

1 **An examination of appetite and disordered eating in active Crohn's**
2 **disease**

3 Richard Anthony Wardle ^{a 1}, Gita Thapaliya ^{a 2}, Adam Nowak ^{a 3}, Shellie Radford ^{a 4}, Michelle Dalton ^b
4 ⁵, Graham Finlayson ^{c 6}, Gordon W. Moran ^{a 7}

5

6 ^a National Institute for Health Research (NIHR) Biomedical Research Centre in Gastrointestinal and
7 Liver Diseases at Nottingham University Hospitals NHS Trust & The University of Nottingham, Queens
8 Medical Centre Campus, E Floor, West block, Nottingham, NG7 2UH, UK

9 ^b School of Social and Health Sciences, Leeds Trinity University, Leeds, UK

10 ^c Human Appetite Research Unit, School of Psychology, Faculty of Medicine and Health, University of
11 Leeds, Leeds, UK

12

13 ¹ Richardwardle@nhs.net

14 ² Gita.thapaliya@nottingham.ac.uk

15 ³ Adam.nowak@nhs.net

16 ⁴ Shellie.Radford@nuh.nhs.uk

17 ⁵ M.dalton@leedstrinity.ac.uk

18 ⁶ G.s.finlayson@leeds.ac.uk

19 ⁷ Gordon.moran@nottingham.ac.uk

20

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25 **Short Title**

26 Eating Behaviour In Crohn's disease: EBIC study

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28 **Corresponding author**

29 G. W. Moran

30 Clinical Associate Professor in Gastroenterology

31 NIHR Nottingham Digestive Diseases Biomedical Research Centre in Gastrointestinal and Liver

32 Diseases, Nottingham University Hospitals NHS Trust & The University of Nottingham, Nottingham,

33 United Kingdom

34 E-mail: Gordon.Moran@nottingham.ac.uk

35 Telephone no: +44 (0)115 9249924 ext 70608

36

37 **Authors' contributions**

38 Richard Anthony Wardle

39 Conception and design of study, acquisition of data, analysis and/or interpretation of data, drafting the
40 manuscript, revising the manuscript critically for important intellectual content, approval of the version
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42

43 Gita Thapaliya

44 Acquisition of data, analysis and/or interpretation of data, drafting the manuscript, approval of the
45 version of the manuscript to be published.

46

47 Adam Nowak

48 Acquisition of data, approval of the version of the manuscript to be published.

49

50 Shellie Radford

51 Acquisition of data, approval of the version of the manuscript to be published.

52

53 Michelle Dalton

54 Analysis and/or interpretation of data, drafting the manuscript, revising the manuscript critically for
55 important intellectual content, approval of the version of the manuscript to be published.

56

57 Graham Finlayson

58 Conception and design of study, analysis and/or interpretation of data, drafting the manuscript,
59 revising the manuscript critically for important intellectual content, approval of the version of the
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61

62 Gordon W. Moran

63 Conception and design of study, acquisition of data, analysis and/or interpretation of data, drafting the
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70 There are no financial conflicts of interest

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95 ABSTRACT

96 Background

97 Crohn's disease (CD) patients suffer from nutritional deficiencies when in active disease. We
98 aim to examine calorific intake, macronutrient choice and disordered eating behaviour in
99 patients with active CD.

100 Methods

101 CD patients with matched healthy volunteers (HV) were recruited. Active disease was defined
102 by faecal calprotectin $>250\mu\text{g/g}$, C-reactive protein $>5\text{mg/dl}$, or active disease seen on
103 endoscopy or imaging. Symptoms were quantified by Harvey-Bradshaw Index (HBI). Calorific
104 intake was assessed by 24-h dietary recall. Disordered eating was assessed using validated
105 questionnaires [Binge Eating Scale (BES); Power of Food Scale (PFS); Control of Eating
106 Questionnaire (CoEQ); Dutch Eating Behaviour Questionnaire (DEBQ); Three Factor Eating
107 Questionnaire (TFEQ)].

108 Results

109 30 CD (18M:12F, Age: 32.3 ± 2.19 , BMI: 24.9 ± 0.8) and 31 matched HV (19M:12F,
110 Age: 32.8 ± 2.0 , BMI: 24.7 ± 0.5) were recruited. Mean faecal calprotectin was
111 $1032.5\pm 176\mu\text{g/g}$, C-reactive protein $83.8\pm 47.1\text{mg/L}$ and HBI 4.8 ± 1 . There were no significant
112 differences in calorific intake between groups. Protein intake was lower in the CD cohort
113 ($p=0.03$). Hospital Anxiety and Depression score was higher ($p=0.01$) and CoEQ-Positive
114 Mood ($p=0.001$) lower in CD. CD were characterised by higher BES ($p=0.01$) and lower CoEQ
115 Craving Control ($p=0.027$) with greater craving for Sweet ($p=0.043$), Savoury ($p=0.021$) foods.
116 PFS food present ($p=0.005$), DEBQ Emotional ($p<0.001$) and External Eating ($p=0.022$) were
117 significantly higher than HV.

118 Conclusions

119 Reduced protein consumption and more prevalent disordered eating behaviour traits were
120 present in CD. Greater binge eating and decreased control of cravings may be attributed to
121 lower mood and higher anxiety observed. Patients may benefit from stronger psychological
122 support with firm dietetic advice for healthy eating.

123 **Keywords**

124 Inflammatory Bowel Disease, Crohn's disease, eating behaviour, nutrition

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141 INTRODUCTION

142 Patients with gastrointestinal disorders are at a greater risk of a disordered eating pattern
143 compared to healthy volunteers with an increased prevalence of a wide range of abnormal
144 eating patterns such as binge eating, meal skipping and food restriction ^{1,2}. Disordered eating
145 behaviour applies to most patients with gastrointestinal disease and may include food
146 restriction, meal skipping and over-eating rather than the more severe eating disorders where
147 patients are diagnosed according to specific narrow criteria ^{3,4}. A disordered eating behaviour
148 may be described with a two-path theoretical model ^{1,2}. The first pathway concerns individuals
149 who experience high levels of anxiety about unfamiliar foods and/or overestimate the negative
150 consequences associated with their condition. These individuals may restrict their intake to
151 self-prepared and familiar foods limiting their diet variety. The second pathway concerns
152 individuals who gain weight when following their prescribed dietary regimen and subsequently
153 employ techniques to reduce this weight gain.

