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Dietary intake of inulin-type fructans in active and inactive Crohn's disease and healthy controls: a case-control study

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ABSTRACT

Background and Aims

Prebiotic inulin-type fructans are widely consumed in the diet and may have contrasting effects in Crohn's disease by stimulating gut microbiota and/or by generating functional gastrointestinal symptoms. The aim of this study was to measure fructan and oligofructose intakes in patients with active and inactive Crohn's disease compared with healthy controls.

Methods

Patients with active Crohn's disease (n=98), inactive Crohn's (n=99) and healthy controls (n=106) were recruited to a case-control study. Dietary intake of inulin-type fructans was measured using a specific food frequency questionnaire and was compared between the three groups and between patients with different disease phenotypes (Montreal classification). Associations between intakes and disease activity (Harvey Bradshaw Index, HBI) were also undertaken.

Results

Patients with active Crohn's disease had lower fructan intakes (median 2.9 g/d, IQR 1.8) than those with inactive Crohn's (3.6 g/d, 2.1, P=0.036) or controls (3.9 g/d, 2.1, P=0.003) and lower oligofructose intakes (2.8 g/d, 1.8) than inactive Crohn's (3.5 g/d, 2.2, P=0.048) or controls (3.8 g/d, 2.1, P=0.003). There were no differences in intakes related to disease site or behaviour. There were negative correlations between HBI wellbeing score and fructan intake (ρ=-0.154, P=0.03) and oligofructose intake (ρ=-0.156, P=0.028) and for the HBI abdominal pain score and fructan (ρ=-0.164, P=0.021) and oligofructose intake (ρ=-0.157, P=0.027).

Conclusions

Patients with active Crohn's disease consume lower quantities of fructans and oligofructose than their inactive counterparts and healthy controls. The impact of lower intakes of prebiotic fructans on gut microbiota are unknown and warrant further research.

Keywords: inflammatory bowel disease, inulin, fructan, oligofructose, fructans, FODMAPs

INTRODUCTION

The aetiology of Crohn's disease includes an inappropriate immune response towards commensal microbiota in genetically susceptible individuals. Many studies utilising in-depth molecular microbiological techniques have consistently demonstrated that the luminal and mucosal microbiota in Crohn's disease are characterised by reduced diversity and lower levels of *Firmicutes* such as Roseburia and *Faecalibacterium prausnitzii*.[1-3] These bacteria ferment dietary substrates, including non-digestible or non-absorbed carbohydrates, to produce short-chain fatty acids such as butyrate,[4] which has been shown to promote immunoregulation.[5] A range of interventions that target the modification of the gastrointestinal microbiota have therefore been investigated in Crohn's disease including antibiotics, probiotics and prebiotics.

Prebiotics selectively stimulate the growth and/or activity of one or a limited number of microbial genera/species in the gut microbiota that confer(s) health benefits to the host.[6] The most widely investigated prebiotics are the inulin-type fructans, and many studies have shown that dietary supplementation stimulates the numbers of bifidobacteria[6] and some studies also report stimulation of *F. prausnitzii*[7] and the production of short-chain fatty acids.[4,6] These findings are important to Crohn's disease since such changes in the luminal and mucosal environment might therefore elicit immunological and therapeutic benefit, for example the evidence of higher levels of *F. prausnitzii* in those with extended remission.[8]

Inulin-type fructans consist of D-fructose monomers linked by β2→1 bonds to form linear polymers, some with a terminal glucose molecule. Inulin-type fructans refer to all molecules ranging in length from 2-60 degrees of polymerisation, whilst oligofructose refers only to shorter molecules of 2-10 degrees of polymerisation.[6] Inulin-type fructans are widely

consumed in the diet, the majority being present as oligofructose in cereals such as wheat and rye and in vegetables such as onions, leeks, and asparagus, although longer polymers (i.e. 11-60 degrees of polymerisation) are also contained within chicory root and artichokes.[9-11]

Despite the potential mechanisms for inulin-type fructans to benefit Crohn's disease through modification of the gastrointestinal microbiota, supplementation studies have failed to result in the induction of remission of active disease.[12,13] Some patients with Crohn's disease also experience functional gastrointestinal symptoms (e.g. abdominal pain, bloating, diarrhoea) that are not the result of active disease, and a significant minority also fulfil criteria for the functional bowel disorder irritable bowel syndrome.[14] Fermentable carbohydrates such as inulin-type fructans have been implicated in the generation of gastrointestinal symptoms in some people with functional bowel disorders.[15,16] This presents a conundrum whereby prebiotic carbohydrates that might beneficially modify the gastrointestinal microbiota and be fermented to produce short-chain fatty acids, may in some also induce functional gastrointestinal symptoms.

