

1 **Associations between Diet and Disease Activity in Ulcerative Colitis Patients using a**
2 **Novel Method of Data Analysis**

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4 Elizabeth A Magee, Laurie M Edmond*, Shiona M Tasker, San Choon Kong, Richard
5 Curno and John H Cummings.

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7 Division of Pathology and Neuroscience, Ninewells Hospital and Medical School,
8 Dundee, DD1 9SY, Scotland, United Kingdom.

9 Email addresses:

10 EAM: e.magee@dundee.ac.uk

11 LME: l.m.edmond@dundee.ac.uk

12 SMT: s.m.tasker@dundee.ac.uk

13 SCK: s.c.kong@dundee.ac.uk

14 RC: r.curno@dundee.ac.uk

15 JHC: j.h.cummings@dundee.ac.uk

16 *corresponding author

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20

20 **Abstract**

21 **Background**

22 The relapsing nature and varying geographical prevalence of ulcerative colitis (UC)
23 implicates environmental factors such as diet in its aetiology.

24

25 **Methods**

26 In order to determine which foods might be related to disease activity in UC a new
27 method of dietary analysis was developed and applied. Eighty-one UC patients were
28 recruited at all stages of the disease process. Following completion of a 7 d diet diary,
29 clinical assessment including a sigmoidoscopic examination (scale 0 (normal mucosa) to
30 6 (very active disease)) was conducted. Food weights for each person were adjusted
31 (divided) by the person's calorific intake for the week. Each food consumed was given a
32 food sigmoidoscopy score (FSS) calculated by summing the products of the (adjusted)
33 weight of food consumed and sigmoidoscopy score for each patient and occurrence of
34 food and dividing by the total (adjusted) weight of the food consumed by all 81 patients.
35 Thus, foods eaten in large quantities by patients with very active disease have high FSSs
36 and vice versa. Foods consumed by <10 people or weighing <1 kg for the whole group
37 were excluded, leaving 75 foods.

38

39 **Results**

40 High FSS foods were characterized by high levels of the anti-thiamin additive sulfite
41 (Mann-Whitney, $p < 0.001$), i.e. bitter, white wine, burgers, soft drinks from concentrates,
42 sausages, lager and red wine. Caffeine also has anti-thiamin properties and decaffeinated

43 coffee was associated with a better clinical state than the caffeine containing version.
44 Beneficial foods (average intake per week) included crackers (70 g), pork (210 g),
45 breakfast cereals (200 g), lettuce (110 g), apples and pears (390 g), sweetcorn (80 g), milk
46 (1250 ml), melon (350 g), cucumber (50 g), bananas (350 g), bacon (120 g), beef and
47 beef products (500 g), tomatoes (240 g), soup (700 g), citrus fruits (300 g), fish (290 g),
48 yogurt (410 g), cheese (110 g), mushrooms (70 g), potatoes (710 g) and legumes (120 g).

49

50 **Conclusions**

51 The dietary analysis method described provides a new tool for establishing relationships
52 between diet and disease and indicates a potentially therapeutic diet for UC.

53

54 Key words: ulcerative colitis, diet, sulfite, thiamin, resistant starch.

55

55 **Background**

56 Ulcerative colitis (UC) is a chronic, relapsing mucosal disorder that extends in
57 continuous fashion proximally from the rectum and is limited to the colon. The aetiology
58 of UC includes a genetic component possibly involving an abnormal cell-mediated
59 immune response to commensal enteric bacteria in the large intestine. The
60 relapse/remission pattern of the disorder and substrate driven nature of microbial
61 metabolism in the large bowel implicate environmental factors such as diet.

62 Apart from nutritional repletion, dietary measures do not play a role in the
63 management of UC. Nonetheless, attempts to link the cause of UC with specific foods
64 date back at least 50 years[1]. Many foods or food groups have been related to UC (table
65 4) [2-13] including sugar, eggs, soft drinks, fruit and vegetables, protein, carbohydrate
66 and fat. However none have been proven to be of significant benefit or to contribute to
67 the cause of UC. This may partly be because both the assessment of disease activity in
68 UC and dietary intake are difficult to measure, or because the actual dietary component
69 that is key to this relationship has not been measured.

70 It has been proposed that sulfide, produced in the large bowel from either amino
71 acid fermentation or sulphate reduction, may be a triggering factor in the inflammatory
72 process of UC[14, 15]. Recently, in a prospective dietary study where foods rich in
73 sulfur compounds were quantitated, evidence that sulfur compounds may increase the
74 likelihood of subsequent relapse in UC was found[16].

75 The main source of inorganic sulfur, predominantly sulfate, in the diet are the S
76 (IV) family of additives; the sulfiting agents. Sulfites have been used as food
77 preservatives since the 17th century and are amongst the most widely accepted and

78 versatile of additives. Sulfiting agents, denoted by E220-228 in Europe and generally
79 recognized as safe (GRAS) substances in the USA, include sulfur dioxide, hydrogen
80 sulfites, sulfites and metabisulfites. Sulfiting agents are cheap, easy to use and extremely
81 effective at preventing microbial growth and reducing spoilage[17]. They serve as
82 antioxidants, inhibit enzymatic and non-enzymatic browning reactions and act as a
83 texture modifier in biscuit dough. Sulfites improve color extraction from, and
84 stabilization of grape must in winemaking and preserve lobsters and shrimps from
85 discoloration during iced storage.