154 In Inflammatory Bowel Disease (IBD), issues regarding food intake are felt to be either
155 important or extremely important in 62.5% of patients, with virtually all Crohn's disease (CD)
156 patients having had problems with unintentional weight loss ⁵. Abnormal eating patterns have
157 been described in IBD with qualitative studies unselectively describing eating behaviour
158 irrespective of disease activity ^{6,7}. Approximately three-fourths of patients with IBD describe a
159 decline in appetite when the disease is active ⁶ with up to 37% of CD patients showing
160 abnormal eating patterns ⁸. Malnutrition is more prevalent in CD than ulcerative colitis with up
161 to 75% of hospitalised patients being malnourished with 50% in negative nitrogen balance ⁹.
162 To this effect, the IBD priority-setting partnership set up by the James Lind Alliance identified
163 a research need to understand a role for diet in disease management ¹⁰. The effect of
164 disordered eating on the nutritional status in CD has never been investigated.

165 Appetite and satiety involve complex interactions between homeostatic and hedonic factors.
166 The enteroendocrine-gut brain axis is central to the homeostatic control of food intake, whilst
167 other neural circuits integrate environmental and emotional cues to constitute the hedonic

168 drive of appetite regulation ¹¹. The cross-link between eating behaviour and active CD is poorly
169 understood. Disordered eating might be associated with a change in the homeostatic and
170 hedonic balance. The aim of this study is to examine free-living calorie and macronutrient
171 intake in patients with active CD compared to healthy volunteers and to determine the
172 prevalence and type of eating behaviour traits and disordered eating in CD patients with active
173 disease.

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190 **METHODOLOGY**

191 **Basic protocol and patient recruitment**

192 This was an open label, qualitative questionnaire-based study with a matched-pair design.
193 The study was conducted between July 2015 and January 2018 at the National Institute of
194 Health Research (NIHR) Nottingham Digestive Diseases Biomedical Research Centre (NDD
195 BRC) at the Queens Medical Centre Campus, Nottingham, UK. Participants were recruited
196 from The Inflammatory Bowel Disease Clinic, via the study flyer and social media. CD patients
197 (aged 16-75yrs) with active disease were recruited as well as age, BMI and gender-matched
198 healthy volunteers. Healthy volunteers (HV) were recruited from an existing participant
199 database in the Nottingham BRC and from the local healthy populations of Nottingham
200 University Hospitals and the University of Nottingham. This study was advertised through
201 study fliers and social media.

202 Disease activity was defined through objective markers of inflammation: faecal calprotectin of
203 $>250\mu\text{g/g}$ or CRP of $>5\text{g/dl}$ or through recent ileocolonoscopy, CT or MR enterography
204 showing active inflammatory and uncomplicated disease (not of a stricturing or penetrating
205 behaviour). CD clinical activity was measured with a Harvey Bradshaw Index¹² (HBI) score
206 recorded at inclusion. Potential participants with recent corticosteroid use (in the last 3
207 months), pregnancy or breast-feeding and patients with significant co-morbidities were
208 excluded from the study. Stable doses of immunosuppressive agents or anti-TNF agents were
209 permitted.

210 All CD patients and healthy volunteers gave their informed consent prior to recruitment.
211 Participants completed a single, spontaneously administered 24hr dietary recall either face-
212 to-face at the NDD BRC or by telephone, the Hospital Anxiety and Depression scale (HADS)
213 and psychometric eating behaviour questionnaires within the study period.

214 **Outcomes**

215 The primary outcome of this study was to compare total 24 hr calorie intake as measured by
216 a single face-to-face or telephone-administered 24-hour dietary recall¹³ between CD with
217 active disease and age-, BMI- and gender-matched HV. Calories consumed were calculated
218 for the recall based on manufacturers' labels and the nutrition analysis tool Nutritics (Nutritics
219 v4.312 Academic Edition, Ireland). Dietary recall did not include caloric intake from weekends
220 or holidays but only days Monday to Thursday. The secondary endpoint for this study was to
221 measure eating behaviour traits through psychometric scales: Three Factor Eating
222 Questionnaire (TFEQ) ¹⁴; the Binge Eating Scale ¹⁵; the Power of Food Scale ¹⁶; the Dutch
223 Eating Behaviour Questionnaire ¹⁷; and the Control of Eating Questionnaire ^{18,19}.

224 **24-h dietary recall**

225 The Automated Multiple-Pass Method (AMPM) was utilised to perform the single
226 spontaneously administered 24hr dietary recall. This five-step questionnaire can accurately
227 assess dietary consumption and may be administered face-to-face or by telephone ^{13,20} RW,
228 AN and GT conducted all interviews. A copy of the dietary assessment textbook Carbs and
229 Cals was provided to each participant to facilitate the dietary recall ²¹. This book contains over
230 1700 food and drink photographs and was primarily used to assist in identifying the appropriate
231 food type and portion size consumed. Diet logs were analysed using Nutritics dietary analysis
232 software (Nutritics v4.312 Academic Edition, Ireland).

233 **Eating Behaviour traits**

234 Eating behaviour traits were measured through five validated self-report questionnaires; the
235 Power of Food Scale (PFS); the Binge Eating Scale (BES); the Control of Eating Questionnaire
236 (COEQ); Three Factor Eating Questionnaire (TFEQ) and the Dutch Eating Behaviour
237 Questionnaire (DEBQ) ¹⁴⁻¹⁸.

