54
Vitamin E (mg/d)	10.5 (9.7, 11.4)	11.0 (10.4, 11.7)	11.6 (10.9, 12.2)	10.6 (9.9, 11.3)	11.1 (10.3, 11.9)	0.22

Potassium (mg/d)	2865 (2692, 3038)	3127 (2983, 3270)	3181 (3038, 3324)	3117 (2971, 3263)	3215 (3049, 3380)	0.051
Sodium (mg/d)	2417 (2262, 2571)	2481 (2352, 2609)	2577 (2450, 2705)	2414 (2284, 2545)	2545 (2397, 2693)	0.31
Phosphorus (mg/d)	1169 (1100, 1238)	1246 (1188, 1303)	1290 (1233, 1347)	1273 (1215, 1332)	1336 (1270, 1402)	**0.041**
Calcium (mg/d)	686.1 (635.4, 736.9)	734.8 (692.6, 777.0)	820.5 (778.6, 862.4)	791.4 (748.1, 834.7)	878.7 (830.1, 927.4)	**<0.001**
Magnesium (mg/d)	248.8 (232.8, 264.7)	272.6 (259.4, 285.9)	276.6 (263.4, 289.7)	269.3 (255.9, 282.7)	283.1 (267.9, 298.3)	**0.041**
Iron (mg/d)	9.1 (8.5, 9.6)	9.8 (9.3,10.3)	9.8 (9.4, 10.3)	9.6 (9.1, 10.1)	10.0 (9.5, 10.6)	0.16
Zinc (mg/d)	7.9 (7.4, 8.4)	8.7 (8.3,9.1)	8.5 (8.1, 9.0)	8.8 (8.3, 9.2)	8.9 (8.4, 9.4)	0.072
Iodine (µg/d)	128.8 (118.9, 138.6)	133.1 (124.9, 141.3)	139.4 (131.2, 147.6)	135.9 (127.6, 144.3)	138.5 (129.0, 148.0)	0.60
Selenium (µg /d)	61.8 (57.3, 66.2)	63.0 (59.4, 66.7)	63.8 (60.1, 67.5)	59.9 (56.1, 63.6)	59.4 (55.1, 63.7)	0.48

NSP Non-starch polysaccharide; RAE Retinol active equivalents

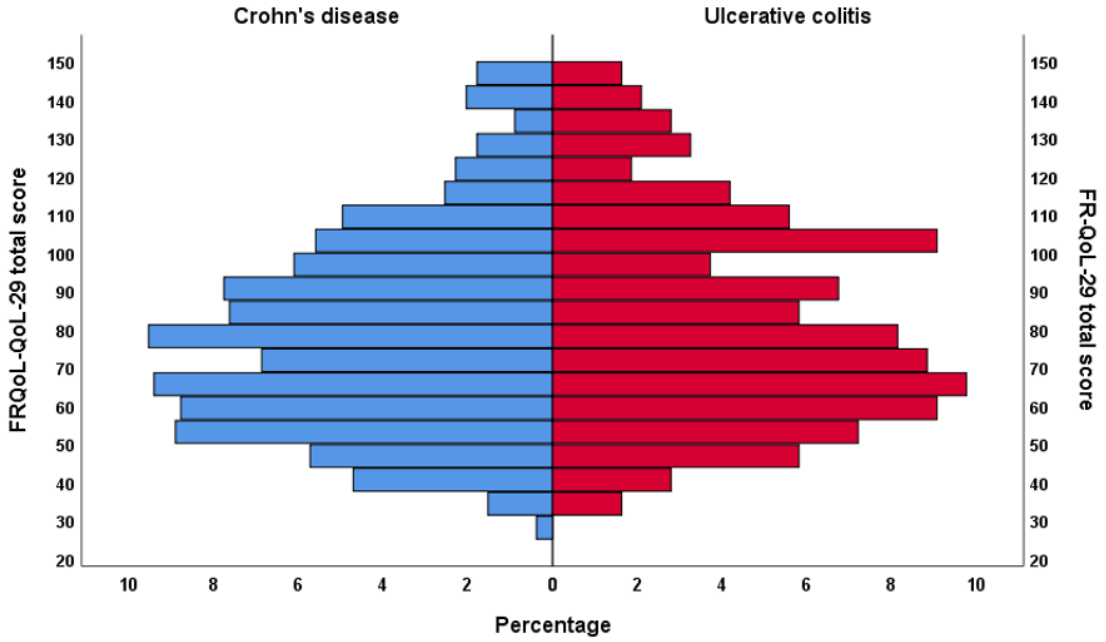
[1] Intakes are estimated marginal mean (95% CI) values

[2] P value across quintiles following general linear model and adjustment for sex, age, ethnicity, current disease activity (active/remission), university education, number of disease flares in past 2 years and scores for quality of life (IBDQ) and distress (IBD-DS).

Figure legend

Figure 1 Distribution of FR-QoL-29 total score in inflammatory bowel disease

Data are presented as the patients in each FR-QoL-29 score boundary as a percent of those with Crohn's disease (n=789, blue) and as a percent of those with ulcerative colitis (n=432, red).



