# Use of complementary and alternative medicine in Swedish patients with inflammatory bowel disease: a controlled study

Lena Oxelmark<sup>a,h</sup>, Annelie Lindberg<sup>b</sup>, Robert Löfberg<sup>d,f</sup>, Berit Sternby<sup>j</sup>, Anders Eriksson<sup>i</sup>, Sven Almer<sup>c,d</sup>, Ragnar Befrits<sup>d</sup>, Bjöörn Fossum<sup>e,g</sup>, Per Karlén<sup>b</sup>, Olle Broström<sup>e</sup> and Curt Tysk<sup>k</sup>; SOIBD, the Swedish Organization for the study of Inflammatory Bowel Disease

**Background** There is an increasing interest in complementary and alternative medicine (CAM) in patients with chronic diseases, including those with inflammatory bowel disease (IBD). Patients may turn to CAM when conventional therapies are inadequate or associated with side effects for symptomatic relief or to regain control over their disease. The objectives were to explore CAM use and perceived effects in IBD patients in comparison with a control group.

**Methods** A cross-sectional, multicenter, controlled study was carried out. IBD patients were invited from 12 IBD clinics in Sweden. Controls were selected randomly from a residence registry. A study-specific questionnaire was used for data collection. **Results** Overall, 48.3% of patients with IBD had used some kind of CAM during the past year compared with 53.5% in controls (P = 0.025, adjusted for age, sex, geographic residence, and diet). The most frequently used CAM among IBD patients was massage (21.3%), versus controls (31.4%) (adjusted P = 0.0003). The second most used CAM was natural products, 18.7% in IBD patients versus 22.3% of the controls (unadjusted P = 0.018). In all, 83.1% of the patients experienced positive effects from CAM and 14.4% experienced negative effects.

**Conclusion** Overall, 48.3% of Swedish IBD patients used some kind of CAM and controls used CAM significantly more. Natural products were used by one-fifth of the patients and even more by controls. This is notable from a patient safety perspective considering the possible risks of interactions with conventional medication. In all, 40% of the patients reported adverse events from conventional medicine. Patients experienced predominantly positive effects from CAM, and so did controls. Eur J Gastroenterol Hepatol 28:1320–1328

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# Introduction

Inflammatory bowel diseases (IBD) are chronic, relapsing bowel conditions including ulcerative colitis (UC), Crohn's disease (CD), and inflammatory bowel disease unclassified (IBDU) when the diagnosis is unclear. Patients with IBD

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<sup>a</sup>Department of Neurobiology, Care Sciences and Society, Division of Nursing, <sup>b</sup>Department of Clinical Sciences, Danderyd Hospital, <sup>c</sup>Center for Digestive Diseases, Karolinska University Hospital, <sup>d</sup>Department of Medicine, Solna, Karolinska Institutet, <sup>e</sup>Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, <sup>f</sup>Stockholm GastroCenter, <sup>g</sup>Sophiahemmet University, Stockholm, <sup>h</sup>Institute of Health and Care Sciences, the Sahlgrenska Academy, University of Gothenburg, <sup>I</sup>Department of Medicine, Geriatrics and Emergency, Sahlgrenska University Hospital/East Hospital, Gothenburg, <sup>I</sup>Department of Gastroenterology, Skane University Hospital, Lund and <sup>k</sup>Faculty of Medicine and Health, School of Health and Medical Sciences, örebro University and Department of Medicine, Division of Gastroenterology, Örebro University Hospital, Örebro, Sweden

Correspondence to Lena Oxelmark, PhD, Institute of Health and Care Sciences, PO Box 457, SE-40530 Gothenburg, Sweden

Tel: +31 786 6089; fax: +31 786 6050; e-mail: lena.oxelmark@gu.se

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This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially. may have disabling symptoms such as frequent diarrhea, often with blood or mucus discharge, abdominal pain, weight loss, malabsorption, malnutrition, and fatigue [1]. Moreover, patients may be affected by extraintestinal manifestations involving other organs such as the joints, eyes, skin, liver, and bile ducts [2]. The cause of IBD is unknown and there is no medical cure, although several therapeutic advances have been made in recent years; medical and surgical treatment for IBD is complex. Current treatment paradigms recommend the use of immunomodulators with or without biological therapy aiming at maintaining clinical and endoscopic remission to reduce the inflammatory burden, minimize complications, and the need for surgery, and as a result achieve an improved quality of life for the patient [3,4].

There is an increasing interest in and use of complementary and alternative medicine (CAM) in patients with chronic diseases, including those with IBD [5–8]. Patients with IBD may turn to CAM for various reasons: for example, when conventional therapies are inadequate [9] or associated with adverse side effects, or for symptomatic relief and to regain control over their disease [10]. The amount of steroid medication may be a predictor of CAM use [11]; moreover, CAM use may indicate psychosocial distress in patients with IBD [12,13].

The terms complementary medicine and alternative medicine refer to a broad set of healthcare practices that

are not part of a country's own tradition and are not fully integrated into the dominant healthcare system. These terms are used interchangeably with traditional medicine (TM) in some countries. TM has a long history and is the sum of the knowledge, skills, and practices on the basis of the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not in the maintenance of health [14]. There are different types of CAM: whole medical systems (homeopathic medicine, traditional Chinese medicine, Avurveda), mind-body medicine (meditation, prayer, healing), natural products (herbs, also known as botanicals, vitamins and minerals, and probiotics, often sold as dietary supplements), manipulative and body-based practices (chiropractic or osteopathic manipulation, massage), and energy medicine (Qi gong, Reiki, therapeutic touch, the use of magnetic fields) [15–17].