86 However, there are some problems with sulfite use[18, 19]. In the early 1980s
87 ingestion or inhalation of sulfites was shown to cause bronchospasm in about 5 % of
88 asthmatics. Sulfite sensitivity can pose a particular threat in the workplace where
89 sulfiting agents are used, but may also occur with ingestion of sulfited foods such as
90 potato products and wine. In addition, skin sensitivity has been reported and there are
91 anti-nutritional effects, particularly the destruction of thiamin[20]. The mechanism
92 involves an initial nucleophilic substitution of thiamin by the sulfite ion. As a result of
93 this anti-nutritional effect the GRAS status for sulfites was reviewed in the USA and in
94 1986 the use of sulfites in fresh and frozen fruit and vegetables revoked and a declaration
95 on the label required[21, 22]. Earlier (in the USA) their use in meat had been prohibited,
96 because these foods are an important source of thiamin.

97 A study of diet and disease activity in UC using a 7 d dietary diary, a full
98 assessment of disease activity and a method of dietary data analysis that allows trends in
99 food consumption not apparent using customary dietary software was therefore
100 undertaken.

101

101 **Methods**

102 *Subjects.* Eighty-one UC patients were recruited and informed consent obtained. Ethical
103 permission was granted by Tayside Committee on Medical Ethics, Dundee, UK (ref
104 007/00). As it was important to have a range of disease activities present, recruitment
105 included patients at all stages of the disease. Patients were excluded if clinical
106 examination or histology indicated Crohn's disease or indeterminate colitis, if there was a
107 positive stool culture for pathogens or if the patient had antibiotic treatment within 3
108 months preceding the start of the study.

109 *Dietary Assessment.* All the UC patients were asked to complete a 7 d diet diary[23].
110 The diet diary used has been validated for use in the European Prospective Investigation
111 into Cancer study (EPIC). Following completion of the diet diary, subjects attended the
112 research clinic and a full clinical assessment (see below) was carried out. The time
113 interval between the first day of the diary and the clinical visit was on average 28 d. Thus
114 the dietary data is prospective.

115 7d diet diaries were coded and analyzed using Tinuviel, WISP v3.0 nutritional
116 analysis software (Warrington, UK). Due to the variation in the sulfiting protocols and
117 widespread use of sulfiting agents, current tables of food composition do not contain
118 inorganic sulfur values and cannot be used to quantify intake. Instead of quantitating the
119 intake of particular dietary components, foods and food groups were assessed in their
120 entirety using the method described in the dietary data analysis section (below).

121 *Clinical Assessment.* Clinical assessment included history, physical examination and
122 global clinical grading, plus full blood count, liver function tests and inflammatory
123 markers. Patients were examined by rigid sigmoidoscopy or flexisigmoidoscopy and

124 graded on a scale 0-6 (integers and half integers used) according to the macroscopic
125 appearances of the rectal mucosa at a distance 5-10 cm from the anal verge[24]. The
126 clinical assessment of disease activity was confirmed in each case by histological
127 examination, by a single histopathologist blinded to the clinical details, of a rectal biopsy
128 taken from the posterior rectal wall 5-10 cm from the anal verge[25]. A simple clinical
129 colitis score was assigned to patients on each visit following Walmsley's scoring
130 system[26], together with blood parameters of disease severity (Hb, plasma viscosity,
131 CRP, serum albumin). A 14 d bowel habit diary[27] was also completed by a sub sample
132 of the population.

133 *Dietary Data Analysis.* Patterns of dietary intake associated with disease activity became
134 apparent through the study of the dietary diaries, e.g. high intakes of sulphite containing
135 foods coupled with a modern processed, convenience diet was associated with a high
136 sigmoidoscopy score. Traditional dietary coding (WISP) did not show any such clear
137 associations between micro or macro nutrient intake and sigmoidoscopy score.
138 Traditional dietary analysis was therefore thought to be missing important patterns in
139 dietary data and a new method of dietary assessment was subsequently developed.

140 This new method used the following procedure. To calculate the association of a
141 particular food with clinical score, each food or food group consumed was given a food
142 sigmoidoscopy score (FSS) calculated by summing the products of food weight and
143 sigmoidoscopy score for each occurrence of the food or food group and dividing by the
144 total weight of the food or food group contained in all diaries. In order for each diary to
145 make equal contributions to the FSSs, the weight of each food was adjusted using the
146 calorific intake for each person. This procedure was carried out separately for every food

147 item recorded in the 7 d diet diaries but is explained below using the example of red
148 wine.

149

150 Red wine score = $(\sum v(i)s(i))/\sum v(i)$ for $i=1$ to 81 equation 1.

151 Where: -

152 i is the 7 d dietary diary number ($n=81$).

153 $v(i)$ is the volume (divided by calorific intake for patient (i) of red wine recorded in 7 d
154 dietary diary i .

155 $s(i)$ is the sigmoidoscopy score associated with 7 d dietary diary (i).

