

Uncomplicated Diverticular disease is not a Common Cause of Colonic Symptoms such as those of Irritable Bowel Syndrome

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Uncomplicated Diverticular disease is not a Common Cause of Colonic Symptoms<u>such as</u> <u>those of Irritable Bowel Syndrome</u>

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Key Words: diverticular disease, abdominal pain, constipation,

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ABSTRACT

Background

Colonic diverticular disease is common among older individuals while colonic symptoms such as those of irritable bowel syndrome are frequent in the general population.

Aim

To determine, among patients in secondary care, if uncomplicated diverticular disease is a common cause of colonic symptoms.

Methods

Patients aged ≥ 50 years attending gastroenterology outpatient clinics or scheduled for colonoscopy or barium enema in a secondary care hospital were invited to take part. Those with structural gastrointestinal diseases were excluded. Participants completed a locally validated Rome II questionnaire on colonic symptoms. Patients with diverticular disease were compared with those without.

Results

784 patients with no structural pathology other than diverticular disease or benign colonic polyps completed the study. 744 patients underwent colonoscopy: 40 barium enema. 281 patients had diverticular disease. Among patients with and without diverticular disease, the frequency of abdominal pain, diarrhoea, constipation and irritable bowel syndrome were 123 (44%) and 226 (46%), 44 (16 %) and 80 (17%), 38 (14%) and 80 (17%) and 66 (25%) and 119 (25%), respectively (NS).

Conclusion

1 2 3	Uncomplicated colonic diverticular disease is not a common cause of colonic symptoms,
4	such as those of irritable bowel syndrome, among patients in secondary care.
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Introduction

Diverticular disease of the colon is a condition in which colonic mucosa protrudes through the outer muscular layers, usually abnormally thickened, to form narrow-necked pouches(1). This condition covers a wide clinical spectrum, from an incidental finding to symptomatic uncomplicated disease to diverticulitis, which can lead to perforation or abscess formation. Diverticular disease of the colon is very common, especially among older individuals. Prevalence rates in western countries range from 5% in the fifth decade of life to 50% by the ninth decade. It has been estimated that only about 20% of patients with diverticular disease of the colon will develop colonic symptoms, which are often similar in nature to those of irritable bowel syndrome. Since both diverticular disease of the colon and irritable bowel syndrome are common conditions, it is difficult to ascertain, in an individual with uncomplicated diverticular disease and irritable bowel syndrome-type symptoms, if the diverticular disease causes the symptoms, or whether it is a matter of two common conditions happening to occur in the same patient.

The aim of the present study is to compare, within a cohort of patients undergoing colonic imaging studies, patients with and without diverticular disease with regard to the frequency of colonic symptoms. If diverticular disease is a common cause of colonic symptoms, we would expect more patients with diverticular disease to have colonic symptoms, such as those of irritable bowel syndrome, compared to patients without diverticular disease. On the other hand, if diverticular disease is not a common cause of colonic symptoms, we would expect the frequency of colonic symptoms to be similar in the two groups of patients.

PATIENTS AND METHODS

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Patients aged 50 years and above who were attending Gastroenterology outpatient clinics at St George's Hospital , Queen Mary's Hospital, Roehampton, and Epsom Hospital, and who were scheduled to undergo colonoscopy or barium enema, were asked to complete a locally validated questionnaire relating to colonic symptoms. Patients aged 50 years and above, attending for colonoscopy by the same clinicians, were also asked to complete the questionnaire prior to the procedure. It was originally envisaged that consecutive patients would be recruited. In practice, however, there were occasions when clinic or endoscopy lists were too busy to allow patient recruitment to take place. However, there was no selection based on symptoms or patient demography.

Patients known to have inflammatory bowel diseases, colorectal carcinoma and other structural gastrointestinal conditions other than diverticular diseases and benign colonic polyps were not invited to take part in the study, and patients found during their colonic imaging or subsequent investigations to have these conditions were also excluded. We studied only patients aged 50 years and over as younger individuals had a low prevalence of diverticular disease of the colon, and we would have required a larger study to achieve the same statistical power.

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Questionnaire Design and Validation:

We used the modular Rome II questionnaire(2), but altered some of the expressions to make them more easily understandable by people in south London. The reproducibility of the questionnaire had previously been validated in our local population (3).