Online Supplementary Material

Food-related quality of life is impaired in inflammatory bowel disease and associated with reduced intake of key nutrients

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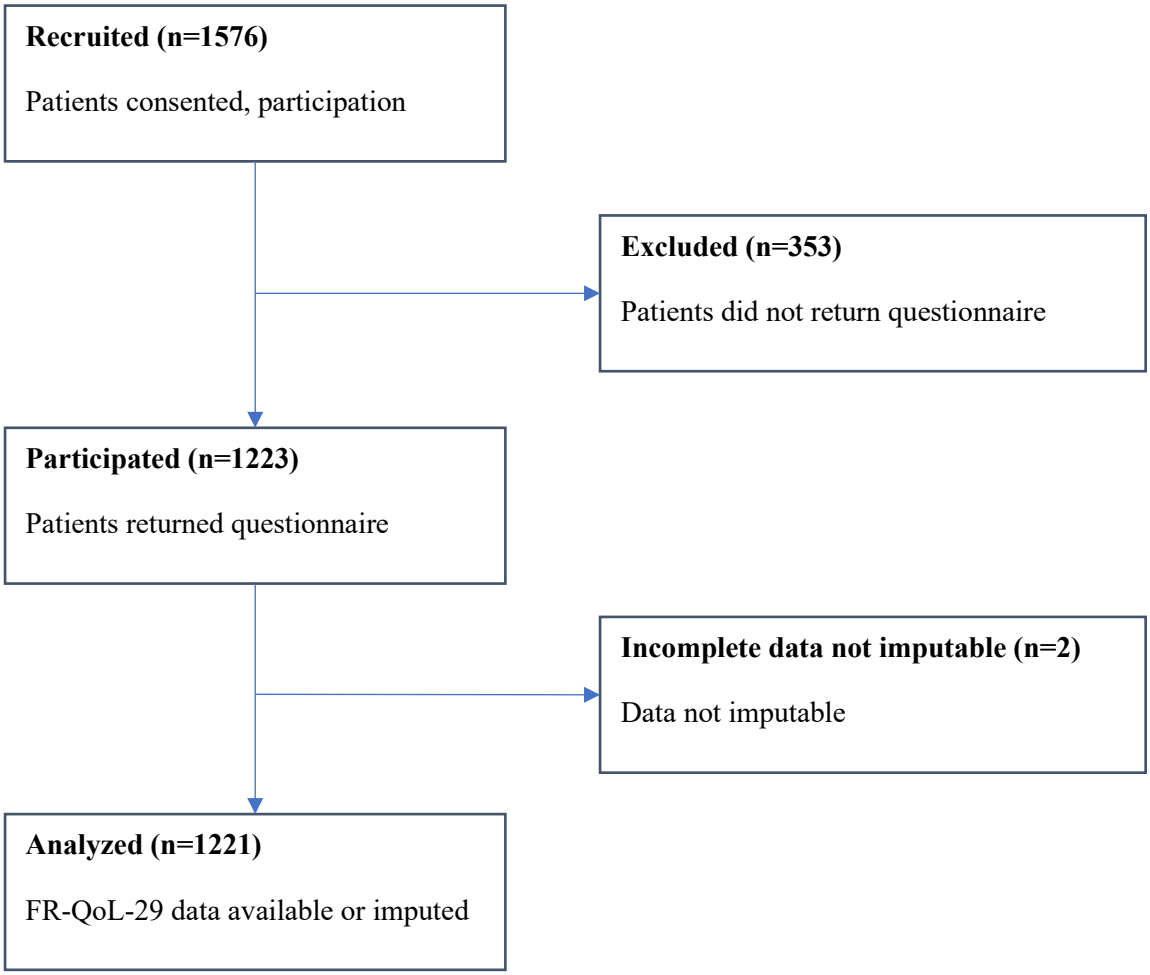
Supplementary Figure 1: Participant flow diagram, the questionnaire survey



Supplementary Table 1: Categorical and continuous variables and their association with FR-QoL-29 total score in univariable and multivariable regression models in the entire inflammatory bowel disease population

	Univariable			Multivariable		
Variables	**β**	**(95%CI)**	**P>t**	**β**	**(95%CI)**	**P>t**
Demographic						
Gender						
Male†	0.00			0.00		
Female	-11.13	(-14.74, -7.51)	**<0.001**	-1.82	(-4.91, 1.27)	0.40
Ethnicity	F(4,1213.0) = 4.04, **p =0.009**			F(4,1174.3) = 1.44, p = 0.53		
Asian/Asian British†	0.00			0.00		
Black/Black British	13.85	(0.17, 27.53)	**0.046**	2.28	(-7.26, 11.81)	0.92
Mixed	12.73	(-2.00, 27.46)	0.11	3.01	(-7.26, 13.28)	0.86
White	9.22	(2.62, 15.83)	**0.003**	2.05	(-2.85, 6.96)	0.68
Any other ethnic group	-4.56	(-22.73, 13.60)	0.91	-8.90	(-21.59, 3.80)	0.25
University degree level education						
No†	0.00			0.00		
Yes	6.15	(2.42, 9.88)	**<0.001**	3.12	(0.29, 5.95)	**0.025**
Partner						
No†	0.00			0.00		
Yes	3.13	(-0.65, 6.92)	0.14	0.40	(-2.61, 3.41)	0.98
Home ownership						
Homeowner†	0.00			0.00		