156

157 Thus foods eaten in large quantities by patients with high levels of disease activity will
158 have high scores and vice versa. The denominator in the above equation is the total
159 volume of the food in question from all diaries (corrected for calorific intakes) so the
160 food scores can be equated with the effect of a typical portion of the food in question on
161 the sigmoidoscopy scores of the patients. This procedure is repeated for every food item.
162 Foods or food groups were excluded from the analysis if 10 or fewer people consumed
163 them or if they made up less than 1 kg of the total intake of the entire population. The
164 decision as to where food group boundaries lay was made depending on the size of the
165 group and whether the differences between the foods were considered important for this
166 study.

167 *Statistics and Data Handling.* Dietary data was exported from WISP to Microsoft
168 EXCEL 98 (Macintosh version, 1998). A worksheet containing the core headings;
169 Patient ID, food description, weight and patient sigmoidoscopy score was completed.

170 The data was then sorted by food description and each food copied to a separate EXCEL
171 file. Equation 1 was then used to calculate food sigmoidoscopy scores for each food in a
172 manner similar to the example in table 2.

173 Correlation values for scatter plots were obtained using the linear regression
174 function in EXCEL. The equation $t=r \sqrt{((n-2)/(1-r^2))}$ combined with t tables provided
175 corresponding significance levels.

176

176 **Results**

177 Of the 81 patients recruited 43 were male and 38 female. The average age (range)
178 of the males and females were respectively 53 (26-78) y and 47 (19-74). The distribution
179 of sigmoidoscopy scores is shown in fig 1. One third of the patients had sigmoidoscopy
180 scores of 0, 0.5 or 1. The mean sigmoidoscopy score for all 81 patients was 2.09.
181 Correlations for the bowel habit diaries with sigmoidoscopy scores, bowel habit diaries
182 with clinical activity indexes, and for the clinical activity indexes with sigmoidoscopy
183 scores were respectively; $r^2=0.39$ (n=44), $r^2=0.39$ (n=44), and $r^2=0.25$ (n=81). The bowel
184 habit diaries data set was not complete because bowel habit diaries were not introduced
185 until later in the study.

186 Table 3 shows the foods and food groups with associated sigmoidoscopy scores
187 and average portion sizes. In total 75 foods (or food groups) were given FSS scores. The
188 higher the FSS value the greater the association with disease activity and vice versa. The
189 total weight of foods in all diaries was 1,681 kg. The average food sigmoidoscopy score
190 (i.e. a food sigmoidoscopy score calculated for the entire dietary intake data set was
191 2.127). Foods excluded from the FSS table (Table 3), by virtue of contributing <1 kg or
192 being consumed by <10 people, made up 8 % of the total weight of all foods and had a
193 score slightly lower (2.001) than that of an average food (2.127). Standard errors are not
194 quoted for the food scores as the data used to generate them (weight * sigmoidoscopy
195 score) was not normally distributed due to the number of sigmoidoscopy scores of 0.

196 The dietary diaries were assessed for completeness by comparing calorific intakes
197 with expected values for the sexes. Expected (calculated from dietary reference tables
198 using age and sex)[28] versus actual values for men and women were respectively 2481

199 kcal/d versus 2326 kcal/d and 1925 kcal/d versus 1887 kcal/d.

200 Foods for which regulations exist in the EU permitting sulfite addition are shown
201 in table 4[29]. Typically a manufacturer will add sulfite up to the maximum permitted
202 level in order to achieve the longest shelf life for the product. A report on sulfite usage in
203 the UK was produced in 2001[30]. Sweet wines, langoustines (prawns), dehydrated
204 potatoes and dried fruit were not given FSS scores because their data quantity fell below
205 the <10 people or <1 kg rule. Soft drinks were split into those known to contain sulphite
206 (drinks made from fruit squash concentrates and lucozade) and the rest. In terms of
207 intake (portion size*sulfite concentration), for this population, the major sources of
208 sulphite (FSS, FSS table position) were bitter beer (3.91, 75), white wine (2.87, 73),
209 burgers (2.84, 72), soft drink concentrates (2.79, 70), sausages (2.68, 68), lager (2.47, 64)
210 and red wine (2.00, 29). A Mann-Whitney test on the FSS positions of these foods gave a
211 significance of $p < 0.001$. The sulfite-containing, alcoholic beverages; wines and beers,
212 were associated with increased UC disease activity, but spirits were not, which suggests a
213 role for sulfite rather than alcohol in the disease process. A plot of alcohol consumption
214 from wine and beer against sigmoidoscopy score revealed a significant positive
215 correlation ($n=81$, $r^2=0.07$, $p < 0.02$).

216 Decaffeinated coffee appeared better for the UC patient than the caffeine-
217 containing counterpart. Decaffeinated tea is not shown on table 3 because it was only
218 drunk by 9 people but had a FSS of 1.71 versus 2.01 for the caffeine-containing product.
219 Whole fruit consumption appeared better than the corresponding juice (e.g. fruit juice
220 scored 2.43 compared to citrus fruits at 1.96 and apples at 1.67).