Overall, 30% of the world's population do not have access to conventional medicine and for these patients, herbal medicines and TM are the main options [14]. A review of the WHO in 142 countries showed that, in 99 countries, CAM, that is, natural products (herbal products and dietary supplements) are sold over the counter without prescriptions [17]. CAM is mostly used for self-care [18], and is often recommended by friends. Many CAM treatments are available in our present-day society and the quality of the information on CAM, often provided by the media and the Internet, is variable. In general, a wide range of CAMs are recommended for many conditions, and a variety of treatments are recommended for the same conditions. The definition of CAM is changing constantly.

Today, some CAM treatments are supported by evidence from randomized-controlled trials, meta-analyses, and systematic reviews [19-22], and there are several interesting studies on CAM for the treatment of IBD [19]. A recent review of clinical trials of various herbal therapies for IBD [23] presents the most important studies on Aloe vera gel [24], polyphenols (green tea) [25–27], wheat grass juice [28], bilberry [29], wormwood [30,31], Boswellia serrata [19,32], cannabis [33], and Chinese herbal medicine [34]. Promising results have been shown for curcumin as maintenance treatment in UC [35,36]. Probiotics have been shown to increase the clinical response and remission rate in mild to moderate UC [37,38] and to prevent pouchitis [39]. Considering the mounting evidence that dietary changes influence gut microbiome, dietary intervention studies have been attempted [40], and as patients are becoming more interested in and are using specific diets to better control the disease [41], diets might be considered CAM. Moreover, acupuncture and moxibustion have been attempted for both CD and UC [42,43]. Studies using psychological interventions comprising relaxation techniques, patient education [44], and psychotherapy, however, showed that psychotherapy had no effect on disease activity, health-related quality of life, or emotional status [45]. However, a recently published study showed improved anxiety, quality of life, and mindfulness after a stress-reduction program on the basis of mindfulness in patients with CD [46]. Additional controlled trials are still needed in many areas [47].

There are safety aspects because some herbal-based CAMs may be associated with adverse side effects and may cause interactions with conventional therapy [48,49]. It is noteworthy that there is emerging evidence that CAM therapies may modulate or disrupt the immune system [32]. Thus, the use of CAM in patients with IBD needs to be considered in daily practice when making clinical decisions. This multicenter survey was conducted to determine the extent of CAM use, the reason for CAM use, and perceived positive or negative effects from CAM in patients with IBD in Sweden.

## Methods

# Sample

Eight hundred and fifty-four patients with IBD from 12 Swedish hospitals were invited to participate in the study. A control group matched for age and sex, urban or rural, and geographic area was recruited. Ten of the IBD centers were university based; one was a large teaching hospital, one was a private clinic, and one was a nonprofit hospital. The centers were spread geographically from the north to the south of Sweden.

#### **Data collection**

# Patients with IBD

The inclusion criterion was an established diagnosis of IBD according to medical records being treated at the clinic. The patients were contacted at the IBD centers by an IBD nurse or a physician who provided oral and written information on the study. If the patients were willing to participate, they filled in a questionnaire either at the clinic or at home using a prestamped, addressed reply envelope. Two reminders were provided either by post or by telephone. The completed questionnaires were interpreted as representing informed consent. All data sampling was performed at each IBD center between August 2008 and June 2009.

#### Control group

The individuals in the control group were selected randomly from a residence registry, Statens personadressregister (SPAR). SPAR includes all individuals who are registered as residents in Sweden and the data are updated continuously from the Swedish Population Register. An age, sex, and residence match was performed after the first 300 patients with IBD had been included. The questionnaire was sent by post to 1400 individuals together with an informative letter explaining the study, and a stamped, addressed reply envelope. Two reminders were sent. Returned questionnaires were interpreted as representing informed consent.

# Study-specific CAM questionnaire

A self-administered questionnaire was used to collect data on CAM. The questionnaire was developed from a previously used questionnaire from an international survey, in which two of the authors (L.O., R.L.) participated [5]. After updating the previous questionnaire with the help of an expert group on integrative care and CAM [50], a final list of 24 different CAMs was extracted. The respondents were asked to indicate the type and frequency of CAM use (use in the past year, use in the last 2 weeks), perceived positive and negative effects of CAM, and their source of CAM information. There was a space for noting 'others' if the particular CAM used was not listed.

Further data on demographic characteristics such as age, sex, education, marital status, employment status, urban versus rural residence, annual income, diet, and lifestyle habits (tobacco and alcohol use) were collected. The questionnaire also included questions on disease characteristics, type of IBD, current symptoms, year of diagnosis, conventional medication use, and perceived adverse events from conventional medication.

# Statistical considerations

For comparison between two groups, Fisher's exact test was used for dichotomous variables, the Mantel–Haenszel  $\chi^2$ -test was used for ordered categorical variables, and the Mann–Whitney *U*-test was used for continuous variables. Univariable logistic regression was performed to predict the use of CAM. Odds ratio and confidence interval (CI) (adjusted for age, sex, residence, and diet) were calculated for the association of CAM use between IBD patients and controls. Two-tailed tests were used. *P*-values less than 0.05 were considered to be statistically significant.

#### **Ethical considerations**

The study was carried out according to the Declaration of Helsinki. The IBD patients received oral and written information about the study. The individuals in the control group received written information. All participators were informed that participation was voluntarily and that they could withdraw at any time without consequences. The study was approved by the Ethical Committee for all participating sites (Dnr 2008/4:6, 2009/852–32).