Not a homeowner	-6.27	(-9.96, -2.59)	**<0.001**	-0.69	(-4.03, 2.64)	0.94
Current work or education						
Currently in work or education†	0.00			0.00		
Not currently in work or education	-4.09	(-8.31, 0.14)	0.062	1.54	(-1.92, 5.01)	0.63
Smoking history	F(2,1214.3) = 5.46, p = **0.013**			F(2,1170.6) = 0.15, p = 1.0		
Never smoker†	0.00			0.00		
Previous smoker	-2.70	(-6.75, 1.34)	0.29	-0.57	(-3.62, 2.48)	0.96
Current smoker	-8.92	(-15.68, -2.16)	**0.005**	0.45	(-4.39, 5.28)	0.99
Clinical						
Confirmed diagnosis						
Ulcerative Colitis†	0.00			0.00		
Crohn's	-3.08	(-6.93, 0.78)	0.16	-2.90	(-6.22, 0.43)	0.11
Current activity						
Remission†	0.00			0.00		
Active	-20.11	(-23.86, -16.35)	**<0.001**	-0.60	(-3.93, 2.72)	0.96
Disease flares in previous two years	F(6,1209.2) = 52.38, p**<0.001**			F(6,1161.9) = 4.26, p **<0.001**		
None†	0.00			0.00		
One	-14.77	(-19.85, -9.69)	**<0.001**	-4.47	(-9.09, 0.14)	0.060
Two	-23.12	(-28.64, -17.59)	**<0.001**	-7.53	(-12.70, -2.35)	**0.002**

Three	-19.86	(-26.62, -13.09)	**<0.001**	-8.00	(-14.03, -1.98)	**0.005**
Four	-23.57	(-30.77, -16.38)	**<0.001**	-7.52	(-13.97, -1.07)	**0.016**
Five	-35.25	(-42.76, -27.74)	**<0.001**	-12.66	(-19.55, -5.77)	**<0.001**
Ongoing disease	-33.97	(-39.04, -28.89)	**<0.001**	-8.17	(-13.57, -2.76)	**0.001**
Severity of symptoms during previous flare	F(3,1195.4) = 19.49, p **<0.001**			F(3,1155.0) = 3.15, p = 0.071		
None†	0.00			0.00		
Mild	-10.88	(-20.57, -1.19)	**0.022**	-0.88	(-7.95, 6.20)	0.99
Moderate	-18.17	(-27.20, -9.14)	**<0.001**	-2.53	(-9.20, 4.14)	0.74
Severe	-23.43	(-32.45, -14.40)	**<0.001**	-5.23	(-11.92, 1.45)	0.17
Previous surgery for IBD						
No†	0.00			0.00		
Yes	-2.91	(-6.84, 1.02)	0.21	-0.69	(-3.84, 2.45)	0.93
Other gastro-intestinal surgery						
No†	0.00			0.00		
Yes	-2.75	(-9.69, 4.20)	0.72	1.37	(-3.55, 6.28)	0.88
Oral 5ASA						
No†	0.00			0.00		
Yes	5.43	(1.31, 9.55)	**0.005**	0.99	(-2.51, 4.48)	0.87

Biologics						
No†	0.00			0.00		
Yes	-6.13	(-9.81, -2.44)	**<0.001**	1.03	(-1.90, 3.97)	0.79
Immune suppressant						
No†	0.00			0.00		
Yes	4.14	(0.46, 7.83)	**0.022**	2.46	(-0.20, 5.11)	0.080
Steroids						
No†	0.00			0.00		
Yes	-11.84	(-17.56, -6.12)	**<0.001**	1.57	(-2.66, 5.80)	0.75
Artificial nutrition						
No†	0.00			0.00		
Yes	-15.06	(-23.17, -6.95)	**<0.001**	-2.36	(-8.33, 3.60)	0.72
MUST risk of malnutrition	F(2,1057.8) = 7.69, p = **0.001**			F(2,1075.5) = 0.11, p = 1.0		
Low†	0.00			0.00		
Medium	-8.29	(-14.92, -1.67)	**0.009**	-0.51	(-5.18, 4.15)	0.99
High	-9.25	(-17.24, -1.26)	**0.017**	-0.98	(-6.60, 4.64)	0.97
Age, y	0.13	(0.01, 0.26)	**0.029**	-0.06	(-0.19, 0.08)	0.68
Duration of diagnosis, y	0.01	(0.00, 0.03)	0.090	0.00	(-0.01, 0.01)	1.00
Years since last disease flare	2.06	(1.47, 2.65)	**<0.001**	0.12	(-0.46, 0.70)	0.94