221 An average thiamin concentration (mg / 100 g) (Holland, 1993 #9) for each food

222 or food group is also shown in table 3. There is a significant correlation ($p < 0.005$)
223 between this thiamin value and the food's sigmoidoscopy score.
224

224 **Discussion**

225 Ulcerative colitis is considered to have a genetic component. Twin studies[31]
226 have shown a 10% concordance of UC in monozygotic and 3% in dizygotic twins
227 suggesting about 90% environmental and 10% genetic contributions. The pool of
228 genetically susceptible individuals is therefore at least 10 times greater than those
229 diagnosed with the condition. A failure to date in identifying the gene(s) responsible
230 points to a complicated genetic component featuring multiple polymorphisms. The first
231 acute episode of UC must disrupt either, the ecology of, or the sensitivity and selectivity
232 of the immune system to, the commensal enteric microflora sufficiently to cause the
233 chronic condition. More extreme versions of the environmental conditions that lead to
234 subsequent relapses could conceivably lead to the first acute episode.

235 Of all the dietary components studied in relation to UC risk and disease severity,
236 milk has probably received the most attention. Andreson[1] was the first to postulate
237 that food allergy was the cause of UC in two-thirds of his patients, and by the use of
238 elimination diets claimed to identify the offending food and remove it. In Andreson's
239 experience, the most common provoking antigen was cow's milk. His views were
240 confirmed by Rowe[32] and later by Truelove[33]. They all postulated that milk protein
241 sensitivity was an aggravating cause of disease in up to 5% of colitic patients, who
242 benefited from a milk-free diet. While able to demonstrate circulating antibodies to milk
243 proteins more frequently and in higher titer than in matched controls, they were unable to
244 correlate the occurrence and titer of these antibodies with the extent, severity, or duration
245 of colitis, or with the response to a milk-free diet. Mishkin[34] concluded, in a review of
246 the subject, that IBD patients avoid dairy products to a much greater extent than the

247 prevalence of lactose malabsorption and/or milk intolerance in this population group
248 would justify. This observation was probably due to the incorrect perceptions of patients
249 and arbitrary advice of physicians and authors of popular diet books.

250 In order to ascertain whether dietary antigens may sustain the mucosal
251 inflammatory response, two prospective controlled trials have investigated the
252 effectiveness of bowel rest and total parenteral nutrition as primary therapy in the
253 management of acute UC[35, 36]. Neither study found any benefit over conventional
254 corticosteroid treatment alone and so the possibility of a dietary antigen driving the
255 chronicity of the disease seems unlikely. These results are in agreement with work
256 demonstrating[37] that a split ileostomy is of little benefit in the management of UC, but
257 the latter observations may have been confounded by the development of diversion
258 colitis[38].

259 The dietary analysis procedure proposed here has the potential to highlight trends
260 in dietary data that would not be apparent using traditional dietary analysis software and
261 could be useful in the study of other diseases with dietary associations. This system
262 would highlight any possible dietary factors both positive and negative, not just sulfite.
263 The proposed method is less reductionist than traditional coding as it assesses the risk of
264 each food item or group rather than the risk from the foods' (quantitated) constituents.
265 Part of the power of this study derives from the availability of a sigmoidoscopic grading
266 (0-6) of the severity and extent of the disease. This grading provides the statistical
267 variable that is normally obtained from a non-UC control group. Other alternative
268 systems for analysis of disease risk for dietary components are; the use of disease
269 occurrence odds ratios between the top and bottom quartiles of intakes, and assessing the

270 correlation coefficients between disease activity and intakes. The odds ratio method loses
271 data and data accuracy by characterizing intakes as high, high middle, low middle and
272 low and then discarding the middle two quartiles. The correlation method is dependent
273 on spread. The proposed system has neither of these disadvantages. The food
274 sigmoidoscopy score calculation does rely on the assumption that the sigmoidoscopy
275 score is an approximately linear scale, i.e. a sigmoidoscopy score of 6 is caused by the
276 consumption of a double portion of a harmful food item of sigmoidoscopy score 3. This
277 could be argued to be reasonable. Both the sigmoidoscopy grading and dietary analysis
278 method are validated methodologies. The food sigmoidoscopy score is simply a
279 mathematical function of these two variables. As all data is transformed according to the
280 same simple rules any statistical treatment of the results is as valid as statistical treatment
281 of the raw data.

282 Whilst bowel habit diaries and clinical activity indices were used to generate
283 analogous scores to the food sigmoidoscopy scores, the results from these measurements
284 are not included in this paper. Bowel habit diary scores are naturally variable and the
285 clinical activity index, as well as using bowel habit diary data, also involves subjective
286 measurements such as a feeling of well being. Thus, the food orders generated by these
287 measurements were not thought to be as accurate as those generated by the
288 sigmoidoscopy scores.

289 The consensus of previous studies on diet and UC pointed to the modern,
290 processed, highly refined, Western diets as being damaging. The results presented here
291 linking diet with disease activity are broadly in agreement with this. Additionally they
292 propose a new risk factor for UC, namely intake of sulfited foods.