#### **Results**

Of the 854 patients with IBD who were invited to participate, 164 did not return the questionnaires (despite two reminders), 40 patients declined participation, and two were excluded owing to incomplete questionnaires. In total, 648 patients with IBD were included, yielding a response rate of 76%.

Fourteen hundred individuals were invited to participate in the control group, of whom 440 responded, yielding a response rate of 32%. Twenty individuals declined participation, 33 letters were returned because of unknown address, one individual had died, and 906 did not return the questionnaires despite two reminders.

#### Nonparticipants

The patients with IBD who did not respond had a mean age of 41.6 years; 48.5% were men, 39.2% had UC, and 42.9% had CD. The nonresponders in the control group had a mean age of 40.8 years and 56.5% were men.

Sociodemographic and disease data are listed in Table 1. Of the 648 patients with IBD included in the study, 324 (50%) had UC, 319 (49.2%) had CD, and five (0.8%) had IBDU. The mean disease duration was 13.3 years and the mean age of the IBD patients with IBD was 42.7 years. The individuals in the control group were significantly older than the patients with IBD (mean age 45.9 years; P = 0.0004). In the IBD group, 48.3% of the

patients were women and 58.1% of the controls were women (P = 0.002). Significantly more of the controls were cohabiting compared with the patients with IBD (P = 0.04). Patients with IBD lived significantly more often in urban areas (P = 0.001) compared with controls. Patients with IBD used various kinds of diets (e.g. lacto vegetarian, lacto ovo vegetarian, vegan, and other types of diets) more often than the controls who used more normal diets (P < 0.0001).

The level of education was similar in the patients and controls. There were also no differences between patients with IBD and controls in occupation. In all, 28% of the patients with IBD were active tobacco users, 13.6% of them smoked and 14.8% used other tobacco (e.g. snuff tobacco), the differences were not significant compared with controls. Current alcohol use was significantly higher among the controls than the patients with IBD (P = 0.005).

Overall, 93% of the patients with IBD reported the use of conventional medicine for IBD and 39.8% reported having experienced an adverse drug event from conventional medicine. The controls often did not reply to the question on conventional medication or adverse events. Differences between patients with IBD and controls were adjusted for when comparing CAM use between groups.

#### CAM use

Patients with IBD and individuals in the control group used different kinds of CAM (Table 2). Of the patients with IBD, 48.3% had used some kind of CAM during the past year compared with 53.5% of the controls (P = 0.11). However, after adjusting for age, sex, geographic residence, and diet in a multivariate analysis, a statistically significant difference was observed [P=0.025, odds ratio 1.16 (95% CI 1.02–1.32)]. The most frequently used CAM among patients with IBD was massage, used by 21.3%, compared with 31.4% of the controls (adjusted P = 0.0003). The second most frequently used CAM was herbal products, which were used by 18.7% of the patients with IBD compared with 22.3% of the controls (adjusted P = 0.018). The most commonly used natural products used by patients were omega 3, probiotics, Aloe vera, vitamins, Arctic root, and other herbal products. The controls used omega 3, Echinacea spp., Kan Yang, Siberian ginseng, Arctic root, and herbal products (data not shown). Relaxation was used by patients with IBD and by controls to a similar extent. Other CAMs used to a similar extent by patients with IBD and the controls were yoga, acupuncture, counseling, chiropractic, and meditation. More controls used naprapathy than did IBD patients (adjusted P = 0.0055), reflexology, and healing (unadjusted P = 0.026).

Patients sought CAM treatments to reduce pain, mainly pain from back, neck, joints, and bowel but also as strategies to handle their disease in order to decrease bowel symptoms and improve well-being. Only a small proportion of the controls stated their reason for CAM use. IBD patients used CAM primarily on their own initiative, but patients were also referred to CAM practitioners or recommended CAM use by healthcare professionals. They obtained information on different CAMs mainly from friends and their next of kin, but also from the media, the Internet, and the literature and from health food stores (Fig. 1).