Blood measurements						
Hemoglobin	0.31	(0.19, 0.44)	**<0.001**	0.01	(-0.11, 0.12)	1.00
Serum albumin	0.44	(0.07, 0.80)	**0.012**	-0.07	(-0.37, 0.23)	0.92
C-reactive protein	-0.07	(-0.17, 0.02)	0.19	-0.03	(-0.10, 0.04)	0.73
Psychosocial						
Distress score (IBD-DS)	-0.42	(-0.45, -0.39)	**<0.001**	-0.26	(-0.31, -0.20)	**<0.001**
Anxiety (HADS-A)	-2.86	(-3.18, -2.53)	**<0.001**	-0.26	(-0.67, 0.16)	0.37
Depression (HADS-P)	-3.46	(-3.84, -3.07)	**<0.001**	-0.11	(-0.65, 0.42)	0.94
Fatigue self-assessment (IBD-FI)	-2.70	(-3.00, -2.41)	**<0.001**	-0.30	(-0.71, 0.11)	0.22
Fatigue impact on daily activities (IBD-FII)	-0.55	(-0.60, -0.49)	**<0.001**	0.09	(-0.01, 0.19)	0.10
Quality of life (UK IBDQ)	0.96	(0.88, 1.04)	**<0.001**	0.33	(0.17, 0.48)	**<0.001**
Intercept				78.51	(50.63, 106.38)	
Overall Model				F(43, 1172.3) = 31.66, p<0.001		

† Reference level against which the other levels of the categorical variables are compared

Supplementary Table 2: Categorical and continuous variables and their association with FR-QoL-29 total score in univariable and multivariable regression models in Crohn's disease only

	Univariable			Multivariable		
Variables	**β**	**(95%CI)**	**P>t**	**β**	**(95%CI)**	**P>t**
Demographic						
Gender						
Male†	0.00			0.00		
Female	-11.90	(-16.33, -7.47)	**<0.001**	-0.43	(-4.45, 3.59)	0.99
Ethnicity	F(4, 782.0) = 0.88, p = 0.86			F(4,737.6) = 0.45, p = 0.99		
Asian/Asian British†	0.00			0.00		
Black/Black British	9.01	(-7.09, 25.11)	0.45	1.38	(-10.16, 12.91)	0.99
Mixed	6.14	(-12.19, 24.46)	0.81	-2.36	(-15.42, 10.70)	0.96
White	2.85	(-5.65, 11.35)	0.81	-1.04	(-7.51, 5.43)	0.97
Any other ethnic group	-7.86	(-30.53, 14.81)	0.79	-8.03	(-24.32, 8.26)	0.56
University degree level education						
No†	0.00			0.00		
Yes	7.61	(3.00, 12.22)	**<0.001**	2.70	(-0.92, 6.32)	0.21
Partner						
No†	0.00			0.00		
Yes	2.81	(-1.80, 7.42)	0.37	2.12	(-1.73, 5.97)	0.46

Home ownership						
Homeowner†	0.00			0.00		
Not a homeowner	-4.20	(-8.73, 0.33)	0.079	0.66	(-3.60, 4.92)	0.98
Current work or education						
Currently in work or education†	0.00			0.00		
Not currently in work or education	-7.86	(-12.98, -2.73)	**<0.001**	1.84	(-2.50, 6.18)	0.67
Smoking history	F(2, 782.6) = 2.38, p = 0.25			F(2,734.9) = 0.76, p = 0.85		
Never smoked†	0.00			0.00		
Previous smoker	-1.56	(-6.71, 3.59)	0.85	1.40	(-2.54, 5.34)	0.78
Current smoker	-6.98	(-14.73, 0.77)	0.090	2.57	(-3.13, 8.27)	0.63
Clinical						
Disease location	F(2, 775.6) = 4.13, p = **0.048**			F(2,729.8) = 2.16, p = 0.31		
Ileal(L1)†	0.00			0.00		
Colonic (L2)	6.17	(-0.19, 12.53)	0.062	3.60	(-1.13, 8.34)	0.19
Ileocolonic (L3)	-0.07	(-5.72, 5.58)	1.00	0.39	(-3.73, 4.51)	0.99
Upper GI(L4)						
No†	0.00			0.00		
Yes	-5.89	(-14.79, 3.00)	0.30	0.86	(-5.61, 7.33)	0.98
Disease characteristics	F(2, 759.3) = 0.99, p = 0.75			F(2,688.2) = 0.67, p = 0.89		

Non-stricturing, non-penetrating (B1)†	0.00			0.00		
Stricturing (B2)	-3.01	(-8.39, 2.37)	0.45	-1.95	(-6.06, 2.16)	0.59
Penetrating (B3)	0.04	(-6.38, 6.45)	1.00	-1.34	(-6.49, 3.80)	0.90
Perianal						
No†	0.00			0.00		
Yes	1.27	(-4.23, 6.78)	0.93	0.69	(-3.42, 4.81)	0.97
Current activity						
Remission†	0.00			0.00		
Active	-19.33	(-23.98, -14.68)	**<0.001**	1.80	(-2.48, 6.08)	0.68
Disease flares in previous two years	F(6, 778.4) = 35.15, p **<.001**			F(6,730.0) = 3.12, p = **0.015**		
None†	0.00			0.00		
One	-13.36	(-19.29, -7.42)	**<0.001**	-4.40	(-9.99, 1.20)	0.17
Two	-23.75	(-30.61, -16.89)	**<0.001**	-7.89	(-14.52, -1.26)	**0.015**
Three	-17.18	(-26.53, -7.83)	**<0.001**	-7.45	(-15.65, 0.75)	**0.087**
Four	-21.01	(-29.70, -12.33)	**<0.001**	-6.18	(-14.20, 1.83)	0.18
Five	-34.27	(-43.57, -24.97)	**<0.001**	-12.62	(-21.27, -3.97)	**0.003**
Ongoing disease	-32.51	(-38.48, -26.54)	**<0.001**	-9.78	(-16.42, -3.15)	**<0.001**
Severity of symptoms during previous flare	F(3, 775.3) = 9.02, p **<0.001**			F(3,721.4) = 1.19, p = 0.67		
None†	0.00			0.00		
Mild	-10.17	(-22.27, 1.92)	0.13	-0.43	(-9.57, 8.71)	1.00
Moderate	-14.92	(-26.20, -3.65)	**0.006**	-0.32	(-8.92, 8.28)	1.00