<u>A symptom was said to be present when it occurred over at least 3 weeks, for at least one</u> <u>day in each week, in the last 3 months.</u> Constipation was defined as the occurrence of at least two of the following symptoms at least one-quarter of the time: hard or lumpy stools, Deleted: A symptom was said to be present when it occurred over at least 3 weeks, for at least one day in each week, in the last 3 months. ¶ We assessed t

Deleted: by asking patients attending a medical clinic to complete it on two occasions 1-7 days apart. We then calculated kappa values to determine the reproducibility of the responses. Perfect agreement was defined as a value of 1.0 and agreement no different from chance by a value of 0. A kappa coefficient of greater than 0.4 was considered to indicate good agreement (3). Seventy-three patients took part in the validation studies. Out of 54 questions, the kappa score was greater than 0.4 in every case, and above 0.7 for 45 questions

straining during a bowel movement, feeling of incomplete emptying after a bowel movement, a sensation that the stool cannot be passed (i.e. blocked) when having a bowel movement, a need to press on or around the bottom or vagina to try to remove stool to complete the bowel movement, and fewer than 3 bowel movements per week. Patients with constipation must not have loose, watery or mushy stools during one-quarter or more of defecations. Diarrhoea was defined as the passage of loose, mushy or watery stools for more than $\frac{3}{4}$ of the bowel movements.

Irritable bowel syndrome was defined as the occurrence of abdominal pain with at least two of the following characteristics: improvement with a bowel movement, a change in stool frequency with onset of pain, and a change in stool consistency with onset of pain. Abdominal pain as reported in this study may or may not be associated with irritable bowel syndrome: the two groups overlapped. Diarrhoea-predominant irritable bowel syndrome was defined as irritable bowel syndrome with either more than three bowel movements per day, loose or mushy stools during at least one quarter of defecations or faecal urgency during at least one quarter of defecations. Patients with diarrhoea-predominant irritable bowel syndrome must not have passed hard or lumpy stools, experienced the need for straining during at least one quarter of defecations, and must not have passed less than three bowel movements a week. Constipation-predominant irritable bowel syndrome was defined as irritable bowel syndrome with either fewer than three bowel movements per week, the passage of hard or lumpy stools or the need for straining during at least one quarter of defecations. Patients with constipation-predominant irritable bowel syndrome must not have passed more than three stools a day, passed loose or mushy stools during at least one quarter of defecations or experienced faecal urgency during at least one quarter of defecations.

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Incontinence was defined as the accidental leakage or passage of stool on more than one occasion a month in the last year. Proctalgia fugax was defined as the occurrence of more than one episode of aching pain or pressure in the anal canal or rectum in the last year.

Statistical analyses:

Statistical analyses were performed using the Statistical Package for the Social Science (SPSS) software version 15. Fisher's exact test and chi-square test were used for comparing categorical variables. As multiple comparisons were made, probability values of <0.01 were taken to denote statistical significance.

Our endoscopy database suggested that approximately 25% of patients aged 50 years and over would have diverticular disease of the colon, and that 30% of all patients undergoing colonic imaging would have symptoms of irritable bowel syndrome. If patients with diverticular disease of the colon had a 50% increase in the prevalence of irritable bowel syndrome compared to patients without, approximately 33% of patients with diverticular disease would fulfill the criteria for irritable bowel syndrome compared to 22% of patients without. To have an 80% chance of detecting this difference, we needed to recruit 722 patients. In the event 36% of our patients had diverticular disease of the colon while the prevalence of irritable bowel syndrome was 25%. The original power calculations was therefore not applicable. We recruited 784 patients, although not all patients answered every question, and calculated the 95% confidence limits of the prevalence of various diagnoses in patients with and without diverticular disease. These give an indication of the chances of a type 2 error for each comparison.

Ethical Considerations

The study protocol was approved by the Wandsworth Research Ethics Committee. Informed consent was obtained from all patients.