#### Table 1. Sociodemographic and disease data, comparison between groups

Variable	IBD <sup>a</sup> (N=648) [n (%)]	UC (N=324) [n (%)]	CD (N=319) [n (%)]	Controls (N=440) [n (%)]	IBD vs. control ( <i>P</i> -value)	UC vs. CD ( <i>P</i> -value)
Age [mean (SD)]	42.7 (15.1)	42.1 (14.7)	43.1 (15.2)	45.9 (15.2)	0.0004	0.42
Median (range)	42.0 (13.0-89.0)	41.0 (15.0-82.0)	42.0 (13.0-89.0)	42.0 (18.0–85.0), n=439		
Sex						
Male	335 (51.7)	176 (54.3)	157 (49.2)	183 (41.9)		
Female	313 (48.3)	148 (45.7)	162 (50.8)	254 (58.1)	0.0018	0.22
Education						
Grammar school	93 (14.7)	39 (12.3)	53 (17.0)	65 (15.1)		
College	256 (40.4)	127 (40.2)	126 (40.4)	161 (37.4)		
Other	12 (1.9)	4 (1.3)	8 (2.6)	7 (1.6)		
University	272 (43.0)	146 (46.2)	125 (40.1)	198 (45.9)	0.47	0.092
Marital status						
Married/cohabitant	422 (65.7)	214 (66.9)	206 (65.0)	315 (71.9)		
Living apart	46 (7.2)	26 (8.1)	20 (6.3)	20 (4.6)		
Single	132 (20.6)	61 (19.1)	69 (21.8)	64 (14.6)	L	
Widow/widower	42 (6.5)	19 (5.9)	22 (6.9)	39 (8.9)	0.04 <sup>b</sup>	NS <sup>D</sup>
Occupation						
Working	433 (66.9)	230 (71.2)	200 (62.7)	306 (69.9)		
Studying	50 (7.7)	29 (9.0)	21 (6.6)	30 (6.8)		
Sick leave/pension	79 (12.2)	24 (7.4)	55 (17.2)	27 (6.2)		
Retired	68 (10.5)	32 (9.9)	35 (11.0)	55 (12.6)		
Other	17 (2.6)	8 (2.5)	8 (2.5)	20 (4.5)	0.34°	0.027 <sup>c</sup>
Residence						
Urban area > 25 000 inhabitants	498 (77.3)	251 (78.0)	242 (76.3)	292 (67.0)		
Small town < 10 000 inhabitants	86 (13.4)	42 (13.0)	44 (13.9)	84 (19.3)		
Village < 500 inhabitants	24 (3.7)	12 (3.7)	12 (3.8)	25 (5.7)		
Countryside	36 (5.6)	17 (5.3)	19 (6.0)	35 (8.0)	0.0012	0.63
Annual income (SEK, thousand krona)	n=552	n = 285	n = 263	n=379		
Mean (SD)	300.7 (188.1)	308.2 (198.6)	290.0 (165.3)	309.8 (326.2)	0.66	0.48
Median (range)	286.5 (0-1500.0)	300.0 (0-1500.0)	280.0 (0-1200.0)	280.0 (0-6000.0)		
Diet						
Normal diet	537 (82.9)	271 (83.6)	262 (82.1)	412 (93.8)		
Other <sup>d</sup>	111 (17.1)	53 (16.4)	57 (17.9)	27 (6.2)	< 0.0001	0.69
Tobacco use						
Current smoker	87 (13.6)	34 (10.4)	53 (16.8)	49 (11.3)	0.20	0.065
Other tobacco use	93 (14.8)	47 (14.9)	46 (14.8)	49 (11.3)	1.00	1.00
Current alcohol use	492 (75.8)	254 (79.4)	236 (74.7)	363 (83.8)	0.005	0.19
(n = 636) Disease duration						
Mean (SD)	13.3 (11.6)	11.9 (11.1)	14.8 (12.0)			
Median (range)	10.0 (1-56)	9.0 (1-50)	11.0 (1-56)			
Current IBD symptoms	374 (57.0)	167 (51.5)	204 (63.9)			
Conventional medication	602 (92.9)	292 (90.1)	285 (90.5)			
Adverse drug event	258 (39.8)	125 (38.5)	130 (40.7)			
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For pairwise comparison between groups, Fisher's exact test was used for dichotomous variables, the Mantel-Haenszel  $\chi^2$ -test was used for ordered categorical variables, and the Mann-Whitney *U*-test was used for continuous variables.

CAM, complementary and alternative medicine; CD, Crohn's disease; IBD, inflammatory bowel disease; NS, nonsignificant; UC, ulcerative colitis.

<sup>a</sup>Five cases with IBD unclassified are included in the IBD cases, but are not analyzed separately.

<sup>b</sup>Living together versus living apart.

<sup>c</sup>Working (n = 433) versus nonworking (n = 214).

<sup>d</sup>Including lacto vegetarian, lacto ovo vegetarian, and vegan diet.

#### Effects of CAM experienced by patients with IBD

The perceived experiences of patients with IBD of CAM are presented in Table 3. In all, 83% of the patients with IBD who had used any CAM during the past year perceived the CAM as a positive experience, whereas 14.4% of them had experienced a negative effect (or effects) of the CAM treatment. The majority of the patients who used massage found it to be positive (i.e. relaxing, providing pain relief, and well-being) and 5.8% experienced negative effects (pain, unease, or ill-being). Natural products were used by 18.7% of the patients with IBD; 66.1% of these patients perceived positive effects, improved disease symptoms, well-being, and general improvement. There

were no negative experiences of relaxation; yoga was experienced as a means to achieve well-being, relaxation, and improved mobility. Patients with IBD who used acupuncture experienced pain relief, well-being, and improved disease symptoms.

#### Discussion

A high percentage of the patients with IBD (48.3%) had used some kind of CAM within the last year, which is in line with previous research (32–68%) in other Western countries [5,8,10,51–54]. The most common CAM use in the current study was massage, followed by natural products, relaxation, yoga, acupuncture, and counseling.