Severe	-20.28	(-31.56, -9.00)	**<0.001**	-3.14	(-11.77, 5.50)	0.77
Previous surgery for IBD						
No†	0.00			0.00		
Yes	-1.94	(-6.49, 2.62)	0.67	1.15	(-2.63, 4.93)	0.85
Other gastro-intestinal surgery						
No†	0.00			0.00		
Yes	-0.95	(-8.46, 6.56)	0.99	1.96	(-3.47, 7.38)	0.77
Oral 5ASA						
No†	0.00			0.00		
Yes	9.01	(1.99, 16.04)	**0.006**	0.56	(-4.83, 5.95)	0.99
Biologics						
No†	0.00			0.00		
Yes	-4.16	(-8.79, 0.47)	0.09	0.90	(-2.77, 4.58)	0.91
Immune suppressant						
No†	0.00			0.00		
Yes	6.48	(1.97, 11.00)	**0.003**	2.71	(-0.66, 6.09)	0.16
Steroids						
No†	0.00			0.00		
Yes	-13.83	(-21.52, -6.14)	**<0.001**	2.42	(-3.46, 8.30)	0.69

Artificial nutrition						
No†	0.00			0.00		
Yes	-13.54	(-22.31, -4.77)	**<0.001**	-2.36	(-9.06, 4.33)	0.78
MUST risk of malnutrition	F(2, 729.0) = 4.26, p = **0.043**			F(2,714.0) = 0.06, p = 1.0		
Low†	0.00			0.00		
Medium	-6.16	(-13.86, 1.54)	0.16	0.48	(-5.05, 6.01)	1.00
High	-9.26	(-18.61, 0.08)	0.053	-0.66	(-7.37, 6.05)	0.99
Age, y	-0.02	(-0.18, 0.14)	0.99	-0.12	(-0.30, 0.05)	0.24
Duration of diagnosis, y	0.00	(-0.02, 0.02)	1.00	0.00	(-0.02, 0.01)	0.97
Years since previous disease flare	1.89	(1.17, 2.62)	**<0.001**	-0.05	(-0.76, 0.66)	1.00
Blood measurements						
Hemoglobin	0.34	(0.17, 0.50)	**<0.001**	0.03	(-0.12, 0.19)	0.94
Serum albumin	0.60	(0.13, 1.07)	**0.009**	0.04	(-0.33, 0.42)	0.99
C-reactive protein	-0.10	(-0.27, 0.06)	0.32	0.02	(-0.11, 0.15)	0.98
Psychosocial						
	-0.41	(-0.45, -0.37)	**<0.001**	-0.26	(-0.33, -0.19)	**<0.001**

Distress score (IBD-DS)						
Anxiety (HADS-A)	-2.76	(-3.16, -2.36)	**<0.001**	0.02	(-0.51, 0.56)	1.00
Depression (HADS-P)	-3.33	(-3.79, -2.87)	**<0.001**	-0.12	(-0.78, 0.55)	0.97
Fatigue self-assessment (IBD-FI)	-2.70	(-3.05, -2.35)	**<0.001**	-0.38	(-0.90, 0.14)	0.23
Fatigue impact on daily activities (IBD-FII)	-0.53	(-0.60, -0.47)	**<0.001**	0.10	(-0.02, 0.23)	0.13
Quality of life (IBDQ)	0.95	(0.86, 1.05)	**<0.001**	0.41	(0.21, 0.61)	**<0.001**
Intercept				59.13	(21.30, 96.96)	
Overall Model				F(48,736.7) = 17.85, p**< 0.001**		

† Reference level against which the other levels of the categorical variables are compared

Supplementary Table 3: Categorical and continuous variables and their association with FR-QoL-29 total score in univariable and multivariable regression models in ulcerative colitis only