Diet and nutrition play an important role in the management of Crohn's disease and have been identified as issues of primary concern in patients.[17] Many patients believe that diet can induce or exacerbate symptoms[17] and self-imposed diet restrictions have been reported, including of foods rich in inulin-type fructans.[18-20] To our knowledge there are no large studies investigating dietary intakes of inulin-type fructans in Crohn's disease. The aim of this case-control study was to measure intakes of inulin-type fructans and oligofructose in patients with both active and inactive Crohn's disease compared with healthy controls.

METHODS

This was a case-control study using interviewer-administered questionnaires to measure intakes of inulin-type fructans from habitual diet in patients with active Crohn's disease, inactive Crohn's disease and healthy controls. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving patients and healthy controls were approved by the National Research Ethics Service (South East Research Ethics Committee, Bromley Local Research Ethics Committee). Written informed consent was obtained from all participants prior to study enrolment.

Participants

Patients with Crohn's disease were recruited from four inflammatory bowel disease outpatient clinics across London, United Kingdom (UK). Patients were eligible if they had a documented diagnosis of Crohn's disease for at least three months, supported by radiological or histological reports and were aged between 18-65 years. Exclusion criteria included a recent change in medication (e.g. change in immunosuppressant or biologic therapy within 12 weeks, oral 5-aminosalicyclic acid or steroids within 4 weeks, use of rectal preparations during the preceding 2 weeks). Patients completed questionnaires prior to any changes in medication at that appointment to ensure that the measurement of disease activity was reflective of their recent disease activity and coincident to the period of survey of inulin-type fructan intake. Further exclusion criteria included pure perianal Crohn's disease, other gastrointestinal disorders (e.g. short bowel syndrome, previous pan-proctocolectomy / significant colonic resection), other severe major organ disorders (e.g. hepatic, renal, endocrine, respiratory, neurological, or cardiovascular disease or previous diagnosis of cancer with disease-free state $\leq$ 2 years) or self-reported pregnancy or lactation, all of which may otherwise impact on dietary intake.

Patients were categorised as having active disease if they had a Harvey Bradshaw Index (HBI) of ≥4 together with a C-reactive protein >10 mg/dL and were categorised as having inactive disease if they had an HBI of ≤3 and a C-reactive protein <10 mg/dL. The combined use of clinical and serum inflammatory markers was used to increase the sensitivity and specificity of the active and inactive definitions. Patients not fulfilling both criteria were not recruited.

Healthy adults (18-65 y) were recruited as controls through a circular email sent to all students and staff at King's College London and through the snowballing technique, in order to recruit subjects from outside of the institution. Exclusion criteria included having Crohn's disease or any other gastrointestinal disorder (e.g. ulcerative colitis, irritable bowel syndrome, chronic constipation, diarrhoea), previous gastrointestinal surgery or other severe major organ disorder as above, including those likely to impact dietary intake (e.g. diabetes, cardiovascular disease) or self-reported pregnancy or lactation.

Data collection

Basic demographic data including sex, age, smoking status and ethnicity were collected at the time of recruitment. For patients with Crohn's disease, a range of clinical information was also recorded. A gastroenterologist recorded each patient's disease activity using the HBI to score general wellbeing, stool frequency, pain, abdominal mass and extra-intestinal manifestations.[21,22] The gastroenterologist also recorded the Crohn's disease phenotype using the Montreal classification to record age at diagnosis, disease location and disease behaviour.[23]

Intakes of inulin-type fructans (hereon referred to as fructans) and oligofructose were measured using a specific food frequency questionnaire (FFQ).[11] The FFQ comprised 23 foods and drinks (eight fruits and vegetables; 15 composite foods e.g. breads, breakfast cereals, pastry products etc) that make contributions to fructan and oligofructose intakes in the UK diet. The FFQ has been shown to be a valid and reliable method for measuring fructan and oligofructose intakes for use in dietary surveys.[11] Patients with Crohn's disease and healthy controls were asked to recall the frequency and portion size of consumption of the 23 items over the preceding week.