Table 2. Type of complementary and alternative medicine used in patients with IBD within the last year, comparison between groups							
Kind of CAM used	IBD (N=648)	UC (N=324)	CD (N=319)	Controls (N=440)	IBD vs. controls (P-value)	Adjusted <i>P</i> -value <sup>a</sup>	Odds ratio (95% Cl) <sup>a</sup>
Any CAM	313 (48.3)	147 (45.5)	163 (51.1)	235 (53.5)	0.11	0.025	1.16 (1.02–1.32)
Massage	138 (21.3)	58 (18.0)	79 (24.8)	138 (31.4)	0.0002	0.0003	1.31 (1.13–1.52)
Natural products	121 (18.7)	51 (15.8)	68 (21.3)	98 (22.3)	0.17	0.018	1.21 (1.03–1.43)
Relaxation	68 (10.5)	29 (9.0)	38 (11.9)	51 (11.6)	0.63	0.33	1.11 (0.90–1.37)
Yoga	52 (8.0)	30 (9.3)	22 (6.9)	42 (9.6)	0.44	0.058	1.26 (0.99–1.60)
Acupuncture	49 (7.6)	21 (6.5)	26 (8.2)	39 (8.9)	0.51	0.53	1.08 (0.85–1.36)
Counseling	47 (7.3)	24 (7.4)	22 (6.9)	27 (6.2)	0.56	0.86	0.98 (0.75-1.26)
Chiropractic	35 (5.4)	16 (5.0)	19 (6.0)	25 (5.7)	0.94	0.88	1.02 (0.78-1.34)
Meditation	31 (4.8)	14 (4.3)	17 (5.3)	21 (4.8)	1.00	0.40	1.14 (0.84–1.55)
Naprapathy	24 (3.7)	15 (4.6)	8 (2.5)	29 (6.6)	0.044	0.0055	1.51 (1.13–2.03)
Religion	23 (3.6)	10 (3.1)	13 (4.1)	20 (4.6)	0.50	0.077	1.35 (0.97–1.90)
Homeopathy	15 (2.3)	8 (2.5)	6 (1.9)	7 (1.6)	0.56	NA	0.83 (0.51-1.34)
Qi gong	13 (2.0)	6 (1.9)	7 (2.2)	15 (3.4)	0.22	NA	1.23 (0.82-1.83)
Dietary change	12 (1.9)	6 (1.9)	6 (1.9)	2 (0.5)	0.055	NA	NA
Reflexology	11 (1.7)	4 (1.2)	5 (1.6)	15 (3.4)	0.11	NA	NA
Self helping group	9 (1.4)	8 (2.5)	1 (0.3)	1 (0.2)	0.086	NA	NA
Acupressure	8 (1.2)	2 (0.6)	5 (1.6)	8 (1.8)	0.59	NA	NA
Healing	7 (1.1)	3 (0.9)	4 (1.3)	14 (3.2)	0.026	NA	NA
TCM	6 (0.9)	5 (1.5)	1 (0.3)	4 (0.9)	1.00	NA	NA
Hypnosis	4 (0.6)	3 (0.9)	1 (0.3)	1 (0.2)	0.66	NA	NA
Anthroposophy	3 (0.5)	1 (0.3)	2 (0.6)	5 (1.1)	0.36	NA	NA
Shiatsu	3 (0.5)	1 (0.3)	1 (0.3)	5 (1.1)	0.36	NA	NA
Aromatherapy	2 (0.3)	1 (0.3)	1 (0.3)	5 (1.1)	0.20	NA	NA
Ayurveda	2 (0.3)	2 (0.6)	0 (0.0)	4 (0.9)	0.37	NA	NA
Rosen method bodywork	1 (0.2)	0 (0.0)	1 (0.3)	2 (0.5)	0.72	NA	NA

For categorical values, n (%) is presented. For a pairwise comparison between groups, Fisher's exact test was used for dichotomous variables.

Odds ratio (OR) and confidence interval (CI) for OR were calculated for IBD patient versus controls. Five cases with IBDU are included in the IBD cases, but were not analyzed separately.

CAM, complementary and alternative medicine; CD, Crohn's disease; IBD, inflammatory bowel disease; IBDU, inflammatory bowel disease unclassified; NA, not available; TCM, traditional Chinese medicine; UC, ulcerative colitis.

<sup>a</sup>Adjusting for age, sex, residence, and diet using logistic regression.



Fig. 1. Sources of information on CAM (%). 'Other' comprised literature (scientific articles, textbooks), own initiative, and wellness at workplace. CAM, complementary and alternative medicine; HCP, healthcare professionals.

The majority of patients using CAM reported positive effects of their CAM use. The use of CAM was significantly higher in the control group (53.1 vs. 48.3%); however, this high use of CAM in the control group must be interpreted with caution because of the low response rate. Patients with IBD may be so used to conventional medication that they dare not use CAM to a greater extent or they may be influenced by healthcare professionals showing a disparaging attitudes toward patients' CAM use [55]. It has been argued that in the absence of critical assessment of CAM, gastroenterologists could simply be supportive, cautious, and open-minded about widely available CAMs [6].

Overall, 93% of the patients with IBD in the present study reported the use of conventional medication and as many as 40% of these reported adverse event from conventional medicine. This high figure of adverse drug events could be because of a selection bias because the patients responding to the questionnaires could be those explicitly interested in CAM and/or those who had experienced adverse effects from conventional medicine. However, patients on IBD medication often report adverse drug reactions, mainly from steroid therapy. A review showed that adverse events lead to cessation of medication in up to 55% of patients being prescribed steroids, and 10-11% of patients prescribed antitumor necrosis factor therapy and immunomodulators, [56]. The IBD patients in our study sought CAM treatments to reduce pain and to handle stress and symptom related to their disease. The majority of the patients perceived positive effects from CAM treatments, but interestingly, no major improvement in disease symptoms was observed.

A significantly higher proportion of the controls (22.3%) used natural products compared with patients with IBD (18.7%), controlled for age, sex, residence, and diet. This was to some degree surprising because patients with a chronic disease were expected to use more CAM compared with a control group. This difference may possibly be explained by the fact that the controls were significantly older, more of them were women, more were living in urban areas/cities, and the controls were following more normal diets.