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239 The Power of Food Scale (PFS)

240 The PFS is a 15-item questionnaire reflecting the psychological influence of the food
241 environment. It measures appetite for, rather than consumption of palatable foods and may
242 be a useful measure of the hedonic impact of food environments replete with highly palatable
243 foods²². Items are grouped into three domains according to food proximity; food available but
244 not physically present, food present but not tasted and food tasted but not consumed.

245 The Binge Eating Scale (BES)

246 The BES is a 16-item questionnaire that assesses the severity of binge eating tendencies.
247 Eight questions describe the behavioural manifestations of binge eating behaviour and eight
248 describe the feelings and cognitions associated with binge eating. Scores are summed to
249 produce a total score ranging from 0 to 46. Cut off points have previously been reported
250 denoting mild (≤ 17), moderate (18–26), and severe (≥ 27) binge eating behaviour^{15,23,24}.

251 The Control of Eating Questionnaire (CoEQ)

252 The CoEQ is a 21-item questionnaire designed to assess the severity and type of food
253 cravings experienced over the previous seven days¹⁸. The CoEQ has four subscales; Craving
254 Control, Craving for Savoury, Craving for Sweet and Positive Mood. Items on the CoEQ are
255 assessed by 100-mm visual analogue scales (VAS) with items relating to each subscale being
256 averaged to create a final score.

257 Three Factor Eating Questionnaire (TFEQ)

258 The TFEQ contains 51-items and measures three dimensions of human eating behaviour;
259 Cognitive Restraint of Eating, Disinhibition and Hunger¹⁴. Restraint refers to concern over
260 weight control and strategies which are adopted to achieve this. Disinhibition reflects a
261 tendency towards over-eating and eating opportunistically in an obesogenic environment.
262 Hunger is concerned with the extent to which hunger feelings are perceived and the extent to
263 which such feelings evoke food intake²⁵. Each item scores either 0 or 1 point. The minimum
264 score for factors I, II and III is therefore 0, with the possible maximum scores being 21, 16
265 and 14 respectively.

266 The Dutch Eating Behaviour Questionnaire (DEBQ)

267 The 33-item DEBQ assesses different eating styles that may contribute to weight gain;
268 emotional eating, external eating, and restraint. 'Emotional eating' occurs in response to
269 emotional arousal states such as fear anger or anxiety, 'external eating' in response to external
270 food cues such as sight and smell of food and 'restraint eating' is overeating after a period of
271 slimming when the cognitive resolve to diet is abandoned ¹⁷.

272 **Statistical Analysis**

273 The sample size was based on published data ²⁶ where the 24hr self-reported calorie intake
274 in CD was 1978.7±169.7Kcal and that in HV was 1854.4 ±129.5Kcal. Assuming α of 0.05,
275 power of 80% and using 2-sided test, 30 participants in each group were needed to show a
276 significant difference in the primary outcome.

277 Data were analysed using SPSS version 20 for Windows. The parametric or non-parametric
278 nature of the data was determined by a normality test. Data is presented as mean \pm standard
279 error of the mean (SEM). Continuous data was compared using paired t-test while categorical
280 data was compared with Chi-Squared test. Total 24hr Kcal intake, macronutrient intake
281 together with outcome data from the individual questionnaires administered to all participants
282 were compared between the groups. An exploratory sub-analysis was undertaken comparing
283 differences between gender. P values <0.05 were deemed significant.

284 **Ethical approval**

285 This study received research ethics committee approval from National Research Ethics
286 Service (NRES) Committee East Midlands (REC reference 15/EM/0142 as of the 27th April
287 2015). The protocol was registered with clinical trials.gov (NTC02379117).

288 **RESULTS**

289 **Demographic data**

290 Thirty CD patients (18M:12F, Age:32.3±2.19, BMI:24.9±0.8) and 31 matched HV (19M:12F,
 291 Age:32.8±2.0, BMI:24.7±0.5) were recruited to this matched pairs cross-sectional study (see
 292 Table 1). There were no significant differences in gender ratio, mean age and mean BMI
 293 between the CD and HV. CD participants had objective evidence of active disease with an
 294 elevated C-reactive protein (83.8±47.1mg/L), or faecal calprotectin (1032.5±176µg/g) or as
 295 assessed by colonoscopy or MR enterography or both (see supplementary table). These
 296 objective investigations have been undertaken as part of the participants standard of care
 297 within a mean of 52.9±14.1 days of recruitment. Mean HBI score was 4.8±1. None of the
 298 participants had any change in management prior to recruitment and data collection. Upon
 299 recruitment, 10 participants (33.3%) were being prescribed immunosuppressant therapy, 6
 300 (20%) anti-TNF therapy and 7 (23.3%) CD participants a combination of anti-TNF therapy and
 301 immunosuppressant therapy. Eleven participants (36%) had a history of CD-related intestinal
 302 surgery with a mean of 0.4±0.1 CD-related operations per patient. Mean disease duration prior
 303 to recruitment was 8.1±1.5 years.

304 Table 1: Summary demographic data of participants

Group	Gender (n)	Age	BMI
CD	M (18)	31.1±2.7	24.1±1.1
	F (12)	34.1±3.8	26.1±1.2
HC	M (19)	32.6±2.3	24.7±0.6
	F (12)	33±3.9	24.8±1.0

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306 **24-hour calorie intake**

307 The total self-reported 24-hour calorie and macronutrient intake for the CD and HV cohorts
 308 are shown in Table 2. There were no significant differences observed in total energy intake
 309 between cohorts. Protein intake was significantly lower in the CD cohort (CD, 70.3g±6.1; HV,

310 92.6g±7.8p=0.03). There was no significant difference in the consumption of all other
311 macronutrients.