	Univariable			Multivariable		
Variables	**β**	**(95%CI)**	**P>t**	**β**	**(95%CI)**	**P>t**
Demographic						
Gender						
Male†	0.00			0.00		
Female	-9.78	(-16.04, -3.51)	**<0.001**	-5.15	(-10.35, 0.06)	0.053
Ethnicity	F(4,424.2) = 5.34, p **<0.001**			F(4,381.4) = 2.45, p = 0.13		
Asian/Asian British†	0.00			0.00		
Black/Black British	21.11	(-5.33, 47.55)	0.16	5.22	(-13.61, 24.05)	0.88
Mixed	22.95	(-1.80, 47.70)	0.079	14.30	(-2.86, 31.46)	0.13
White	19.10	(8.59, 29.60)	**<0.001**	8.06	(0.05, 16.06)	**0.047**
Any other ethnic group	-0.19	(-30.44, 30.05)	1.00	-6.36	(-27.63, 14.91)	0.85
University degree level education						
No†	0.00			0.00		
Yes	3.16	(-3.23, 9.54)	0.56	2.40	(-2.21, 7.01)	0.51
Partner						
No†	0.00			0.00		
Yes	3.29	(-3.36, 9.94)	0.56	-1.34	(-6.48, 3.80)	0.90

Home ownership						
Homeowner†	0.00			0.00		
Not a homeowner	-9.68	(-16.05, -3.31)	**<0.001**	-1.77	(-7.39, 3.85)	0.83
Current work or education						
Currently in work or education†	0.00			0.00		
Not currently in work or education	3.23	(-4.15, 10.60)	0.65	-0.64	(-6.74, 5.47)	0.99
Smoking history	F(2,427.0) = 3.74, p = .072			F(2,381.3) = 2.43, p = 0.24		
Never smoked†	0.00			0.00		
Previous smoker	-5.25	(-11.88, 1.39)	0.17	-4.24	(-9.26, 0.78)	0.13
Current smoker	-13.23	(-27.01, 0.55)	0.065	-5.21	(-15.06, 4.64)	0.50
Clinical						
Disease location	F(2,421.9) = 0.48, p = 0.95			F(2,372.2) = 2.23, p = 0.29		
Proctitis (E1)†	0.00			0.00		
Distal (E2)	-3.46	(-12.71, 5.80)	0.75	-5.07	(-11.44, 1.31)	0.16
Pancolitis (E3)	-3.33	(-12.36, 5.71)	0.76	-5.14	(-11.44, 1.16)	0.15
Disease characteristics	F(3,425.5) = 15.11, p**< 0.001**			F(3,379.3) = 1.31, p = 0.61		
Clinical remission (S0)†	0.00			0.00		
Mild (S1)	-13.67	(-20.75, -6.59)	**<0.001**	-4.02	(-9.61, 1.56)	0.23
Moderate (S2)	-20.55	(-29.02, -12.08)	**<0.001**	-3.53	(-11.21, 4.16)	0.61
Severe (S3)	-21.39	(-41.68, -1.10)	**0.036**	2.45	(-13.74, 18.65)	0.98

Current activity						
Remission†	0.00			0.00		
Active	-21.48	(-27.86, -15.09)	**<0.001**	-2.52	(-8.57, 3.52)	0.68
Disease flares in previous two years	F(6,422.7) = 20.18, p **< 0.001**			F(6,380.9) = 1.34, p = 0.56		
None†	0.00			0.00		
One	-20.17	(-29.77, -10.57)	**<0.001**	-4.02	(-12.52, 4.49)	0.59
Two	-26.62	(-36.31, -16.94)	**<0.001**	-7.39	(-16.20, 1.43)	0.13
Three	-27.87	(-38.50, -17.23)	**<0.001**	-6.95	(-16.64, 2.75)	0.24
Four	-31.28	(-44.07, -18.48)	**<0.001**	-8.14	(-19.37, 3.10)	0.23
Five	-40.52	(-53.41, -27.62)	**<0.001**	-11.93	(-23.82, -0.04)	0.050
Ongoing disease	-39.53	(-49.04, -30.02)	**<0.001**	-5.12	(-15.09, 4.85)	0.52
Severity of symptoms during previous flare	F(3,424.5) = 11.65, p **<0.001**			F(3,380.2) = 3.31, p = 0.059		
None†	0.00			0.00		
Mild	-12.03	(-28.23, 4.17)	0.21	2.34	(-9.64, 14.31)	0.95
Moderate	-23.79	(-38.86, -8.72)	**<0.001**	-4.43	(-15.61, 6.74)	0.72
Severe	-28.88	(-43.98, -13.78)	**<0.001**	-6.25	(-17.40, 4.90)	0.45
Previous surgery for IBD						
No†	0.00			0.00		
Yes	-2.20	(-14.31, 9.91)	0.96	-0.91	(-9.69, 7.86)	0.99
Other gastro-intestinal surgery						

No†	0.00			0.00		
Yes	-8.42	(-27.31, 10.48)	0.64	3.02	(-10.52, 16.57)	0.93
Oral 5ASA						
No†	0.00			0.00		
Yes	1.87	(-4.54, 8.28)	0.86	2.52	(-2.31, 7.35)	0.51
Biologics						
No†	0.00			0.00		
Yes	-8.72	(-15.06, -2.37)	**0.003**	1.63	(-3.74, 6.99)	0.85
Immune suppressant						
No†	0.00			0.00		
Yes	0.71	(-5.73, 7.16)	0.99	3.53	(-1.10, 8.16)	0.19
Steroids						
No†	0.00			0.00		
Yes	-10.64	(-19.34, -1.94)	**0.012**	0.57	(-5.87, 7.01)	1.00
Artificial nutrition						
No†	0.00			0.00		
Yes	-19.88	(-40.79, 1.02)	0.067	-1.12	(-15.84, 13.60)	1.00
MUST risk of malnutrition	F(2,406.9) = 3.63, p = 0.080			F(2,355.3) = 0.67, p = 0.88		
Low†	0.00			0.00		
Medium	-12.62	(-25.24, 0.01)	0.050	-3.54	(-12.59, 5.50)	0.72