With respect to patient safety, it is notable that as many as 18.7% of the patients with IBD in our study used natural products. The patients also used other CAMs (but to a lesser extent): anthroposophy (0.5%), Ayurveda (0.3%),

# **Table 3.** Perceived effects of CAM in patients with IBD (n = 648)

CAM treatment	Use of CAM specified [n (%)]	Positive effect of CAM [ <i>n</i> (%)]	Negative effect of CAM [n (%)]
Massage	138 (21.3)	107 (77.5)	8 (5.8)
Pain relief		30 (21.7)	
Well-being		29 (21.0)	
Relaxing		33 (23.9)	
Improved mobility		15 (10.9)	
Improved symptoms		5 (3.6)	
Unspecified		21 (15.2)	
Pain			4 (2.9)
III-being, unease			2 (1.5)
liredness			1 (0.7)
Other			2 (1.5)
Unspecified			1 (0.7)
Natural products	121 (18.7)	80 (66.1)	12 (9.9)
Pain relief		4 (3.3)	
Well-being		20 (16.5)	
Relaxing		1 (0.8)	
Improved symptoms		3 (31.4)	
Unspecified		24 (19.8)	
Pain			1 (0.8)
III-being, unease			1 (0.8)
Increased symptoms			5 (4.1)
Liredness			1 (0.8)
Other			1 (0.8)
Unspecified			3 (2.5)
Relaxation	68 (10.5)	58 (85.3)	0
Pain relief		4 (5.9)	
Well-being		12 (17.7)	
Relaxing		19 (27.9)	
Improved symptoms		5 (7.4)	
Unspecified		22 (32.4)	
Yoga	52 (8.0)	44 (84.6)	5 (9.6)
Pain relief		2 (3.9)	
Well-being		18 (34.6)	
Relaxing		12 (23.1)	
		8 (15.4)	
Improved symptoms		2 (3.9)	
Unspecified		9 (17.3)	0 (0 0)
III-being, unease			2 (3.9)
Increased symptoms			1 (1.9)
	40 (70)		3 (5.8)
Pain roliof	49 (7.6)	15 (20.6)	9 (18.4)
		7 (14.2)	
Pelaving		8 (163)	
Improved symptoms		8 (16.3)	
Upproved symptoms		0 (19.4)	
Pain		9 (10.4)	4 (8.2)
Improved symptoms			(0.2)
Tiredness			2(4.1) 2(4.1)
Other			1 (0 1)
Unspecified			1 (2.1)
Counseling	47 (73)	42 (89 A)	4 (85)
Well-being	(1.0)	28 (59.6)	1 (0.0)
Relaxing		3 (64)	
Improved symptoms		2 (4.3)	
Unspecified		10 (21.3)	
III-being unease		10 (2110)	4 (9.5)
Chiropractic	35 (54)	29 (82.9)	4 (11.4)
Pain relief	00 (0.1)	16 (45.7)	. ()
Well-being		3 (8.6)	
Improved mobility		3 (8.6)	
Improved symptoms		5 (14.3)	
Unspecified		6 (171)	
Pain		0 (11.1)	2 (5.7)
Other			2 (5.7)
Unspecified			1 (2.9)
Meditation	31 (4.8)	28 (90.3)	0
Well-being	01 (1.0)	13 (41.9)	0
Relaxing		8 (25.8)	
Improved symptoms		4 (12 9)	
Unspecified		8 (25.8)	
Naprapathy	24 (37)	21 (875)	3 (125)
Pain relief	21(0.7)	11 (45.8)	0 (12.0)
Well-being		3 (12.5)	
Relaxing		1 (4.2)	
Improved mobility		1 (4 2)	
protod mobility		1 (7.2)	

Table 2 (Caption and

CAM treatment	Use of CAM specified [ <i>n</i> (%)]	Positive effect of CAM [ <i>n</i> (%)]	Negative effect of CAM [ <i>n</i> (%)]
Unspecified		7 (29.2)	
Pain			2 (9.5)
Unspecified			1 (4.8)
Religion	23 (3.5)	18 (78.3)	0
Well-being		6 (26.1)	
Relaxing		1 (4.4)	
Unspecified		11 (47.8)	
Homeopathy	15 (2.3)	10 (66.7)	1 (6.7)
Pain relief		1 (6.7)	
Well-being		1 (6.7)	
Relaxing		1 (6.7)	
Improved mobility		1 (6.7)	
Improved symptoms		5 (33.3)	
Unspecified		3 (20.0)	

Percentage shows the positive or the negative experience of those who used specific CAM.

CAM, complementary and alternative medicine; IBD, inflammatory bowel disease.

homeopathy (2.3%), and traditional Chinese medicine (0.5%), which are not included in the 'natural products', and yet involve a certain amount of herbal products. The definition of CAM used in this study in terms of natural products includes a variety of products, herbals (botanicals), vitamins and minerals, and probiotics (often sold as dietary supplements) [16]. Research on the importance of vitamin D is increasing and clinicians may recommend IBD patients such products as vitamins, omega 3, and probiotics [57–59]; however, the patients in the present study did identify these products as CAMs, indicating that they were not recommended these by their physicians.

A review showed that herbal therapy appeared to be effective in IBD, but the safety profile and long-term efficacy require further research [60]. Certain herbal therapies have been reported to have anti-inflammatory properties, and the use of these CAMs may theoretically cause interactions with conventional medicines. Herbal treatments may have toxic side effects, and some treatments are contraindicated and may be dangerous [49]. Liver toxicity has been described in the literature, for example, in relation to the consumption of Noni juice [61,62]; none of the IBD patients in the present study had used Noni. The results from the present study highlight the importance of healthcare professionals being aware of the potential effects, potential side effects, and interactions of such therapies and the fact that our patients are using these CAMs.