312 In a sub-analysis of this dataset aimed at investigating difference by gender, the 24hr calorie
313 intake of male CD participants was not significantly different to male HV participants. In female
314 participants, 24-hour calorie intake was significantly reduced in the CD cohort compared with
315 HV participants (CD, 1519.3±136.5; HV, 2039.4Kcal±133.8; p=0.01). In female participants
316 consumption of carbohydrate (CD, 187.9g±19.9 HV, 270.1g±22.3, p=0.01), sugar (CD,
317 78.9±8.5; HV, 107.5±9.3; p=0.03) and fibre (CD, 15.9g±2.6; HV, 25.9g±3.8; p=0.04) were
318 significantly less than in HV participants.

319

320 Table 2. 24-hour self-reported calorie and macronutrient intake in CD and HV. Data is
321 presented as mean and Standard error of the mean

	CD (total)	CD (male)	CD (female)	HV (total)	HV (male)	HV (female)
Total (Kcal)	1900.9± 138.6	2187.0± 193.7	1519.3± 136.5	2054.3± 110.7	2065.0± 167.0	2039.4± 133.8
Carbohydrate (g)	248.4± 20.7	293.7± 28.5	187.9± 19.9	255.9± 17.3	245.9± 25.3	270.1± 22.3
Sugar (g)	97.8± 8.1	112.0± 11.6	78.9± 8.5	101.7± 7.4	97.6± 10.9	107.5± 9.3

Protein (g)	70.3± 6.1	74.0± 8.5	65.4± 8.8	92.6± 7.8	101.6± 12.2	79.9± 6.8
Fat (g)	69.7± 6.2	79.4± 8.2	56.9± 8.3	72.3± 5.3	73.8± 8.1	70.2± 6.2
Saturated Fat (g)	23.1± 2.1	26.2± 2.5	18.9± 3.3	23.1± 2.2	23.6± 3.4	22.5± 2.5
Fibre (g)	18.9 ± 2.1	21.2± 3.0	15.9± 2.6	23.4± 2.3	21.7± 2.8	25.9± 3.8
Alcohol (g)	3.5± 1.8	5.0± 2.9	1.5± 1.5	4.6± 1.9	5.5± 2.8	3.4± 2.2

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323 Hospital Anxiety and Depression Scale

324 CD participants had significantly higher scores on the Hospital Anxiety and Depression scale
 325 compared to HV participants (CD, 13.4±1.6; HV, 7.4±1.5; p=0.01) (see Table 3). This was
 326 evident for both anxiety (CD, 8.6±0.9; HV, 4.2±0.7; p=0.001) and depression (CD, 6±0.9; HV,
 327 1.8±0.3; p=<0.001) subscales.

328 Both male (CD 13.5±2.1; HV, 4.3±1; p=0.001) and female (CD, 15.9±2.9; HV, 8.6±1.6; p=0.04)

329 CD participants showed significant difference in HADS when compared with HV participants.

330 Male CD participants scored significantly higher than HV participants in both anxiety (CD

331 7.9±1.2; HV, 2.9±0.7; p=0.002) and depression (CD 5.5±1.2; HV, 1.3±0.4; p=0.005)

332 subscales. Female participants however were only significantly different in the depression

333 subscale (CD 6.5±1.5; HV, 2.5±0.6; p=0.02).

334 **Eating Behaviour traits**

335 Table 3 shows the outcomes from the psychometric eating behaviour questionnaires for CD
 336 and HV. CD participants scored higher on BES compared to HV participants (CD, 10.9±1.9;
 337 HV, 5.2±1.0; p=0.01) and a greater proportion of CD participants (29%) scored above the
 338 clinical cut-off criteria for moderate levels of binge eating (>17 BES) compared to HV (3.3%)
 339 [χ^2 (1) = 7.0, p=0.008].

340 CD participants reported lower levels of CoEQ Craving Control (CD, 56.16±3.5; HV, 66.4±2.9;
 341 p=0.027) and greater craving for sweet (CD, 48.9±4.4; HV, 37.3±3.5; p=0.043) and savoury
 342 (CD, 48.9±3.5; HV, 38.3±2.7; p=0.021) foods compared to HV participants. CD participants
 343 scored significantly lower on the CoEQ Positive Mood subscale (CD, 50.8±3.3; HV, 64.8±2.5;
 344 p=0.001).

345 CD participants had higher scores on the PFS food present (CD, 11.7±0.7; HV, 9.0±0.6;
 346 p=0.005) subscale. No significant difference was seen however for overall PFS score or food
 347 available or tasted subscales.

348 In addition, CD participants scored higher on the DEBQ Emotional Eating (CD, 36.4±3.7; HV,
 349 20.0±1.7; p=<0.001) and External Eating (CD, 30.8±1.9; HV, 25.2±1.2; p=0.022) subscales
 350 compared to HV participants. However, there was no difference in restraint assessed by either
 351 or DEBQ (CD, 23.7±2.7; HV, 21.6±1.9; p=0.528) the TFEQ (CD, 6.4±0.9; HV, 8.4±0.9; p=NS)
 352 between CD and HV participants.

353

354 Table 3. Eating behaviour traits in CD participants and age-, BMI- and gender-matched HV.

	CD	HV	Sig. (2-tailed)
HADS	13.4±1.6	7.4±1.5	0.01
HADS: Anxiety	8.6±0.9	4.2±0.7	0.001

HADS: Depression	6.0±0.9	1.8±0.3	<0.001
BES	10.9±1.9	5.2±1.0	0.01
PFS	35.6±2.4	31.0±1.9	NS
PFS: Available	12.1±1.2	10.5±0.9	NS
PFS: Present	11.7±0.7	9.0±0.6	0.005
PFS: tasted	11.7±0.8	11.7±0.8	NS
CoEQ: Control	56.2±3.5	66.4±2.9	0.027
CoEQ: Sweet	48.9±4.4	37.3±3.5	0.043
CoEQ: Savoury	48.9±3.5	38.2±2.7	0.021
CoEQ: Mood	50.7±3.3	64.8±2.5	0.001
TFEQ: R	5.9±0.9	8.4±0.9	NS
TFEQ: D	6.1±0.8	4.5±0.6	NS
TFEQ: H	5.5±0.8	4.0±0.5	NS