High	-8.06	(-23.25, 7.13)	0.50	-3.34	(-14.28, 7.60)	0.85
Age, y	0.37	(0.17, 0.58)	**<0.001**	0.03	(-0.21, 0.27)	0.99
Duration of diagnosis, y	0.05	(0.03, 0.08)	**<0.001**	0.02	(-0.01, 0.04)	0.30
Years since previous disease flare	2.47	(1.51, 3.43)	**<0.001**	0.41	(-0.51, 1.33)	0.64
Blood measurements						
Hemoglobin	0.29	(0.08, 0.49)	**0.003**	-0.01	(-0.20, 0.17)	1.00
Serum albumin	0.20	(-0.40, 0.79)	0.81	-0.31	(-0.85, 0.23)	0.43
C-reactive protein	-0.06	(-0.18, 0.06)	0.57	-0.06	(-0.14, 0.02)	0.22
Psychosocial						
Distress score (IBD-DS)	-0.43	(-0.48, -0.38)	**<0.001**	-0.26	(-0.34, -0.17)	**<0.001**
Anxiety (HADS-A)	-3.04	(-3.58, -2.50)	**<0.001**	-0.62	(-1.32, 0.08)	0.10
Depression (HADS-P)	-3.70	(-4.39, -3.02)	**<0.001**	-0.40	(-1.35, 0.56)	0.68
Fatigue self-assessment (IBD-FI)	-2.71	(-3.26, -2.17)	**<0.001**	-0.08	(-0.80, 0.64)	0.99
	-0.58	(-0.68, -0.48)	**<0.001**	0.10	(-0.07, 0.28)	0.41

Fatigue impact on daily activities (IBD-FII)						
Quality of life (IBDQ)	0.98	(0.84, 1.12)	**<0.001**	0.21	(-0.05, 0.46)	0.14
Intercept				107.54	(63.18, 151.90)	
Overall Model				F(47, 381.6) = 12.49, p**< 0.001**		

† Reference level against which the other levels of the categorical variables are compared

Supplementary Table 4: Unadjusted energy, nutrient and alcohol intakes per day across the quintiles of food-related quality of life in patients with inflammatory bowel disease

	Intakes in each quintile of FR-QoL-29 score, mean (95% CI)					
	Q1 (29-56)	**Q2 (57-70)**	**Q3 (71-86)**	**Q4 (87-105)**	**Q5 (106-145)**	**p value**
Energy (kcal/d)	1734 (1648,1820)	1781 (1698,1863)	1881 (1795,1967)	1774 (1690,1858)	1855 (1769,1940)	0.10
Protein (g/d)	74.9 (70.8,79.0)	79.9 (76.0,83.8)	80.5 (76.5,84.6)	79.1 (75.2,83.1)	81.3 (77.3,85.4)	0.21
Fat (g/d)	70.7 (66.4,74.9)	71.0 (66.9,75.1)	76.9 (72.7,81.2)	70.9 (66.7,75.1)	76.9 (72.7,81.2)	**0.050**
Saturated (g/d)	26.8 (25.0,28.6)	26.7 (25.0,28.4)	29.6 (27.8,31.4)	26.9 (25.1,28.6)	29.7 (27.9,31.5)	**0.017**
Monounsaturated (g/d)	26.2 (24.6,27.9)	26.3 (24.7,27.9)	28.3 (26.6,30.0)	26.4 (24.8,28.1)	28.5 (26.8,30.2)	0.11
Polyunsaturated (g/d)	11.5 (10.7,12.2)	11.9 (11.2,12.6)	12.4 (11.6,13.1)	11.5 (10.7,12.2)	12.1 (11.4,12.9)	0.35
Carbohydrate (g/d)	209.0 (197.7,220.3)	213.2 (202.4,224.0)	221.1 (209.8,232.3)	207.8 (196.8,218.8)	209.4 (198.3,220.6)	0.47
Total sugars (g/d)	101.2 (94.2,108.1)	103.2 (96.5,109.8)	105.2 (98.3,112.1)	101.5 (94.7,108.2)	103.0 (96.2,109.9)	0.93
Glucose (g/d)	18.3 (16.8,19.8)	18.8 (17.4,20.3)	18.2 (16.7,19.7)	18.1 (16.7,19.6)	18.0 (16.5,19.4)	0.93
Fructose (g/d)	18.2 (16.5,19.9)	19.6 (18.0,21.2)	18.5 (16.8,20.2)	18.9 (17.2,20.5)	18.9 (17.3,20.6)	0.83
Galactose (g/d)	0.37 (0.27,0.47)	0.38 (0.28,0.47)	0.51 (0.41,0.61)	0.52 (0.42,0.62)	0.50 (0.40,0.60)	0.059
Sucrose (g/d)	46.8 (42.9,50.8)	46.3 (42.5,50.1)	47.3 (43.3,51.2)	44.7 (40.8,48.5)	44.5 (40.6,48.4)	0.81
Lactose (g/d)	12.9 (11.6,14.1)	13.4 (12.2,14.6)	14.9 (13.7,16.2)	14.6 (13.4,15.8)	16.3 (15.1,17.5)	**0.001**
Maltose (g/d)	2.6 (2.3,2.9)	2.6 (2.4,2.9)	2.9 (2.6,3.2)	2.6 (2.3,2.9)	2.7 (2.4,3.0)	0.72
Starch (g/d)	105.0 (98.9,111.2)	106.7 (100.9,112.6)	112.5 (106.4,118.7)	103.1 (97.1,109.2)	103.3 (97.1,109.4)	0.19
Fiber (NSP, g/d)	12.1 (11.2,12.9)	13.8 (13.0,14.7)	13.6 (12.8,14.5)	13.3 (12.4,14.2)	14.2 (13.3,15.1)	**0.011**
Alcohol (g/d)	2.3 (1.1,3.5)	3.4 (2.2,4.5)	5.6 (4.4,6.8)	5.9 (4.7,7.1)	7.6 (6.4,8.8)	**<0.001**
Vitamin A (RAE, µg/d)	975 (854,1096)	1000 (884,1116)	1013 (892,1134)	1058 (939,1176)	1116 (996,1237)	0.50
Thiamin (mg/d)	1.22 (1.15,1.29)	1.33 (1.27,1.40)	1.34 (1.27,1.41)	1.28 (1.21,1.35)	1.36 (1.30,1.43)	**0.022**
Riboflavin (mg/d)	1.56 (1.47,1.65)	1.64 (1.56,1.73)	1.73 (1.64,1.82)	1.68 (1.59,1.77)	1.82 (1.73,1.91)	**0.001**
Niacin (mg/d)	19.8 (18.6,21.0)	21.3 (20.2,22.4)	21.2 (20.0,22.4)	21.1 (19.9,22.2)	21.7 (20.6,22.9)	0.22
Pyridoxine (mg/d)	1.91 (1.81,2.00)	2.05 (1.96,2.14)	2.06 (1.97,2.16)	2.02 (1.93,2.12)	2.08 (1.98,2.17)	0.098