The FFQ was administered by the researcher using standardised questioning procedures in order to minimise administrator bias. Flash cards were available if participants were unfamiliar with some food items (e.g. asparagus, globe artichoke, Jerusalem artichoke, chicory root). Data from the FFQ's were subsequently checked by a dietitian and entered into a bespoke food composition database. Dietary intake of fructans and oligofructose from food commodities (e.g. onion, asparagus etc) was calculated using food composition data.[9] Dietary intake from composite foods was assessed by first calculating the food commodity content (e.g. total wheat, total rye) of each composite food on the FFQ (e.g. breads, pastry products) using the Food Commodity Intake Database (US Department of Agriculture and the US Environmental Protection Agency, United States) and then calculating the fructan and oligofructose content of these food commodities. Values for small, medium and large portion sizes were taken from standard food portion values in the UK.[24]

Statistical Analysis

Statistical analyses were performed using SPSS software package version 20 (IBM SPSS Software, NY, US). Categorical data were compared between groups using the chi-square test

or the Fisher's Exact test (where more than 25% of cells had counts less than 5). Parametric continuous data (e.g. demographic data) was compared between the groups using an unpaired t-test or one-way analysis of variance (ANOVA), as appropriate. Fructan and oligofructose intakes were tested for equality of variances using Levene's test and for normality using and Kolomogorov-Smirnov and Shapiro-Wilk tests. Where necessary data was transformed to achieve a satisfactory residual plot. Fructan and oligofructose intakes were found to be not normally distributed and therefore were compared between two groups using a Mann Whitney test and between three groups using a Kruskal Wallis test and Bonferroni *post hoc* correction. Fructan and oligofructose intake data was also divided into tertiles, which were compared between groups using the chi-square test. Relationships between fructan and oligofructose intakes and HBI score(s) were analysed using Spearman's rho. The results of all tests were considered significant if $P \leq 0.05$. Categorical data is reported as n (%) and continuous data as mean (SD) and/or median (IQR) as appropriate.

RESULTS

A total of 303 participants were recruited (98 active Crohn's disease, 99 inactive Crohn's disease, 106 healthy controls). There were no significant differences between the groups in key demographic data including age, sex or ethnicity (**Table 1**). Although not statistically significant, more patients with active Crohn's disease were current smokers (28.6%) than those with inactive disease (17.2%) or healthy controls (19.8%) (P=0.127), perhaps reflecting the impact of smoking on exacerbation of Crohn's disease.[25] Patients in the active group had mild/moderately active Crohn's disease (HBI median 9, min 4 – max 19) and those in the inactive group had only mildly elevated disease (HBI median 1, min 0 – max 3).

There were significant differences in intakes of total fructans (p<0.001) and oligofructose (p=0.001) between groups (**Table 2**). Following *post hoc* corrections, patients with active Crohn's disease were shown to have lower fructan intakes (median 2.9 g/d, IQR 1.8) than both those with inactive Crohn's disease (3.6 g/d, 2.1, P=0.036) or healthy controls (3.9 g/d, 2.1, P=0.003) and lower oligofructose intakes (median 2.8 g/d, IQR 1.8) than those with inactive Crohn's disease (3.5 g/d, 2.2, P=0.048) or healthy controls (3.8 g/d, 2.1, P=0.003). There were no significant differences in intakes of total fructans or oligofructose between the inactive Crohn's disease group and healthy controls. When all 303 participants were divided into tertiles of intake, the highest tertile of fructan intake (≥ 4.19 g/d) consisted of fewer patients with active Crohn's disease (21.4%) than those with inactive Crohn's (35.4%) and healthy controls (42.5%) (P=0.006), with the same pattern for tertiles of oligofructose intake (**Table 2**).