DEBQ: R	23.7±2.7	21.6±1.9	NS
DEBQ: Em	36.4±3.7	20.0±1.7	<0.001
DEBQ: Ex	30.8±1.9	25.2±1.2	0.022

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356 When analysed by gender, male CD participants showed significant difference in BES (CD,
357 7.3±1.6; HV, 3.4±0.8; p=0.04) CoEQ: Control (CD 58.9±4.4; HV, 70.5±3.3; p=0.04) CoEQ:
358 Sweet (CD, 51.5±6.2; HV, 32.9±4.1; p=0.01), TFEQ: Restraint (CD, 4.1±0.8; HV, 8.3±1.1;
359 p=0.005) and DEBQ: Emotional (CD, 31.4±4.2; HV, 18.9±1.9; p=0.02) when compared with
360 male HV participants.

361 Female CD participants showed significant difference in PFS: Present (CD, 12.8±1; HV, 9.6±1;
362 p=0.04), CoEQ: Mood (CD, 44.1±5.2; HV, 64.1±4.1; p=0.006) and DEBQ: Emotional (CD,
363 43.8±6; HV, 22±3.4; p=0.01) when compared with female HV participants.

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370 **DISCUSSION**

371 A poor nutritional status has always been associated with CD but a detailed analysis of eating
372 behaviour in this cohort compared to matched HV has never been undertaken. The primary

373 aim of this study was to compare the total self-reported 24 hr calorie intake in CD with active
374 disease and HV. The main secondary aim was to examine whether CD participants with active
375 disease had a greater prevalence of disordered eating patterns compared to HV. We found
376 no substantial difference in the 24-hour self-reported calorie intake between CD participants
377 with objective evidence of intestinal inflammation and age-, BMI- and gender-matched HV
378 participants. Analysing the data further by gender reveals that a significant decrease in calorie
379 intake is observed in female rather than male CD participants with this reduction in food intake
380 consisting mainly of a reduction in carbohydrates in females and protein in males. This finding
381 is novel and contrasts with observations made in previous studies that have showed no
382 difference in energy intake in CD patients with both active and inactive disease ^{27,28}. These
383 differences in food intake may be explained by the two-path theoretical model; with CD
384 patients experiencing high levels of anxiety to food intake, thus restricting food variety to
385 minimise symptom aversion ^{1,2}.

386 An increased prevalence of disordered eating behaviour traits was observed in CD with a
387 greater prevalence of binge eating, food craving, lower mood and higher anxiety states
388 observed in this group. Patients with gastrointestinal disorders are reported to suffer from
389 disordered eating behaviour with more than a third of CD patients thought to be affected ⁸. In
390 the present study, it was demonstrated that CD participants scored significantly higher on
391 measures of binge eating and hedonic responsiveness compared to HV participants. Binge
392 eating traits were more prevalent as revealed by a significantly higher BES together with
393 significantly stronger cravings with less ability of self-control. The CoEQ showed that CD
394 participants had less control of their cravings, with significantly greater cravings for both sweet
395 and savoury foods.

396 Significantly higher scores on the hedonic eating traits (i.e. BES, PFS, DEBQ-External) in CD
397 may be associated with increased food monitoring behaviour that occurs in patients with
398 dietary-controlled conditions. These findings are consistent with previous research that have
399 demonstrated a higher level of disordered eating patterns in individuals with gastrointestinal

400 disorders ^{1,2}. In a questionnaire-based study in 400 consecutive IBD patients in the UK ⁶,
401 approximately half of the patients felt that diet was the initiating factor in IBD and subsequent
402 relapses. The majority of patients' symptoms were triggered by food with two-thirds of the
403 patients depriving themselves of their favourite food to achieve symptom control. A case-
404 control study of 104 patients with an established diagnosis of IBD ²⁹ concluded that avoidance
405 of meat, nuts, fruit and vegetables are more common among patients with IBD than healthy
406 controls. This corresponds with the findings of this study where the consumption of protein
407 was significantly reduced overall and carbohydrate, sugar and fibre intake were reduced in
408 females.

409 The current study also demonstrated that CD participants had lower levels of positive mood
410 as measured by the CoEQ and higher scores on the HAD scale. Greater levels of
411 psychological distress have been linked to increased binge eating prevalence and in the
412 current study we found that scores on the BES were negatively associated with positive mood
413 (data not shown). Similarly, we found a higher prevalence of emotional eating in the DEBQ.
414 These findings have important implications for the role of mood and psychological distress in
415 the aetiology of gastrointestinal disorders and their association with abnormal eating patterns
416 ³⁰. For example, it is possible that psychological distress may serve as both a cause and a
417 consequence of disordered eating behaviours ³. Arigo et al suggested that fear and anxiety
418 surrounding gastrointestinal symptoms may lead to disordered eating practices of a restrictive
419 nature, as observed in this study ³¹. This increased anxiety may link directly to the personal
420 attitudes and beliefs that patients hold about food. In a French survey of 244 IBD patients,
421 nearly half of the study patients reported that the disease had changed the pleasure of eating
422 ⁷ with only a quarter of the patients eating a normal diet when they relapse. Such a behaviour
423 influenced patients' social life in 25% of the cases. This might have a negative effect on mood
424 and depressive symptoms.

425 Disease activity has been quantified with objective markers of disease activity and intestinal
426 inflammation present in our entire recruited cohort. Clinical scores were quantified through

427 HBI. Gastrointestinal symptom severity may also play an important role in the development
428 of disordered eating patterns, with greater symptom severity correlating positively with the risk
429 of disordered eating ³².