A number of herbal-based and traditional medical products are registered and controlled by the Swedish Medical Products Agency [63]. An European Union directive incorporated into the WHO has a strategy that encourages countries to incorporate CAMs into conventional healthcare [14]. Legalization in Sweden guides Swedish healthcare professionals on how to relate to and recommend these herbal products. This and the fact that patients with IBD do use these natural-based CAMs should be considered when making decisions in clinical care. However, there are some practical issues in Sweden. There is no general CAM policy and CAMs have not been officially approved in healthcare or within the educational system; thus, policy development is essential [64].

We conclude that patients with IBD in Sweden are using CAM treatment to a large extent (48.3%), but the control group used CAM to a greater extent (53.1%). This should be interpreted with caution because of the low response rate in the control group. Patients with IBD might very well be influenced by healthcare professionals showing disapproving attitudes toward patients' CAM use [55], thus hindering CAM use. The majority of the patients experienced positive effects from CAMs, mainly well-being, whereas no major improvement in disease symptoms was observed. In all, 40% of the patients had experienced adverse events from conventional medication, which may be a reason for CAM use; furthermore, the patients in this study experienced predominantly positive effects from CAM therapies. A high level of use of natural products was noted, more common in controls (22.3%) compared with patients with IBD (18.7%), but still used by about one-fifth of the patients. The possible risk of interaction with CAM must be considered when prescribing conventional medication. Consequently, an open-minded dialog with our patients is necessary to determine their CAM use.

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# **Conflicts of interest**

There are no conflicts of interest.

#### References

- 1 Hanauer SB. Inflammatory bowel disease: epidemiology, pathogenesis, and therapeutic opportunities. *Inflamm Bowel Dis* 2006; 12 (Suppl 1): S3–S9.
- 2 Ott C, Schölmerich J. Extraintestinal manifestations and complications in IBD. *Nat Rev Gastroenterol Hepatol* 2013; 10:585–595.

- 3 Stallmach A, Hagel S, Bruns T. Adverse effects of biologics used for treating IBD. Best Pract Res Clin Gastroenterol 2010; 24:167–182.
- 4 De Vroey B, Colombel JF. IBD in 2010: optimizing treatment and minimizing adverse events. Nat Rev Gastroenterol Hepatol 2011; 8:74–76.
- 5 Rawsthorne P, Shanahan F, Cronin NC, Anton PA, Löfberg R, Bohman L, Bernstein CN. An international survey of the use and attitudes regarding alternative medicine by patients with inflammatory bowel disease. *Am J Gastroenterol* 1999; 94:1298–1303.
- 6 Bernstein CN. Complementary and alternative medicine use by patients with inflammatory bowel disease: are Canadian physicians failing with conventional therapy, or not? *Can J Gastroenterol* 2004; 18:47–48. discussion 8.
- 7 Bensoussan M, Jovenin N, Garcia B, Vandromme L, Jolly D, Bouché O, *et al.* Complementary and alternative medicine use by patients with inflammatory bowel disease: results from a postal survey. *Gastroenterol Clin Biol* 2006; 30:14–23.
- 8 Opheim R, Bernklev T, Fagermoen MS, Cvancarova M, Moum B. Use of complementary and alternative medicine in patients with inflammatory bowel disease: results of a cross-sectional study in Norway. *Scand J Gastroenterol* 2012; 47:1436–1447.
- 9 Weizman AV, Ahn E, Thanabalan R, Leung W, Croitoru K, Silverberg MS, et al. Characterisation of complementary and alternative medicine use and its impact on medication adherence in inflammatory bowel disease. *Aliment Pharmacol Ther* 2012; 35:342–349.
- 10 Hilsden RJ, Verhoef MJ, Rasmussen H, Porcino A, DeBruyn JC. Use of complementary and alternative medicine by patients with inflammatory bowel disease. *Inflamm Bowel Dis* 2011; 17:655–662.
- 11 Langhorst J, Anthonisen IB, Steder-Neukamm U, Lüdtke R, Spahn G, Michalsen A, Dobos GJ. Amount of systemic steroid medication is a strong predictor for the use of complementary and alternative medicine in patients with inflammatory bowel disease: results from a German national survey. *Inflamm Bowel Dis* 2005; 11:287–295.
- 12 Langmead L, Chitnis M, Rampton DS. Use of complementary therapies by patients with IBD may indicate psychosocial distress. *Inflamm Bowel Dis* 2002; 8:174–179.
- 13 Cámara RJ, Schoepfer AM, Pittet V, Begré S, von Känel R. Swiss Inflammatory Bowel Disease Cohort Study (SIBDCS) Group. Mood and nonmood components of perceived stress and exacerbation of Crohn's disease. *Inflamm Bowel Dis* 2011; 17:2358–2365.
- 14 WHO. WHO traditional medicine strategy 2014–2023. Geneva: World Health Organization; 2013.
- 15 Wiesener S, Falkenberg T, Hegyi G, Hök J, Roberti di Sarsina P, Fønnebø V. Legal status and regulation of complementary and alternative medicine in Europe. *Forsch Komplementmed* 2012; 19 (Suppl 2):29–36.
- 16 National Center for Complementary and Integrative Health (NCCIH). Complementary, alternative, or integrative health: What's in a name?; 2008. Available at: http://nccih.nih.gov. [Accessed 30 June 2016].
- 17 WHO. Legal status of traditional medicine and complementary/alternative medicine (WHO/EDM/TRM/20012). Geneva, Switzerland: WHO Unit on Traditional Medicine; 2002.
- 18 Thorne S, Paterson B, Russell C, Schultz A. Complementary/alternative medicine in chronic illness as informed self-care decision making. *Int J Nurs Stud* 2002; 39:671–683.
- 19 Langhorst J, Wulfert H, Lauche R, Klose P, Cramer H, Dobos GJ, Korzenik J. Systematic review of complementary and alternative medicine treatments in inflammatory bowel diseases. *J Crohns Colitis* 2015; 9:86–106.
- 20 Joos S. Review on efficacy and health services research studies of complementary and alternative medicine in inflammatory bowel disease. *Chin J Integr Med* 2011; 17:403–409.
- 21 Pittler MH, Ernst E. Systematic review: hepatotoxic events associated with herbal medicinal products. *Aliment Pharmacol Ther* 2003; 18:451–471.
- 22 Rahimi R, Mozaffari S, Abdollahi M. On the use of herbal medicines in management of inflammatory bowel diseases: a systematic review of animal and human studies. *Dig Dis Sci* 2009; 54:471–480.
- 23 Triantafyllidi A, Xanthos T, Papalois A, Triantafillidis JK. Herbal and plant therapy in patients with inflammatory bowel disease. *Ann Gastroenterol* 2015; 28:210–220.
- 24 Langmead L, Makins RJ, Rampton DS. Anti-inflammatory effects of Aloe vera gel in human colorectal mucosa in vitro. Aliment Pharmacol Ther 2004; 19:521–527.
- 25 Oz HS, Chen TS, McClain CJ, de Villiers WJ. Antioxidants as novel therapy in a murine model of colitis. J Nutr Biochem 2005; 16:297–304.
- 26 Oz HS, Chen T, de Villiers WJ. Green tea polyphenols and sulfasalazine have parallel anti-inflammatory properties in colitis models. *Front Immunol* 2013; 4:132.