In all participants, the majority of total fructans and oligofructose came from wheat, onion, banana and garlic, with a range of other commodities contributing very small amounts

('other' e.g. leeks, rye, artichoke). There were significant differences in the contribution of the major food commodities to intakes of total fructans and oligofructose between groups (**Table 3**). Following *post hoc* corrections, patients with active Crohn's disease consumed a greater proportion of total fructans from wheat (median 69.6%, IQR 40.6%) than both those with inactive Crohn's disease (62.8%, 37.5%, P=0.039) or healthy controls (57.9%, 34.4%, P=0.003) and a greater proportion of oligofructose from wheat (median 70.5%, IQR 39.8) than those with inactive Crohn's disease (64.6%, 34.6%, P=0.042) or healthy controls (60.9%, 32.0%, P=0.006). Furthermore, those with active Crohn's disease consumed a lower proportion of total fructans (median 12.8%, IQR 25.3%) and oligofructose (13.4%, 25.7%,) from onion than patients with inactive Crohn's disease (fructan 20.1%, 22.4 P=0.042; oligofructose 20.9%, 22.4 P=0.033). Healthy controls consumed considerably more fructans and oligofructose form other sources (e.g. leeks, rye, artichoke) than patients with Crohn's disease, irrespective of whether disease was active or not (**Table 3**).

In terms of Montreal disease classification, neither disease site nor disease behaviour had a significant effect on intakes of total fructans or oligofructose, either when data was analysed for the combined Crohn's disease population or when active and inactive groups were analysed separately (**Table 4**).

There was a significant, though small, negative correlation between patients' HBI wellbeing score and both total fructan intake (ρ= -0.154, P=0.03) and oligofructose intake (ρ= -0.156, P=0.028) and for the HBI abdominal pain score and total fructan (ρ= -0.164, P=0.021) and oligofructose intake (ρ= -0.157, P=0.027) (**Table 5**). As the scores for these increased, indicating poorer wellbeing and more severe abdominal pain, total fructan and oligofructose intakes decreased. When analysed within patient groups, there was only a significant

correlation between higher abdominal pain score and intakes of total fructans (ρ= -0.216, P=0.032) and oligofructose (ρ= -0.208, P=0.040) in patients with active Crohn's disease. There were no significant associations between intakes of total fructans and oligofructose and any of the other components of the HBI.

DISCUSSION

This is the first study to report intakes of fructans and oligofructose in a large sample of patients with Crohn's disease, and therefore to our knowledge there are no data with which to directly compare our findings. We identified lower intakes of total fructans and oligofructose in patients with active disease compared to those with inactive disease and healthy controls, despite no differences between patients with inactive Crohn's disease and healthy controls. There were small but significant associations between lower intakes of fructans and oligofructose and both impaired wellbeing and more severe abdominal pain, especially in those with active disease.

The lower intakes of fructans and oligofructose in active Crohn's disease could be the result of a variety of factors, including the result of specific diets to induce remission, the restriction of foods or food components to reduce gastrointestinal symptoms or impaired overall dietary intake.

Firstly, patients with active Crohn's disease could be following specific diets to induce remission. Elimination diets such as the low fat, fibre limited, exclusion (LOFFLEX) diet are sometimes used during active disease to assist in induction of remission,[26] although in the current study nobody reported to be following a specific elimination diet. A systematic review of randomised controlled trials recently reported little evidence of benefit of fibre restriction or fibre supplementation for inducing remission in Crohn's disease.[27] Secondly, patients with Crohn's disease sometimes restrict fibre intake in order to reduce gastrointestinal symptoms, with dietary fibre exclusion the most common form of dietary advice provided by gastroenterologists to patients with inflammatory bowel disease in the

UK.[28] Consequently, some studies report lower fibre intakes in active Crohn's disease compared with inactive disease.[29]

However, it is important to highlight that reducing fibre intake does not necessarily equate to reducing fructan intake. For example, the major dietary source of fructan is wheat, and switching from wholemeal bread to refined white bread will reduce fibre intake but would have little impact on fructan intake.[30] Therefore, the lower fructan intake in active Crohn's disease reported here is unlikely to be merely the result of patients reducing their fibre intake to induce disease remission or to reduce gastrointestinal symptoms.