430 When analysed by gender, female CD participants consumed significantly less calories than
431 female HV participants with reduced consumption of carbohydrate, sugar and fibre. This was
432 not observed in male participants. Male CD participants displayed greater hedonic
433 responsiveness with higher BES, lower CoEQ Control and TFEQ:Restraint compared with
434 male HV participants. In female CD participants, significantly higher PFS: present and DEBQ:
435 Emotional with lower CoEQ: mood when compared with female HV participants might imply
436 that female CD participants may be predisposed to emotional eating. These results may
437 suggest that female CD participants have similar level of self-control over dietary consumption
438 as HV. Consequently, females with CD may be less likely to binge eat during active disease,
439 being more likely to display inadequate calorie consumption as displayed by this study. Male
440 CD participants display greater hedonic responsiveness, with higher prevalence of binge
441 eating with the consequence of normalising calorie consumption. It is important to highlight
442 that this study was not powered to analyse the difference in eating behaviour by gender, so
443 such conclusions are hypothesis-generating.

444 We believe that for the first time, this study highlights in detail the important behavioural
445 differences that may be observed in patients with active CD. This study has some limitations
446 that need to be considered. This was a prospective study aiming to compare calorific intake
447 and the eating behaviour of CD patients with active disease to matched healthy volunteers.
448 The BMI of the recruited cohort was BMI:24.9±0.8 in CD and 24.7±0.5 in HV participants.
449 These values are at the upper limit of what the World Health Organisation considers as normal
450 weight. Nevertheless, these BMIs are representative of present world-wide trends making our
451 cohorts more representative ^{33 34}. The sample size despite being relatively small was
452 appropriately powered based on the group's previous pilot data ²⁶. Daily activity level is an
453 important confounder that was not routinely measured to try and minimise participant research

454 burden. Physical inactivity has already been shown in CD ^{35,36} and has been significantly
455 correlated to disease activity but is still prevalent in remission ³⁷. Due to the small sample size,
456 we did not investigate the effect of disease burden surrogates: disease duration, concomitant
457 medication and surgical history in CD patients on eating behaviour. The effect of these
458 variables on eating behaviour should be investigated in downstream studies. Nevertheless,
459 the CD cohort recruited is representative of a CD cohort with moderate disease burden,
460 making our findings generalizable to world-wide healthcare systems.

461 The use of the AMPM as a single administered 24-hour recall is limited, and accuracy may
462 have been improved if this was performed on three consecutive days rather than one day.
463 However, this method has been used successfully in previous research ²⁰. The 24-hour recall
464 technique is also memory dependent and participants' potential bias in reporting "good/bad"
465 foods may affect the accuracy of the outcome. In this study, the 24-hour recall data was
466 collected by three interviewers, which may have introduced inter-rater variability in the data
467 collected. Additionally, during dietary recall, if a manufacturer's nutritional label was not
468 available, portion size was obtained using the Carbs and Cals textbook as a visual aid, which
469 may have affected the estimation of portion size. When assessing eating behaviours, the use
470 of multiple behavioural questionnaires may have introduced an element of participant fatigue
471 that may have decreased the specificity of the responses given. The order of these
472 questionnaires was administered randomly to all participants throughout the study to mitigate
473 this risk. Future studies should use additional methods such as weighed food records, and
474 laboratory test meals to measure food intake in patients with active CD and to confirm the
475 caloric intake findings of the present study.

476 Biochemical, endoscopic and radiological objective measures of disease activity have been
477 acquired as part of routine standard of care rather than as a specific screening process for
478 this study. For this reason, there was a variable lag between the dates of these assessments
479 and recruitment to this study. None of these patients changed their maintenance therapy after
480 these investigations and prior to recruitment within this study.

481 In conclusion, this study has highlighted the significantly higher prevalence of emotional eating
482 and food monitoring behaviour in CD. Clinically these results imply that stronger psychological
483 and firm dietetic education may be of benefit in CD. Nearly half of the IBD patients have never
484 received dietetic advice and two-thirds feel they need more support ⁶. Questioning patients on
485 their attitudes and beliefs through counselling or psychotherapy may alter these behaviours.
486 Firm dietetic advice for healthy eating should also be advocated. Additionally, combating
487 underlying anxiety and depression in these patients may improve disordered eating traits. The
488 UK IBD standards in 2013 highlighted the need for formal psychological support in IBD teams
489 with only 24% of adult IBD services have defined access to a psychologist with an interest in
490 IBD ³⁸.

491 This study has provided new evidence regarding the complexity of disordered eating
492 behaviour traits in active CD. A more objective understanding is needed regarding the fine
493 balance between homeostatic and hedonic control of food intake in intestinal inflammation.

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544 **REFERENCES**

545 1. Satherley R, Howard R, Higgs S. Disordered eating practices in gastrointestinal disorders.

546 *Appetite* 2015;**84**:240-50.