RESULTS

Patient Characteristics

The study took place from October 2004 to March 2008. Eight hundred and forty-six patients were recruited. In 9 patients the imaging was not performed or was incomplete. Fifty-three patients were excluded because of inflammatory bowel disease (32) or colorectal cancer (21). One patient with colonic angiodysplasia and another with melanosis coli were included because these conditions were not considered to be relevant to colonic symptoms. Seven hundred and eighty-four patients were therefore eligible for analysis. There were 333 males and 451 females. Their mean age was 65.8 years (SD 10.3). A few questions were left unanswered in a small number of questionnaires and the numbers of patients on whom various analyses are based on are detailed in the Table.

Indications for colonic imaging include: change in bowel habit 356 (45.4%), rectal bleeding 154 (19.6%), anaemia 152 (19.4%), follow-up of colonic polyps 80 (10.2%), family history of colorectal cancer 73 (9.3%) and other indications 52 (6.6%). Some patients had more than one indication for imaging.

Seven hundred and forty-four patients were investigated by colonoscopy and 40 by barium enema. There was no difference in gender and age between patients who underwent colonoscopy and those imaged by barium enema. All 153 patients undergoing surveillance colonoscopy for a family history of colorectal cancer or past history of colonic polyps underwent colonoscopy rather than barium enema.

Presence or absence of diverticular disease

Two hundred and eighty-one patients had diverticular disease of the colon while 503 patients did not. Patients with diverticular disease were older than those without (mean age 69.6 years (SD 9.4) vs 63.6 years (SD 10.1), p<0.001), but there was no gender difference. One hundred and twenty-three of 281 patients with diverticular disease (44%) reported abdominal pain compared to 226 of 494 patients (46%) without diverticular disease (no significant difference). The proportion of patients with irritable bowel syndrome was the same whether they had diverticular disease (66/266=25%) or not (119/474=25%). Ninetyfive per cent confidence limits of the difference ranged from -0.06 to 0.07 (Table 1). There was no significant difference between patients with diverticular disease of the colon and those without in terms of the frequency of constipation, diarrhoea, bloating, incontinence or proctalgia fugax (Table 1). More female patients had colonic symptoms compared to males. However, when the sexes were separately considered, there were no significant differences in the proportions of patients with or without diverticular disease having colonic symptoms. For example 45/137 women (33%) with diverticular disease had irritable bowel syndrome compared to 79/282 (28%) without diverticular disease. The corresponding figures for men are 21/129 (16%) and 40/192 (21%) respectively.

Site of diverticular disease of the colon

Only seven patients in our series had diverticular disease confined to the right colon, while another 33 had diverticular disease in both the left and right colons. These patients did not differ from patients with isolated or predominant left sided diverticular disease with regards to the frequency of various colonic symptoms.

Colonoscopy or barium enema

Seven hundred and forty four patients underwent colonoscopy while 40 had barium enemas performed. One hundred and fifty three patients in the colonoscopy group underwent imaging because of a family history of colorectal cancer (73) or a past history of colonic polyps (80). No patient underwent barium enema examinations for these indications (p<0.001). Diverticular disease was detected in 262 patients (35%) at colonoscopy compared to 19 patients (48%) who underwent barium enema examinations (NS). Colonic polyps were found in 205 of the 744 patients (28%) undergoing colonoscopy but not in any of the 40 patients who underwent barium enema (p<0.00001).

Of the patients who underwent colonoscopy, 321 of 735 (43%) reported abdominal pain while 168 of 702 (24%) fulfilled Rome II criteria for irritable bowel syndrome, compared to 28 of 40 (70%) and 17 of 38 (45%) patients who had barium enemas performed (p<0.01 in each case). This can probably be explained by barium enema studies not being used for polyp screening, a group of subjects who may be asymptomatic,

Effect of age and gender

There was no difference in age between the 333 men and 451women included in this study (65.9 years, SD 10.2 and 65.7 years, SD 10.3 respectively). There were no differences in the proportions of males and females imaged because of rectal bleeding, anaemia or family history of colorectal cancer. However 232 women (51%) were imaged because of change in bowel habit compared to 124 men (37%, p<0.001).