Thirdly, gastrointestinal symptoms (e.g. abdominal pain, bloating) may be triggered by other foods or food components and patients with active Crohn's disease may reduce their intake of these to avoid such symptoms.[17] For example, one study found that 19% of patients with Crohn's disease reported wheat triggered gastrointestinal symptoms,[17] whilst another found that gastrointestinal symptoms were induced by a range of fructan-containing food items, including breakfast cereals (15.2%), breads (18.2%), cakes and biscuits (22.6%) and vegetables (19.6%).[18] A randomised controlled trial in active Crohn's disease reported greater abdominal pain, flatulence and borborygmi during fructan/oligofructose supplementation, albeit in doses of up to 15 g/d.[12] However, in the current study those with more severe abdominal pain (higher HBI abdominal pain score) actually had lower intakes of fructan. Rather than suggesting low intakes result in pain it is likely that patients with more severe pain choose to avoid consumption of foods that exacerbate symptoms, such as fructan-containing foods. In the current study, patients with active Crohn's disease consumed lower proportions of fructan and oligofructose from onion and other vegetables (e.g. leeks,

asparagus, artichokes). This perhaps may be the result of a move towards consumption of less diverse diets and the adoption of more basic dietary intake.

Functional gastrointestinal symptoms including abdominal pain, flatulence and diarrhoea are common in Crohn's disease, with up to 44% of patients with active disease and 35% of patients with inactive disease also fulfilling criteria for the functional bowel disorder irritable bowel syndrome.[14] Indeed a retrospective uncontrolled study found that restriction of a range of short-chain fermentable carbohydrates (fermentable oligo-, di- and monosaccharides and polyols, termed FODMAPs) resulted in a significant reduction of abdominal pain (50% of patients), flatulence (56%) and diarrhoea (46%) in patients with Crohn's disease, with ongoing dietary restriction of fructans being a significant factor associated with reduction in gastrointestinal symptoms.[31] The current study only measured intakes of fructans, and did not measure intakes of other FODMAPs (e.g. α-galacto-oligosaccharides, polyols etc) that are relevant to gastrointestinal symptom generation, and such studies are now warranted.

Surprisingly we showed no association between liquid stools and fructan intake. However, the HBI is a validated measure of disease activity rather than a specific measure of stool output and it records liquid stools, rather than liquid/loose stools or the subjective symptom of diarrhoea.[21,22] We also failed to show that disease location or disease behaviour had a significant effect on fructan intake. Other studies have also shown no difference across Crohn's disease types in the intake of micronutrients[32] or in the prevalence of fructose malabsorption.[33]

Our study showed no difference in intakes of fructans and oligofructose between patients with inactive Crohn's disease and healthy controls. Indeed a number of studies,[29,34] though

not all,[35] fail to find any differences in total energy intake (as a marker of global food intake) between inactive Crohn's disease and healthy controls. The lack of difference in fructan intakes between inactive disease and the healthy controls is unlikely due to poor estimates of intake in the latter (e.g. due to sampling bias) as intakes in our healthy control population (fructans 3.9 g/d, oligofructose 3.8 g/d) were similar to that previously reported in the UK (fructans 4.0 g/d, oligofructose 3.8 g/d).[11]

Clinical consequences and clinical application

The consequence of lower intakes of fructans and oligofructose in active Crohn's disease is unclear. On one hand it may be viewed as an attempt by patients to select foods that do not trigger gastrointestinal symptoms, whereas alternatively there may be concern that lower intakes may negatively impact the gastrointestinal microbiota. Numerous studies indicate that fructans stimulate the numbers of bifidobacteria and some studies also report stimulation of *Faecalibacterium prausnitzii*.[6,7] These microbiological findings are important since higher bifidobacteria have been associated with greater IL-10 positive dendritic cells and higher *F. prausnitzii* are associated with lower IL-6 positive dendritic cells.[36] In addition, patients with higher *F. prausnitzii* are more likely to have extended remission.[8] The differences in gastrointestinal microbiota between active and inactive Crohn's disease has been extensively investigated,[1-3] but the potential modifying effect of differences in dietary intake on this association (including that of fructan and oligofructose) has not been explored and is now warranted.