293 The involvement of diet in UC is controversial. Differences in dietary intake
294 between patients and controls could be a result of changes in diet brought on by the
295 symptoms of the disease process[4]. While this explanation is possible it does not seem
296 likely that patients would increase their beer and wine intake as a consequence of feeling
297 unwell. The relationship between sulfite intake and sigmoidoscopy score in this study
298 was extremely strong and therefore an explanation for why sulfite should be a risk factor
299 for UC is required. Sulfite has a number of effects that may be relevant to this
300 discussion. Sulfite may be important because it is a precursor of sulfate. Sulfate can
301 potentially be reduced to sulfide by sulfate reducing bacteria in the colon. Sulfide is a
302 plausible metabolic toxin in UC. Supplementing patients with sulfate decreases the
303 microbial incorporation of hydrogen into methane (as measured by breath methane) and
304 increases the in vitro sulfide production rate of feces[39]. The end metabolic product of
305 both sulfite and protein is sulfate. Sulfate from both sources can be reduced to sulfide in
306 the gut. The absence of a significant relationship between protein intake and disease
307 activity in this study does not support a mechanism for UC that involves a common
308 pathway for sulfite and protein.

309 Alternatively, the relevance of sulfite to UC may be because of its ability
310 to degrade thiamin. Thiamin deficiency manifests itself in the nervous and
311 cardiovascular systems. It is unlikely that it is the status of the patient that is important,
312 but rather the amount of thiamin available to the gut microflora. An example of the
313 importance of thiamin to the gut microflora is the requirement of the probiotic bacteria,
314 lactobacilli, for thiamin. Thiamin status is influenced by a number of factors. Firstly,
315 thiamin intake; in foods such as pork, fortified cereals and legumes which are good

316 sources of thiamin, intakes were associated with improved clinical state. Traditional
317 dietary analysis did not reveal a significant correlation between thiamin intake and
318 sigmoidoscopy scores though no allowance is made in dietary coding software for the
319 reduction in thiamin content caused by sulfite usage. Secondly, carbohydrate intake;
320 Elmadfa *et al.* demonstrated that the thiamin status of adult humans depends on
321 carbohydrate intake[40]. Carbohydrate (and sugar) intakes have previously been
322 associated with UC relapse (table 1). Finally, thiamin status can be affected by caffeine's
323 anti-thiaminergic properties. For both coffee and tea intake, the decaffeinated version
324 was associated with better clinical state.

325 However, there was a sub group (n=8) of this population who recorded an intake
326 of either vitamin B complex or multivitamins. This sub group did not have a mean
327 sigmoidoscopy score significantly lower than the general UC population. It is likely that
328 vitamin B1 is a factor in the disease process but not the only nutritional one.

329 An additional possible interpretation for the experimentally determined food order
330 is the carbohydrate nature and content of the foods. Carbohydrates, such as the α -
331 amylase resistant starch (RS) and prebiotics, escape digestion in the small intestine and
332 provide an energy substrate for the colonic microflora. Both prebiotics (found in chicory,
333 legumes, artichokes alliums, and in small amounts in cereals) and resistant starch
334 (potatoes, bananas, lentils and legumes) have been hypothesised to improve the colonic
335 health of the host. For RS, resistance to digestion is a function of the morphology of the
336 starch granules and their crystalline organisation, which is determined by the botanical
337 source of the starch and the processing it has undergone before being eaten[41].
338 Prebiotics are non-digestible carbohydrates that selectively stimulate the growth of

339 lactobacilli and bifidobacteria with benefit to health. Prebiotics are mainly fructose and
340 galactose polymers with a degree polymerisation of between 2 and 60. Of the prebiotic
341 sources; chicory and artichokes were not found in typical diets, legumes and cereals were
342 seen to have probable benefits in this study and alliums were not. This study therefore
343 provides only limited support for the use of prebiotics in UC. The foods containing RS
344 were all found to be of benefit in this study and therefore the role of RS in UC is strongly
345 supported.

346 Any dietary advice provided to ulcerative colitis patients should be based on the
347 FSS table. The table is of course imperfect because of experimental error, natural
348 variation and the associations between foods. For example, milk and cereal are coded
349 separately but are often consumed together. Thus the magnitude of the difference in the
350 FSSs for these two foods is less than if they'd been independent variables. Suggestions
351 have been made in this discussion as to the factors responsible for the FSS order and to
352 distill these factors into the advice given in Table 5. This table is speculation, as this diet
353 has not been formally tested in the UC population. It does however represent the only
354 comprehensive dietary advice available to ulcerative colitis patients at this time.

355 The list of dietary risk factors for colon cancer[42] bears a similarity to the dietary
356 risk factors presented here for UC. UC patients have an increased risk of colorectal
357 cancer and it is probable that factors responsible for inflammation in UC patients are also
358 responsible for neoplasia in the colon cancer population.

359

359

360 **Conclusion**

361 A dietary analysis method is described that provides a new tool for establishing
362 relationships between diet and disease. This method has been applied to the study of
363 ulcerative colitis and points to sulfite and caffeine as being harmful, with thiamin and
364 resistant starch being potentially therapeutic. For the first time, dietary guidelines for
365 ulcerative colitis patients, including food portion sizes have been developed.

366

366

367 **Abbreviations**

368 Ulcerative colitis (UC); Food sigmoidoscopy score (FSS); European Union (EU);

369 Odds ratio (OD) and Confidence interval (CI).

370

370

371 **Competing interests**

372 The authors declare they have no competing interests.

373

373 **Authors' contributions**

374 JHC, EAM and LME contributed to the study design and the writing of the
375 manuscript. EAM was the co-ordinator of the study and along with ST had responsibility
376 for managing the patients and coding the diaries. LME developed the dietary data
377 analysis protocol assisted by RC. CK and JHC performed the sigmoidoscopic
378 examinations of the patients. All authors read and approved the final manuscript.
379

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386 **Tables and figures legends**

387 Figure 1: Frequency distribution of sigmoidoscopy scores (n=81) for ulcerative colitis
388 patients recruited at all stages of disease.