Only 29 women were imaged for follow-up of colonic polyps (6%) compared to 51 men (15%, p<0.001). Women were more likely to have abdominal pain (223 or 50%), irritable bowel syndrome (124 or 30%), functional bloating (106 or 25%) and gross incontinence (43 or 11%) compared to men (126 or 38%, 61 or 19%, 49 or 15% and 12 or 4% respectively,

p<0.01 in each case). One hundred and forty-eight women (33%) had diverticular disease of the colon compared to 133 men (40%, NS).

Effect of indications for imaging

Patients who underwent imaging because of a family history of colorectal cancer (n= 73) or past history of polyps (n= 80) were less likely to have abdominal pain or to fulfil Rome II criteria of irritable bowel syndrome compared to the patients imaged for other indications (44/142 = 31 % and 305/633 = 48 % for abdominal pain, p <0.001, 18/138 = 13 % and 167/602 = 28 % for irritable bowel syndrome, p < 0.001). Of 145 patients imaged because of a family history of colorectal cancer or past history of colonic polyps, 64 (44 %) had colonic polyps compared to 141/639 patients (26%) imaged for other indications (p<0.0001).

Colonic polyps and irritable bowel syndrome

There were 205 patients with benign polyps. Their mean age was 66.6 years (SD 10.3) compared to 65.5 years (SD 10.2) for those without polyps. One hundred and eleven of 333 males (33%) had colonic polyps compared to 94/451 females (21%) (p<0.001). Sixty-nine of 205 (34%) patients with colonic polyps also had diverticular disease compared to 212 of 579 patients without polyps (37%). Patients with polyps were less likely to fulfil the criteria for irritable bowel syndrome (32 of 191 = 17%) compared to those without polyps (153 of 549 = 28%) (p<0.01).

Considering only patients who presented with a family history of colorectal cancer or personal history of colonic polyps, 15/62 patients (24%) with polyps had abdominal pain and 2/59 patients (3%) had irritable bowel syndrome. This compares with 29/80 patients (36%) without polyps having abdominal pain (NS versus those with polyps) and 16/79 (20%) having irritable bowel syndrome (p<0.01 versus those with polyps). If males and females among this group of patients are considered separately, 1/39 men with polyps and 1/20 women

with polyps had irritable bowel syndrome compared to 6/34 men without polyps and 10/45 women without polyps (NS for either sex).

DISCUSSION

Diverticular disease of the colon is classified according to the presence or absence of symptoms. Asymptomatic disease is termed diverticulosis whereas symptomatic diverticular disease may be uncomplicated, associated with mild symptoms, usually abdominal pain and/or change in bowel habit, or complicated, associated with haemorrhage, abscess, perforation or fistula formation(4). Diverticulitis is symptomatic diverticular disease with evidence of inflammation (4). It has been estimated that only 10-25 % of subjects with diverticulosis will develop diverticulitis over their life-time(5). However, many more will experience abdominal pain, episodic diarrhoea, constipation and bloating. These symptoms are also symptoms of irritable bowel syndrome, which occurs in 5 - 25 % of the general population, depending on the criteria used(6). In patients with colonic symptoms and uncomplicated diverticular disease of the colon, it would therefore not be easy to distinguish between symptoms caused by the diverticular disease from those of concomitant, incidental irritable bowel syndrome.

In a Canadian study, the frequency of colonic symptoms was studied using a questionnaire in a group of patients undergoing barium enema examination. Colonic symptoms were equally prevalent among 27 patients with diverticular disease of the colon and 49 patients who did not (7). In a Danish study of 69 patients with irritable bowel syndrome (8), the frequency of pain, flatulence, diarrhoea and constipation were similar in the 19 patients with diverticular disease compared to the 50 patients without.

These studies were inadequately powered to avoid a possible beta error. Further, unlike in our study, the authors did not use standardized definitions or validated questionnaires.

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Results from our present study also show that, among a cohort of patients presenting for colonic imaging, the frequency of various colonic symptoms and irritable bowel syndrome is similar among patients with and without diverticular disease. If diverticular disease were a common cause of colonic symptoms, a sizeable proportion of patients undergoing colonic imaging for colonic symptoms would be expected to have diverticular disease as the cause of their symptoms, in which case patients with diverticular disease would have a higher frequency of colonic symptoms compared to those without. Our results are therefore consistent with the hypothesis that uncomplicated diverticular disease of the colon is not a common cause of colonic symptoms among patients presenting for colonic imaging in secondary care.