Recent guidelines for the dietetic management of patients with Crohn's disease have recommended that exclusion diet be considered in maintenance of Crohn's disease, and that restriction of short-chain fermentable carbohydrates may potentially be useful in those who

experience functional gastrointestinal symptoms.[37] However, only a minority of patients with inflammatory bowel disease are given tailored dietary advice by a gastroenterologist or dietitian[17,28] and therefore patients with IBD may seek alternative and potentially less evidence-based alternatives.[26] This may lead to the unnecessary avoidance of foods that contribute important nutritional and non-nutritional components to the diet.

Strengths and limitations

The data presented here are from a large cohort of patients with active and inactive Crohn's disease and a large healthy control group with similar demographic characteristics. The use of prebiotic supplements containing fructans and/or oligofructose is generally low in this patient group[38] and none of the patients in the current study were using such supplements and therefore the fructan intakes reported here constitute the total amounts consumed. However, we did not measure body weight, body mass index or total dietary intake, and therefore the findings may reflect lower intake of all foods, rather than just those containing fructans and oligofructose specifically. However the evidence for reduction in global food intake during active Crohn's disease is equivocal.

The FFQ used in this study has been validated in a healthy population, but not in patients with Crohn's disease. Whilst our cohort were similar in gender and age to those in the validation study, dietary assessment tools should be validated in the population in which they are to be used. It was also developed using the standard food composition data available at the time[9] which did not include subsequent data for the fructan and oligofructose content of a wider range of foods including various other vegetables[40] and cereals.[41] We may therefore have underestimated fructan and oligofructose intakes, although this would have occurred consistently across all three groups, unless these additional foods are differentially consumed

between active and inactive disease and health. Finally, the FFQ measured short-term intake only. We therefore cannot comment on longer term intakes of fructans and oligofructose and do not attempt to make any associations with the pathogenesis of disease activity. Further research on whole diet intake in Crohn's disease that includes analysis of intakes of a range of carbohydrates is required in order to explore the relationship between diet, disease activity and gastrointestinal symptoms further.

CONCLUSION

Patients with active Crohn's disease consume lower amounts of fructans and oligofructose than their inactive counterparts and healthy controls. This is particularly the case for those with poorer well-being and more severe abdominal pain. Vegetable such as onion, leeks and artichokes etc contributed lower proportions to fructan and oligofructose intakes in patients with active Crohn's disease. The lower intakes of fructan and oligofructose may be the result of specific diets to induce remission, the restriction of foods or food components to reduce gastrointestinal symptoms or impaired dietary intake. The impact of the lower intakes of these prebiotic compounds in active Crohn's disease are unknown and warrant further research.

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AUTHORSHIP

KW, JOL and AJS formulated the research question; JLA and KW designed the study; JLA, CRH, JLB, AK, SN, AH, AF and JOL recruited participants and performed all measurements; JLA and KW analysed data; JLA and KW wrote the manuscript; all authors critically commented on and approved the final manuscript.

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Table 1 Participant demographic and clinical data