389 Table 1: Review of studies of diet and ulcerative colitis (UC).

390 Table 2: Food sigmoidoscopy score (FSS) calculation example for red wine (NB
391 incomplete data set used). In this example the food sigmoidoscopy score for red wine is
392 $2.614/0.883=2.96$.

393 Table 3: Foods consumed in order of food sigmoidoscopy scores (FSS). No foods
394 contribute to more than one category (with the exception of the field "all foods"). The
395 thiamin levels are the best estimate based on the distribution of foods within each
396 group[43].

397 Table 4: Permitted levels of sulfite in the UK.

398 Table 5: Proposed dietary advice for ulcerative colitis patients. The list of potentially
399 protective foods includes the average 7 d intakes for foods. The total calorific content of
400 the protective foods is approximately 30 % of that required for a whole week. Grams (g)
401 can be converted to ounces by dividing by 28.4. It is recommended that the majority of
402 the protective foods be consumed in the quantities listed. Provided sulfite containing
403 foods and coffee (except decaffeinated) are restricted all other foods can be eaten freely.
404 A varied, fresh, balanced diet is recommended.

405 *Carrageenan is to be avoided because of its link to ulcerative colitis in animal
406 models[44]. It is a type of seaweed that contains sulphur (used as a thickening agent in a
407 wide range of desserts, e.g. chocolate mousse). This study was not able to determine

408 whether or not this additive is harmful so advice is precautionary.

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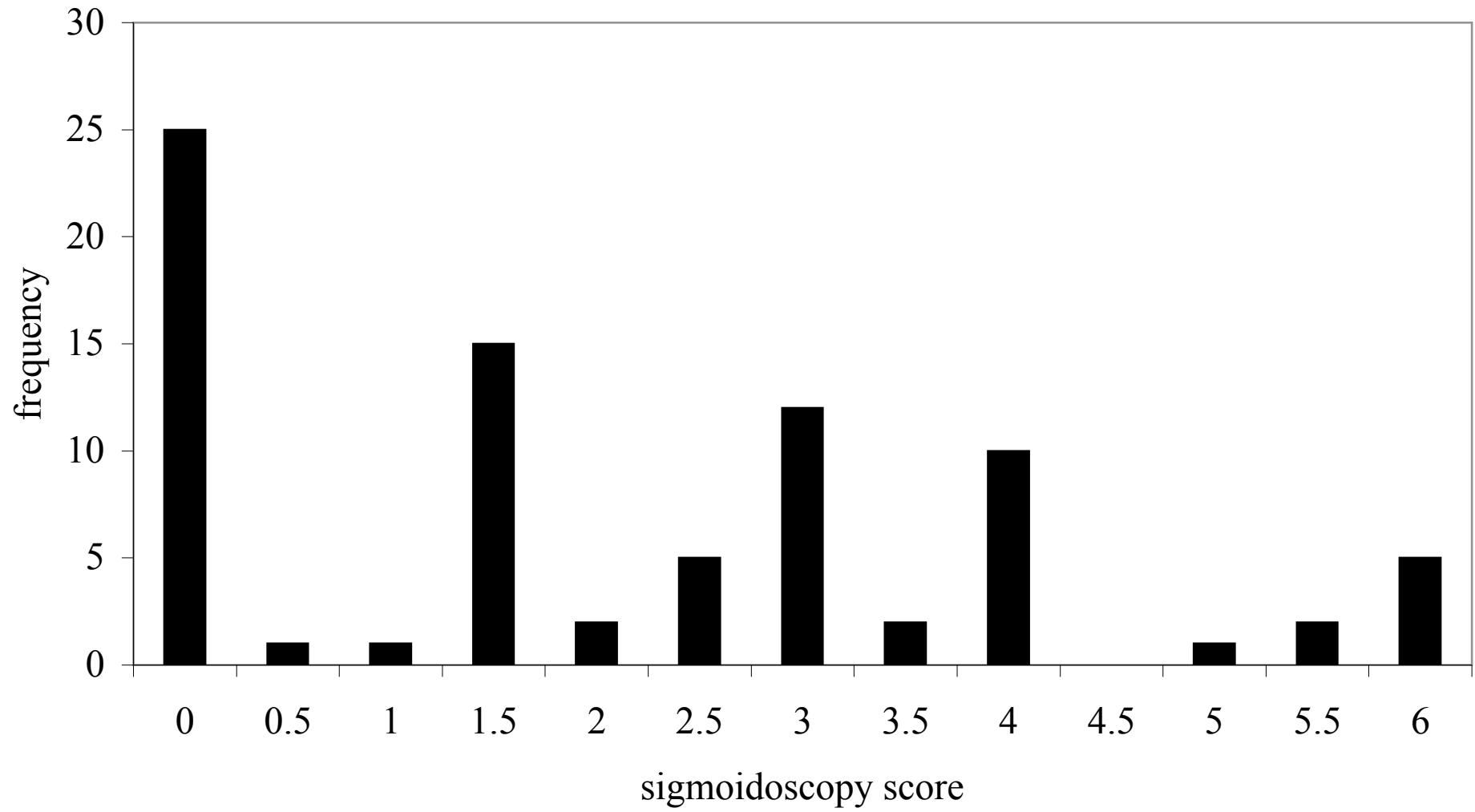