- 547 2. Satherley R-M, Howard R, Higgs S. The prevalence and predictors of disordered eating in
548 women with coeliac disease. *Appetite* 2016;**107**:260-7.
- 549 3. Quick, V. M., Byrd-Bredbenner, C., & Neumark-Sztainer, D. (2013). Chronic illness
550 and disordered eating. A discussion of the literature. *Advances in Nutrition*, 4,
551 277–286.
- 552 4. Nicholas, D. B., Otley, A., Smith, C., Avolio, J., Munk, M., & Griffiths, A. M. (2007).
553 Challenges and strategies of children and adolescents with inflammatory bowel
554 disease. A qualitative examination. *Health and Quality of Life Outcomes*, 28, 1–8.
- 555 5. Prince A, Whelan K, Moosa A, Lomer MC, Reidlinger DP. Nutritional problems in
556 inflammatory bowel disease: The patient perspective. *Journal of Crohn's & colitis*
557 2011;**5**:443-50.
- 558 6. Limdi JK, Aggarwal D, McLaughlin JT. Dietary practices and beliefs in patients with
559 inflammatory bowel disease. *Inflammatory bowel diseases* 2016;**22**:164-70.
- 560 7. Zallot C, Quilliot D, Chevaux JB, *et al.* Dietary beliefs and behavior among inflammatory
561 bowel disease patients. *Inflammatory bowel diseases* 2013;**19**:66-72.
- 562 8. Addolorato G, Capristo E, Stefanini GF, Gasbarrini G. Inflammatory bowel disease: A study of
563 the association between anxiety and depression, physical morbidity, and nutritional status.
564 *Scandinavian journal of gastroenterology* 1997;**32**:1013-21.
- 565 9. Lochs H, Dejong C, Hammarqvist F, *et al.* Espen guidelines on enteral nutrition:
566 Gastroenterology. *Clinical nutrition (Edinburgh, Scotland)* 2006;**25**:260-74.
- 567 10. Hart AL, Lomer M, Verjee A, *et al.* What are the top 10 research questions in the treatment
568 of inflammatory bowel disease? A priority setting partnership with the James Lind Alliance.
569 *Journal of Crohn's & colitis* 2017;**11**:204-11.
- 570 11. Berthoud H-R. Metabolic and hedonic drives in the neural control of appetite: Who's the
571 boss? *Current Opinion in Neurobiology* 2011;**21**:888-96.
- 572 12. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. *Lancet* 1980;**1**:514.

- 573 13. Moshfegh AJ, Rhodes DG, Baer DJ, *et al.* The us department of agriculture automated
574 multiple-pass method reduces bias in the collection of energy intakes. *The American journal*
575 *of clinical nutrition* 2008;**88**:324-32.
- 576 14. Stunkard AJ, Messick S. The three-factor eating questionnaire to measure dietary restraint,
577 disinhibition and hunger. *Journal of psychosomatic research* 1985;**29**:71-83.
- 578 15. Gormally J, Black S, Daston S, Rardin D. The assessment of binge eating severity among
579 obese persons. *Addictive behaviors* 1982;**7**:47-55.
- 580 16. Lowe MR, Butryn ML, Didie ER, *et al.* The power of food scale. A new measure of the
581 psychological influence of the food environment. *Appetite* 2009;**53**:114-8.
- 582 17. van Strien T, Frijters, J. E. R., Bergers, G. P. A., & Defares, P. B. The dutch eating behavior
583 questionnaire (debq) for assessment of restrained, emotional and external eating behavior.
584 *International Journal of Eating Disorders* 1986;**5**:295-315.
- 585 18. Dalton M, Finlayson G, Hill A, Blundell J. Preliminary validation and principal components
586 analysis of the control of eating questionnaire (coeq) for the experience of food craving.
587 *European journal of clinical nutrition* 2015;**69**:1313-7.
- 588 19. Dalton M, Finlayson G, Walsh B, *et al.* Early improvement in food cravings are associated
589 with long-term weight loss success in a large clinical sample. *Int J Obes* 2017;**41**:1232-6.
- 590 20. Dalton M, Blundell J, Finlayson GS. Examination of food reward and energy intake under
591 laboratory and free-living conditions in a trait binge eating subtype of obesity. *Frontiers in*
592 *psychology* 2013;**4**:757.
- 593 21. Cheyette C BY. *Carbs & cals: Count your carbs & calories with over 1,700 food & drink*
594 *photos*: Chello Publishing Limited; 2013.
- 595 22. Cappelleri JC, Bushmakin AG, Gerber RA, *et al.* Evaluating the power of food scale in obese
596 subjects and a general sample of individuals: Development and measurement properties.
597 *International journal of obesity (2005)* 2009;**33**:913-22.

- 598 23. Marcus MD, Wing RR, Hopkins J. Obese binge eaters: Affect, cognitions, and response to
599 behavioural weight control. *Journal of consulting and clinical psychology* 1988;**56**:433-9.
- 600 24. Freitas SR, Lopes CS, Appolinario JC, Coutinho W. The assessment of binge eating disorder in
601 obese women: A comparison of the binge eating scale with the structured clinical interview
602 for the dsm-iv. *Eating behaviors* 2006;**7**:282-9.
- 603 25. Bryant EJ, King NA, Blundell JE. Disinhibition: Its effects on appetite and weight regulation.
604 *Obesity reviews : an official journal of the International Association for the Study of Obesity*
605 2008;**9**:409-19.
- 606 26. Wardle RA, Thapaliya G, Nowak A, Dalton M, Finlayson G, Moran G. An experimental
607 examination of appetite and disordered eating in Crohn's disease patients. Hard Copy Poster
608 P105 Presented at *12th Congress of ECCO - Inflammatory Bowel Diseases 2017* February 15-
609 18, 2017 in Barcelona, Spain
- 610 27. Aghdassi E., Wendland B.E., Stapleton M., Raman M., Allard J.P. Adequacy of Nutritional
611 Intake in a Canadian Population of Patients with Crohn's Disease. *Journal of the American*
612 *Dietetic Association* 2007. 107 (9) (pp 1575-1580), 2007.
- 613 28. Filippi J, Al-Jaouni R, Wiroth JB, Hebuterne X, Schneider SM. Nutritional deficiencies in
614 patients with crohn's disease in remission. *Inflammatory bowel diseases* 2006;**12**:185-91.
- 615 29. Chen T.-C., Cruz G., Sellin J., Hou J. Food avoidance and use of dietary supplements among
616 patients with inflammatory bowel disease. *American Journal of Gastroenterology*.2014
617 Conference: 79th Annual Scientific Meeting of the American College of Gastroenterology
618 Philadelphia, PA United States. Conference Start: 20141017 Conference End: 20141022.
619 Conference Publication: (var.pagings). 109 (pp S507)
- 620 30. Peat CM, Huang L, Thornton LM, *et al*. Binge eating, body mass index, and gastrointestinal
621 symptoms. *Journal of Psychosomatic Research* 2013;**75**:456-61.
- 622 31. Arigo D, Anskis AM, Smyth JM. Psychiatric comorbidities in women with celiac disease.
623 *Chronic illness* 2012;**8**:45-55.