	Active Crohn's (n= 98)		Inactive Crohn's (n=99)		Healthy controls (n=106)		P value
Age, *y, mean (SD)*	38. 5	(12.8)	36.2	(11.2)	36.6	(8.5)	0.283*
Females, *n (%)*	61	(62.2)	54	(54.5)	64	(60.4)	0.516†
Current smoker, *n (%)*	28	(28.6)	17	(17.2)	21	(19.8)	0.127†
Ethnicity, *n (%)*							0.651†
White	67	(68.4)	74	(74.7)	76	(71.7)	
Asian	22	(22.4)	15	(15.2)	23	(21.7)	
Black	5	(5.1)	8	(8.1)	5	(4.7)	
Mixed/other	4	(4.1)	2	(2.0)	2	(1.9)	
Harvey Bradshaw Index, *median (IQR)*	9	(4)	1	(2)	-	-	<0.001‡
Montreal Classification							
Disease duration, *y, mean (SD)*	10.5	(7.6)	14.0	(10.6)	-	-	0.008§
Disease Location, *n (%)*							0.061†
L1 Ileal	13	(13.3)	26	(26.3)	-	-	
L2 Colon	22	(22.4)	22	(22.2)	-	-	
L3 Ileocolonic	63	(64.3)	51	(51.5)	-	-	
L4 Disease site modifier	4	(4.1)	6	(6.1)	-	-	0.747‖
Disease Behaviour, *n (%)*					-	-	0.454†
B1 Non-stricturing/penetrating	50	(51)	57	(57.6)	-	-	
B2 Stricturing	29	(29.6)	29	(29.3)	-	-	
B3 Penetrating	19	(19.4)	13	(13.1)	-	-	
P Perianal disease modifier	20	(20.4)	22	(22.2)	-	-	0.862‖

* P values are the result of an ANOVA

† P values are the result of a chi-squared test

‡ P values are the result of a Mann Whitney test

§ P values are the result of an unpaired t-test

ǁ P values are the result of a Fisher's exact test

Table 2 Total fructan and oligofructose intakes (g/d) and tertiles of intake among patients with Crohn's disease and healthy controls

	Active Crohn's (n=98)		Inactive Crohn's (n=99)		Healthy controls (n=106)		P value
Total fructans							
Daily intakes, g/d, *median (IQR)*	2.9	(1.8)[a]	3.6	(2.1)[b]	3.9	(2.1)[b]	<0.001[*]
Tertiles of fructan intake, *n (%)*							0.006[†]
Low (≤ 2.77 g/d)	45	(45.9)	30	(30.3)	26	(24.5)	
Medium (2.78 - 4.18 g/d)	32	(32.7)	34	(34.3)	35	(33.0)	
High (≥ 4.19 g/d)	21	(21.4)	35	(35.4)	45	(42.5)	
Oligofructose							
Daily intakes, g/d, *median (IQR)*	2.8	(1.8)[a]	3.5	(2.2)[b]	3.8	(2.1)[b]	0.001[*]
Tertiles of oligofructose intake, *n (%)*							0.018[†]
Low (≤ 2.69 g/d)	44	(44.9)	30	(30.3)	27	(25.5)	
Medium (2.70 – 4.05 g/d)	32	(32.7)	34	(34.3)	35	(33.0)	
High (≥ 4.06 g/d)	22	(22.4)	35	(35.4)	44	(41.5)	

Values within a row with unlike superscript letters were significantly different following a Mann Whitney test and Bonferroni *post hoc* correction.

[*] P values are the result of a Kruskal Wallis test

[†] P values are the result of a chi-squared test

Table 3 Percentage contribution of food commodities to intakes of total fructans and oligofructose among patients with Crohn's disease and healthy controls

Percentage contribution to intakes, *median (IQR)*	**Active Crohn's (n=98)**		**Inactive Crohn's (n=99)**		**Healthy controls (n=106)**		**P value***
Total fructans							
Wheat	69.6	(40.6)[a]	62.8	(37.5)[b]	57.9	(34.3)[b]	0.003
Onion	12.8	(25.3)[a]	20.1	(22.4)[b]	17.4	(23.6)[a,b]	0.048
Banana	0.0	(5.8)[a]	2.2	(7.3)[a]	2.8	(8.0)[b]	0.033
Garlic	0.9	(2.1)[a]	1.8	(4.1)[b]	0.9	(3.3)[a,b]	0.001
Other†	0.02	(6.3)[a]	0.03	(9.6)[a]	7.4	(27.0)[b]	<0.001
Oligofructose							
Wheat	70.5	(39.8)[a]	64.6	(34.6)[b]	60.9	(32.0)[b]	0.005
Onion	13.4	(25.7)[a]	20.9	(22.4)[b]	17.6	(23.6)[a,b]	0.036
Banana	0.0	(6.2)[a]	2.2	(7.3)[a]	3.1	(8.5)[b]	0.026
Garlic	0.4	(0.8)[a]	0.7	(1.9)[b]	0.4	(1.4)[a,b]	0.001
Other†	0.02	(5.5)[a]	0.03	(6.8)[a]	5.3	(22.5)[b]	<0.001

Values within a row with unlike superscript letters were significantly different following a Mann Whitney test and Bonferroni *post hoc* correction.