Figure 1

Food group(s)	Association with UC	Number	Comment (s)	Author (s)
Sugar	Positive Positive Positive Positive	100 UC, 100 controls 124 UC, 250 controls 54 UC, 108 matched controls 20 UC	NS OR 2.37 p=0.05 NS	Mayberry <i>et al</i> 1980 ² Porro & Panza 1985 ³ Reif <i>et al</i> 1997 ⁴ Hart <i>et al</i> 2002 ⁵
Carbohydrate	Positive Positive	20 UC 53 UC, 106 controls	NS p<0.001	Hart <i>et al</i> 2002 ⁵ Tragnone <i>et al</i> 1995 ⁶
Fibre	No benefit	39 UC	6 months high fibre diet	Davies & Rhodes 1978 ⁷
Breakfast cereals	No benefit Negative	61 UC, 61 matched controls 114 UC, 114 controls	NS p<0.05	Archer & Harveys 1978 ⁸ Brandes <i>et al</i> 1979 ⁹
Fruit, fruit juice and vegetables	Negative Negative Negative Negative	114 UC, 114 controls 197 UC, 394 matched controls 54 UC, 108 matched controls 124 UC patients, 250 controls	p<0.05 OR 0.77 (CI 0.45-1.35) Fruit OR p=0.36 Veg OR p=0.57 Fruit OR 0.3, Veg OR 0.38	Brandes <i>et al</i> 1979 ⁹ Gilat <i>et al</i> 1981 ¹⁰ Reif <i>et al</i> 1997 ⁴ Porro and Panza 1985 ³
Eggs	Positive	54 UC, 108 matched controls	p=0.05	Reif <i>et al</i> 1997 ⁴
Protein	Positive Positive	53 UC, 106 controls 54 UC, 54 controls	p<0.001 p=0.65	Tragnone <i>et al</i> 1995 ⁶ Reif <i>et al</i> 1997 ⁴
Margarine	No effect Positive	80 UC, 73 controls 101 UC, 143 controls	NS p=0.005	Chuah <i>et al</i> 1992 ¹¹ Kono <i>et al</i> 1994 ¹²
Fat	Positive	20 UC	NS	Hart <i>et al</i> 2002 ⁵
Western foods	Positive	101 UC, 143 controls	p=0.04	Kono <i>et al</i> 1994 ¹²
Soft drinks	Positive	54 UC, 108 matched controls	p=0.02	Reif <i>et al</i> 1997 ⁴
Fish	Negative Negative	54 UC, matched controls 20 UC	p=0.36 NS	Reif <i>et al</i> 1997 ⁴ Hart <i>et al</i> 2002 ⁵
Fast foods	Positive	145 UC, 305 matched controls	OR 3.9 95% CI (1.4-10.6)	Persson <i>et al</i> 1992 ¹³

	patient ID	food description	weight ml	diary energy kcal/day	weight / diary energy	sigmoidoscopy score	sig score *amount / diary energy
	3	red wine	750	2087	0.359	3.5	1.258
	4	red wine	188	1800	0.104	6	0.627
	23	red wine	525	2159	0.243	3	0.730
	28	red wine	375	2132	0.176	0	0.000
sum			1838		0.883		2.614