We studied two groups of patients: firstly, those presenting to medical gastroenterological clinics for elective investigation of colonic symptoms, and secondly, those who were screened for a family history of colorectal cancer or a past history of colonic polyps. We did not include patients with acute diverticulitis, who would generally have presented to the Emergency Department in the first instance, and who would have undergone CT scan rather than barium enema or colonoscopy. Patients who have suffered a previous episode of acute diverticulitis and subsequently attend for colonic symptoms, on the one hand and a personal history of colonic polyps or a family history of colorectal cancer, on the other, findings in patients who attend for surveillance colonoscopy should approximate what would be found if a sample of community subjects were to undergo colonic imaging.

Our findings are not strictly applicable to individuals <u>under the age of 50</u> but there are no conceptual reasons why the patho-physiological effects of diverticular disease should vary according to age. <u>Our study design does not exclude the possibility that those patients with</u>

Deleted: We excluded patients under the age of 50 because younger subjects have a lower prevalence of diverticular disease of the colon, and we would have required a larger study to achieve the same statistical power.

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colonic symptoms but no diverticular disease may have a predisposition to diverticular disease and may develop it over the next few years.

In western countries diverticular disease of the colon occurs most commonly in the sigmoid and descending colon, associated with thickening of the muscle layer(1). In contrast, in oriental countries, colonic diverticula occur predominantly in the right colon (9). The right colon is more voluminous than the left, although colonic pressure changes in patients with right-sided diverticular disease of the colon were reported to be similar to those described for western, left-sided disease (10). We studied a London population with mainly left-sided disease. The frequency and type of symptoms in right–sided diverticular disease may be different but may not have been evident in this study because of small numbers.

We have included patients undergoing either colonoscopy or barium enema. Colonoscopy is now the first-line imaging modality for the colon and this is reflected in the small number imaged by radiology in this study. Barium enema has a lower sensitivity for the diagnosis of small polyps and mucosal lesions, although it is still an acceptable imaging procedure for iron deficiency anaemia(11). Although the proportion of patients found to have diverticular disease of the colon in our study was higher among patients undergoing barium enema compared to those who underwent colonoscopy, the difference did not reach statistical significance. The frequency of colonic symptoms in patients with and without diverticular disease was similar whether colonoscopy or barium enema was the imaging modality used.

We cannot explain why patients with colonic polyps were less likely to have symptoms of irritable bowel syndrome than those without. One contributory factor is that patients attending for surveillance colonoscopy because of a family history of colorectal cancer or a past history of colonic polyps are more likely to have polyps and to be asymptomatic, compared to patients presenting with colonic symptoms. However, even when patients attending for surveillance colonoscopy were considered as a group, those with colonic

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polyps were still less likely to fulfill the criteria for irritable bowel syndrome than those without polyps, although there was no difference in the proportions reporting abdominal pain. There was no difference when males and females were separately considered but this could be a function of small numbers.

Our conclusion that diverticular disease of the colon seldom causes colonic symptoms is consistent with the observation that the prevalence of irritable bowel syndrome in the community does not increase with age(12). If diverticular disease of the colon does cause colonic symptoms, the community prevalence of symptoms of irritable bowel syndrome should increase with age, pari passu with the increase in prevalence of diverticular disease.

Patients with symptomatic uncomplicated diverticular disease of the colon have heightened visceral perception of rectal sigmoid distension stimuli not limited to the diverticular bearing sigmoid colon, resembling irritable bowel syndrome patients(13). In contrast, asymptomatic patients with diverticular disease of the colon did not show this pattern of heightened visceral hypersensitivity(14). These observations are consistent with our hypothesis that in patients with both diverticular disease and colonic symptoms, the association between the two may be due to the colonic symptoms leading to the discovery of the diverticular disease rather than the symptoms being caused by the diverticular disease.