* P values are the result of a Kruskal Wallis test

† "Other" represents the combined percentage contribution from leeks, asparagus, barley, globe artichoke, jerusalem artichoke, rye and dandelion; each of which contributed <1% of total fructan and oligofructose OF intake for >80% participants.

Table 4 Total fructan and oligofructose intakes of patients with Crohn's disease comparing different Montreal disease classifications

Disease Site	**Ileal**		**Colonic**		**Ileocolonic**		**P value***
Total fructan intakes, g/d, *median (IQR)*							
All Crohn's disease (n=39, 44, 114)	3.4	(2.1)	3.3	(2.1)	3.1	(2.3)	0.265
Active Crohn's (n=13, 22, 63)	2.8	(2.4)	2.7	(1.6)	3.0	(1.9)	0.942
Inactive Crohn's (n=26, 22, 51)	3.9	(3.4)	3.6	(1.9)	3.2	(2.6)	0.224
Oligofructose intakes, g/d, *median (IQR)*							
All Crohn's disease	3.4	(1.7)	3.2	(2.0)	2.9	(2.1)	0.281
Active Crohn's	2.8	(2.1)	2.5	(1.6)	2.9	(1.9)	0.910
Inactive Crohn's	3.6	(3.4)	3.5	(1.8)	2.9	(2.7)	0.215
Disease Behaviour	**Non stricturing, non-penetrating**		**Stricturing**		**Penetrating**		**P value***
Total fructan intakes, g/d, *median (IQR)*							
All Crohn's disease (n=107, 58, 32)	3.1	(2.3)	3.3	(2.7)	2.9	(1.3)	0.597
Active Crohn's (n=50, 29, 19)	2.5	(1.7)	3.2	(2.0)	2.9	(1.7)	0.508
Inactive Crohn's (n=57, 29, 13)	3.6	(1.9)	3.6	(3.3)	3.1	(1.5)	0.832
Oligofructose intakes, g/d, *median (IQR)*							
All Crohn's disease	3.1	(2.1)	3.2	(2.6)	2.9	(1.3)	0.498
Active Crohn's	2.3	(1.8)	3.0	(2.0)	2.8	(1.7)	0.424
Inactive Crohn's	3.4	(1.8)	3.6	(3.0)	3.1	(1.5)	0.832

* P values are the result of a Kruskal Wallis Test

Table 5 Spearman's rho correlation between Harvey Bradshaw Index total score, and component scores, and intakes of total fructans and oligofructose

	All Crohn's (n=197)		Active Crohn's (n=98)		Inactive Crohn's (n=99)	
	ρ*	P value	ρ*	P value	ρ*	P value
Total fructan intake						
HBI Total Score	-0.131	0.066	-0.081	0.429	0.182	0.071
Wellbeing	-0.154†	0.030	-0.115	0.260	0.082	0.417
Abdominal Pain	-0.164†	0.021	-0.216†	0.032	0.170	0.093
Liquid stools	-0.127	0.075	-0.001	0.990	0.141	0.163
Abdominal Mass	-0.040	0.573	0.034	0.740	-	-
Complications	-0.014	0.844	0.162	0.112	0.027	0.787
Oligofructose intake						
HBI Total Score	-0.128	0.073	-0.084	0.413	0.169	0.095
Wellbeing	-0.156†	0.028	-0.114	0.262	0.051	0.615
Abdominal Pain	-0.157†	0.027	-0.208†	0.040	0.152	0.132
Liquid stools	-0.121	0.089	-0.004	0.970	0.146	0.149
Abdominal Mass	-0.033	0.648	0.038	0.712	-	-
Complications	-0.010	0.891	0.158	0.120	0.028	0.785

* Spearman's rho correlation coefficient (ρ)

† Correlation is significant at the 0.05 level (2-tailed)