Figure 3

FSS order	food	FSS score	n	total weight g	average portion	thiamin ⁴³ mg/100g
1	crackers	1.003	22	1465	67	0.24
2	pork	1.219	35	7511	215	0.61
3	coffee (decaffeinated)	1.24	15	30298	2020	Trace-0.04
4	corn flakes	1.451	14	1557	111	1.2
5	breakfast cereals (not cornflakes)	1.465	46	8866	193	1.16
6	lettuce	1.553	48	5427	113	0.12
7	butter	1.557	48	3795	79	Trace
8	pizza	1.6	25	5599	224	0.2
9	custard	1.624	16	3034	190	0.09
10	apples, raw	1.668	42	13508	322	0.03
11	sweetcorn	1.747	22	1852	84	0.07
12	spirits	1.776	32	6339	198	0.00
13	milk, all types	1.807	74	92733	1253	0.04
14	melon	1.816	14	4846	346	0.03
15	pears, raw	1.82	19	5261	277	0.02
16	cucumber	1.854	26	1259	48	0.03
17	ice cream	1.856	36	4666	130	0.08
18	bananas	1.892	58	20400	352	0.04
19	bacon	1.901	50	5925	119	1.03
20	beef (and products)	1.905	64	32009	500	0.08
21	tomatoes	1.912	60	14634	244	0.09
22	jam and marmalade	1.941	45	2984	66	Trace
23	chocolate (and products)	1.946	74	17200	232	0.1
24	sugar and sweets	1.95	58	5409	93	0.0
25	soup	1.953	55	38829	706	0.05
26	Miscellaneous wheat flour products	1.957	43	9382	218	0.21
27	citrus fruits	1.961	35	10309	295	0.09
28	mayonnaise	1.985	23	2375	103	0-0.02
29	red wine	2.000	20	10082	504	Trace
30	tea (caffeine)	2.008	64	258121	4033	Trace
31	fish	2.038	59	16869	286	0.08
32	yogurt	2.049	44	18215	414	0.1
33	cheese	2.074	61	6779	111	0.04
34	mushroom	2.076	21	1389	66	0.09
35	potatoes (new and old)	2.077	74	38039	514	0.2
36	peas and beans	2.082	56	6669	119	0.16
37	chips	2.102	56	16286	291	0.12
38	soft drinks (not from concentrate)	2.104	53	72169	1362	0-Trace
39	white bread	2.107	78	36673	470	0.22
	all foods	2.127	81	1680750	20750	
40	turkey	2.131	16	2786	174	0.07
41	ham	2.132	48	5088	106	0.58
42	crisps	2.141	49	4312	88	0.21
43	eggs	2.158	65	10397	160	0.07
44	biscuits	2.162	55	4613	84	0.15
45	margarine	2.198	56	5071	91	Trace
46	cakes	2.209	62	12342	199	0.13
47	cream	2.215	17	1677	99	0.03
48	cranberry	2.224	10	3549	355	Trace
49	vegetables (miscellaneous)	2.235	32	6635	207	0.1
50	gravy (instant)	2.242	25	1892	76	0
51	coffee (caffeine)	2.247	57	130423	2288	Trace-0.04
52	porridge	2.269	17	7411	436	0.08
53	peppers	2.28	20	2067	103	0.01
54	baked beans	2.311	30	5371	179	0.09
55	rice	2.315	47	15614	332	0.04
56	strawberry and raspberry	2.324	11	1195	109	0.03
57	brown bread	2.356	50	15910	318	0.26
58	chicken (and products)	2.358	69	31208	452	0.07
59	fruit pies	2.362	26	3909	150	0.08
60	pasta	2.377	45	16519	367	0.03
61	peaches	2.396	10	2460	246	0.02
62	fruit juice (pure)	2.429	45	32904	731	0.06
63	onions (including leeks)	2.466	37	2351	64	0.07
64	lager	2.468	16	24111	1507	Trace
65	brassicas	2.562	55	10069	183	0.07
66	lamb	2.582	12	2205	184	0.12
67	carrots	2.653	47	5010	107	0.08
68	sausages	2.679	37	7184	194	0.01
69	grapes	2.713	22	3744	170	0.05
70	soft drinks (from concentrate)	2.794	31	37279	1203	Trace-0.02
71	cereal bars	2.831	14	1253	90	0.24
72	burgers	2.838	10	1125	113	0.07
73	white wine	2.868	16	11951	747	Trace
74	kiwi fruit	3.471	13	1474	113	0.01
75	bitter	3.906	10	51408	5141	Trace

Product	Permitted sulfite level ²⁹
beer	20 mg/kg (50 mg/kg 2nd fermentation)
white wines	210 mg/L
red wines	160 mg/L
sweet wines	300-400 mg/L
breakfast sausages	450 mg/kg
burgers	450 mg/kg
soft drink concentrates	20 mg/l, 250 mg/L or 350 mg/L
dried fruit	50 (dried coconut)- 2000 mg/kg
dehydrated potatoes	400 mg/kg
carbonated drinks	20 mg/L (carry over from concentrates only)
langoustines	150 mg/kg edible part (raw)
jams and marmalade	50 mg/L
dry biscuits	50 mg/kg
frozen potatoes	100 mg/kg
peeled potatoes	50 mg/kg
jams, jellies and marmalades made with sulfited fruit	100 mg/L

Figure 5

POTENTIALLY PROTECTIVE DIET

(weight per week)

- ◆ crackers (70 g)
- ◆ pork (210 g)
- ◆ breakfast cereals (200 g), with milk
- ◆ lettuce (110 g)
- ◆ apples or pears, raw (390 g)
- ◆ sweetcorn (80 g)
- ◆ melon (350 g)
- ◆ cucumber (50 g)
- ◆ bananas (350 g)
- ◆ bacon (120 g)
- ◆ beef (250 g), or beef products (500 g)
- ◆ tomatoes (240 g)
- ◆ soup (700 g), not dried
- ◆ citrus fruits (300 g)
- ◆ fish (290 g)
- ◆ yogurt (410 g)
- ◆ cheese (110 g)
- ◆ mushrooms (70 g)
- ◆ potatoes, including chips (710 g)
- ◆ legumes (peas and beans) (120 g)

FOODS TO AVOID OR REDUCE

- ◆ Beer
(except German beer which is sulphite free)
- ◆ Wine
(particularly white)
- ◆ Sausages and burgers
(unless not sulphited, e.g. some organic brands)
- ◆ Sulfite containing soft drinks
(e.g. fruit squash concentrates)
- ◆ Prawns, scampi and shellfish
(usually sulfited)
- ◆ Sulfited dried fruit and vegetables
(e.g. dried potatoes, dried apricots)
- ◆ Processed fruit pies and fruit cakes
- ◆ Coffee
(except decaffeinated)
- ◆ Any other foods containing the sulfite additives E220-228
- ◆ Any foods containing carrageenan (Irish moss), E407*.

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