- 624 32. Pariente B, Mary JY, Danese S, *et al.* Development of the lemann index to assess digestive
625 tract damage in patients with crohn's disease. *Gastroenterology* 2015;**148**:52-63.e3.
- 626 33. World Health Organisation. <http://apps.who.int/bmi>
- 627 34. NCD Risk Factor Collaboration. Trends in adult body-mass index in 200 countries from 1975
628 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million
629 participants. *Lancet*. 2016 Apr 2;**387**(10026):1377-1396.
- 630 35. van Langenberg DR, Della Gatta P, Hill B, *et al.* Delving into disability in crohn's disease:
631 Dysregulation of molecular pathways may explain skeletal muscle loss in crohn's disease.
632 *Journal of Crohn's & colitis* 2014;**8**:626-34.
- 633 36. van Langenberg DR, Papandony MC, Gibson PR. Sleep and physical activity measured by
634 accelerometry in crohn's disease. *Alimentary pharmacology & therapeutics* 2015;**41**:991-
635 1004.
- 636 37. Vogelaar L, van den Berg-Emons R, Bussmann H, *et al.* Physical fitness and physical activity in
637 fatigued and non-fatigued inflammatory bowel disease patients. *Scandinavian journal of*
638 *gastroenterology* 2015;**50**:1357-67.
- 639 38. IBD Standards 2013 Update [https://www.crohnsandcolitis.org.uk/improving-care-](https://www.crohnsandcolitis.org.uk/improving-care-services/health-services/ibd-standards)
640 [services/health-services/ibd-standards](https://www.crohnsandcolitis.org.uk/improving-care-services/health-services/ibd-standards)
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	SEX	AGE (YR.)	BMI (KG/M ²)	MONTREAL	DIS. DUR. (YR.)	MED	HBI	CRP (MG/L)	FCP (µG/G)	MRI	COLONOSCOPY
P01	F	48	24.9	A1L3B2	41	Nil	4	-	-	-	Post op recurrence Rutgeerts i3
P02	M	22	21.8	A2L1B3	3	AZA	2	-	-	-	Post op recurrence Rutgeerts i3
P03	M	51	21.4	A2L1B2	18	HUM, MTX	1	-	316	multifocal active small bowel disease	
P04	F	23	26.7	A2L3B1	4	AZA	5	-	-	-	Diffuse punched out ulcerations in terminal ileum
P05	M	30	25.5	A2L3B3	10	Nil	9	-	-	-	Colonoscopy - Rutgeerts i2
P06	M	25	26.2	A2L3B1	6	HUM	2	-	1763	-	-
P07	M	23	20	A2L3B3	1	HUM	11	-	-	30cm of TI disease with an enter-enteric fistula	-
P08	F	37	24.3	A2L1B2	14	Nil	9	-	-	Terminal ileitis	-
P10	F	23	23.1	A2L1B1	1	MP	5	-	-	-	Diffuse punched out ulcerations in terminal ileum
P11	M	35	33.7	A2L3B1p	2	HUM	9	52	-	-	rectosigmoid inflammation with a perianal fistula
P13	F	29	36	A2L1B1	10	Nil	7	-	-	6cm terminal ileum inflammatory disease	-
P14	M	32	29.6	A2L3B3p	14	HUM, AZA,P	5	-	-	pancolonic inflammatory disease with distal sparing. Has a desc colon stricture. Distal 3cm TI inflamed	-
P15	M	57	18.6	A3L1B3	15	AZA,P	10	-	-	mixed inflammatory and stricturing disease in the ileum	-
P16	F	33	24.9	A2L2B1	13	INF, AZA	6	-	449	-	severe colonic disease with punched out ulcers
P17	F	40	27.6	A3L1B3	0	Nil	5	-	-	30cm of terminal ileal inflammatory disease	-
P19	M	49	25.7	A3L3B1	1	P	2	-	-	15cm of terminal ileal inflammatory disease	-
P20	M	33	22.5	A2L3L4B2	8	INF, AZA	0	-	1800	extensive jejunal disease	-
P23	M	20	19.37	A2L3B3	4	MP	7	-	-	-	Post op recurrence Rutgeerts i2
P24	M	28	18.6	A2L1B1	1	Nil	3	-	-	-	Diffuse punched out ulcerations in terminal ileum
P25	M	23	23.4	A2L3B1p	1	AZA	1	-	-	Diffuse terminal ileal inflammatory disease	-
P26	M	38	30.6	A2L3B2	11	AD, AZA	8	-	785	-	-
P27	F	35	30.3	A2L2B2	13	HUM	8	-	1226	-	-

P28	F	22	23	A2L1 B2	7	HUM, AZA	0	38		Ruterts i2
P29	M	20	19.3	A2L2B1	3	AZA	4	-	1027	
P30	F	68	21.4	A3L2B2/B3	1	MTX	8	224	-	extensive transverse colonic disease with fistulisation
P31	M	31	25.5	A2L1B1	9	AD	1	-	607	chronic disease
P32	F	28	30	A2L2B1	4	INF, MP	1	-	319	
P33	F	24	22	A2L2 B1	12	HUM	1	-	-	mild patchy colitis with loss of vascular pattern, erythema in R colon.
P34	M	25	29.7	A2L1B1	9	MP	2	-	1800	Thickening of the terminal ilium
P35	M	18	22	A2L2B1	6	MP	8	-	1266	

Supplementary Table: CD Participant Demographic

AD=ADALIMUMAB, AZA=AZATHIOPRINE, HUM=HUMIRA, INF=INFLIXIMAB, MP=MERCAPTOPYRINE, MTX=METHOTREXATE, P=PENTASA