Folate (µg/d)	227.0 (213.4,240.6)	247.9 (234.8,260.9)	247.9 (234.4,261.5)	243.4 (230.0,256.8)	258.5 (245.0,271.9)	**0.028**
Vitamin B_{12} (µg/d)	5.9 (5.3,6.5)	6.1 (5.5,6.7)	6.2 (5.6,6.8)	6.5 (5.9,7.0)	6.4 (5.8,7.0)	0.69
Vitamin C (mg/d)	82.1 (73.9,90.2)	99.4 (91.6,107.2)	91.3 (83.2,99.4)	93.6 (85.7,101.5)	95.9 (87.9,103.9)	**0.039**
Vitamin D (µg)	3.03 (2.75,3.31)	2.97 (2.70,3.24)	3.07 (2.79,3.35)	2.98 (2.71,3.25)	2.84 (2.57,3.12)	0.083
Vitamin E (mg/d)	10.4 (9.7,11.0)	10.9 (10.3,11.6)	11.5 (10.8,12.2)	10.7 (10.0,11.3)	11.3 (10.7,12.0)	0.11
Potassium (mg/d)	2895 (2753,3038)	3135 (2998,3271)	3178 (3036,3320)	3099 (2960,3237)	3199 (3059,3339)	0.024
Sodium (mg/d)	2397 (2267,2528)	2476 (2351,2601)	2587 (2458,2717)	2402 (2276,2529)	2572 (2443,2700)	0.11
Calcium (mg/d)	718.2 (676.2,760.2)	747.7 (707.5,787.9)	816.0 (774.2,857.8)	774.9 (733.8,816.1)	855.4 (814.1,896.8)	**<0.001**
Phosphorus (mg/d)	1180 (1123,1238)	1251 (1195,1306)	1291 (1234,1348)	1260 (1204,1316)	1332 (1275,1389)	**0.005**
Magnesium (mg/d)	247.0 (233.9,260.2)	271.6 (259.0,284.2)	276.0 (262.9,289.1)	269.5 (256.7,282.2)	286.2 (273.3,299.2)	**0.001**
Iron (mg/d)	8.8 (8.3,9.2)	9.6 (9.2,10.1)	9.9 (9.4,10.3)	9.7 (9.3,10.2)	10.3 (9.9,10.8)	**<0.001**
Zinc (mg/d)	7.8 (7.4,8.3)	8.7 (8.3,9.1)	8.6 (8.2,9.0)	8.7 (8.3,9.1)	9.0 (8.6,9.4)	**0.003**
Iodine (µg/d)	131.0 (122.9,139.2)	134.0 (126.1,141.8)	138.6 (130.4,146.7)	134.8 (126.8,142.7)	137.4 (129.3,145.4)	0.73
Selenium (µg /d)	59.9 (56.2,63.6)	62.4 (58.9,66.0)	63.9 (60.2,67.6)	60.3 (56.7,64.0)	61.2 (57.6,64.9)	0.57