Recently, a population-based study of patients who have undergone colonic imaging was reported from Olmsted County, comprising 76% of subjects who responded to a symptom questionnaire(15). An association was described between irritable bowel syndrome and colonic diverticulosis, although not diverticulitis, among individuals aged 65 years or above, but not among younger subjects. Diarrhoea-predominant IBS and mixed IBS were particularly correlated with colonic diverticular disease. We cannot explain why our findings are different. The Olmsted County study included approximately twice as many patients as ours, but our confidence limits do not suggest that a type 2 error is likely. We studied a

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cohort of patients presenting for colonic imaging in a secondary care setting while Talley's study was population-based. Many patients with diverticular disease have minimal or no symptoms and may therefore not seek medical attention. Findings from community based studies are more likely to be applicable to the general population than hospital-based studies.

The main strength of our study is that we have a large number of patients, some with symptoms and some without, selected only on the basis of attendance for colonic imaging. We used a locally validated Rome II questionnaire with standardized and generally accepted definitions of irritable bowel syndrome and other colonic symptoms. Previous studies(7,8), with the exception of Jung's(15), involved small numbers of patients and symptoms were not assessed in a standardized way.

The major weakness of our study is that it is not community based and referral bias may therefore reduce the ability of our results to be applied to other patient populations. Most of our patients presented for colonic imaging because of symptoms and the relationship between diverticulosis and colonic symptoms in patients attending Gastroenterology clinics may differ from the situation in community subjects, who are less likely to be symptomatic. On the other hand, since colonic diverticular disease can only be diagnosed by imaging studies, it would not be possible to study this condition among subjects who have not presented to medical attention and undergone imaging at some stage. Even if a communitybased study were performed in the United Kingdom, a similar cohort of patients to the present study would have been evaluated, since diverticular disease can only be diagnosed or excluded in secondary care. Further, a significant minority of our patients attended because of a family history of colorectal cancer or past history of colonic polyps rather than a personal history of symptoms. In a sense this subgroup is more like community subjects than patients who underwent colonic imaging for colonic symptoms. We analyzed data

collected in a previous study from 128 randomly selected community subjects above the age of 50(3). The frequency of irritable bowel syndrome among the subgroup of patients in the present study with a family history of colorectal cancer or personal history of colonic polyps at 7/73 (10%) for males and 11/65 (17%) for females is in between that of community controls, at 3/59 (5%) for men and 8/61 (13%) for women, and that of our patients who were imaged because of colonic symptoms at 54/248 (22%) for men and 113/354 (32%) for women. Within the subgroup of patients with a family history of colorectal cancer or personal history of colonic polyps, 5/49 (10%) with diverticular disease fulfilled the criteria for irritable bowel syndrome compared to 13/89 (15%) of those without diverticular disease (NS)

Yet another weakness of our study is that patients were not recruited consecutively. Bias could have been introduced, but this was unlikely to have skewed the results since selection was not made on the basis of the presence or absence of symptoms.

All negative studies are potentially subject to a beta error. We did a power calculation but unfortunately the prevalence of diverticular disease and irritable bowel syndrome in our patients differed from what was expected from our database. However, the small 95% confidence limits of the various differences indicate that a beta error of any magnitude is unlikely.

In conclusion, the prevalence of colonic symptoms among patients undergoing colonic imaging in a secondary care setting is unaffected by whether diverticular disease is present. Diverticular disease of the colon is not a common cause of irritable bowel syndrome and other colonic symptoms in this patient population. Acknowledgements

Preliminary data from this study were presented at the March 2006 meeting of the British

Society of Gastroenterology. Dr J Poloniecki kindly gave statistical advice.

Table: Colonic symptoms in patients with and without diverticular disease of the colon

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15		775	123	43.8%	226	45.7%	NS	0.02
16	Irritable Bowel Syndrome	740	66	24.8%	119	25.1%	NS	0.00 (
17	Diarrnoea predominant	740	25	9.4%	70	14.8%	NS	0.05 (
18	Constipation predominant							
10	irritable bowel syndrome	740	15	5.6%	21	4.4%	NS	0.01 (
20	Diarrhoea	742	44	16.4%	80	16.9%	NS	0.01 (
20	Constipation	740	38	14.3%	80	16.9%	NS	0.03
21	Abdominal Bloating	740	49	18.4%	106	22.4%	NS	0.04 (
22	Functional Incontinence	725	61	23.6%	118	25.3%	NS	0.020
23	Proctalgia Fugax	652	15	6.3%	44	10.6%	NS	0.04
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