- 27 Ferguson LR, Shelling AN, Browning BL, Huebner C, Petermann I. Genes, diet and inflammatory bowel disease. *Mutat Res* 2007; 622:70–83.
- 28 Ben-Arye E, Goldin E, Wengrower D, Stamper A, Kohn R, Berry E. Wheat grass juice in the treatment of active distal ulcerative colitis: a randomized double-blind placebo-controlled trial. *Scand J Gastroenterol* 2002; 37:444–449.
- 29 Biedermann L, Mwinyi J, Scharl M, Frei P, Zeitz J, Kullak-Ublick GA, et al. Bilberry ingestion improves disease activity in mild to moderate ulcerative colitis – an open pilot study. J Crohns Colitis 2013; 7:271–279.
- 30 Krebs S, Omer TN, Omer B. Wormwood (Artemisia absinthium) suppresses tumour necrosis factor alpha and accelerates healing in patients with Crohn's disease – a controlled clinical trial. *Phytomedicine* 2010; 17:305–309.
- 31 Omer B, Krebs S, Omer H, Noor TO. Steroid-sparing effect of wormwood (*Artemisia absinthium*) in Crohn's disease: a double-blind placebo-controlled study. *Phytomedicine* 2007; 14:87–95.
- 32 Clarke JO, Mullin GE. A review of complementary and alternative approaches to immunomodulation. *Nutr Clin Pract* 2008; 23:49–62.
- 33 Weiss A, Friedenberg F. Patterns of cannabis use in patients with inflammatory bowel disease: a population based analysis. *Drug Alcohol Depend* 2015; 156:84–89.
- 34 Chen ZS, Nie ZW, Sun QL. Clinical study in treating intractable ulcerative colitis with traditional Chinese medicine. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 1994; 14:400–402.
- 35 Lang A, Salomon N, Wu JC, Kopylov U, Lahat A, Har-Noy O, et al. Curcumin in combination with mesalamine induces remission in patients with mild-to-moderate ulcerative colitis in a randomized controlled trial. *Clin Gastroenterol Hepatol* 2015; 13:1444.e1–1449.e1.
- 36 Hanai H, Sugimoto K. Curcumin has bright prospects for the treatment of inflammatory bowel disease. *Curr Pharm Des* 2009; 15:2087–2094.
- 37 Gionchetti P, Rizzello F, Habal F, Morselli C, Amadini C, Romagnoli R, Campieri M. Standard treatment of ulcerative colitis. *Dig Dis* 2003; 21:157–167.
- 38 Shen J, Zuo ZX, Mao AP. Effect of probiotics on inducing remission and maintaining therapy in ulcerative colitis, Crohn's disease, and pouchitis: meta-analysis of randomized controlled trials. *Inflamm Bowel Dis* 2014; 20:21–35.
- 39 Gionchetti P, Rizzello F, Helwig U, Venturi A, Lammers KM, Brigidi P, et al. Prophylaxis of pouchitis onset with probiotic therapy: a doubleblind, placebo-controlled trial. *Gastroenterology* 2003; 124:1202–1209.
- 40 Serban DE. Microbiota in inflammatory bowel disease pathogenesis and therapy: is it all about diet? *Nutr Clin Pract* 2015; 30:760–779.
- 41 Khandalavala BN, Nirmalraj MC. Resolution of severe ulcerative colitis with the specific carbohydrate diet. Case Rep Gastroenterol 2015; 9:291–295.
- 42 Joos S, Brinkhaus B, Maluche C, Maupai N, Kohnen R, Kraehmer N, et al. Acupuncture and moxibustion in the treatment of active Crohn's disease: a randomized controlled study. *Digestion* 2004; 69:131–139.
- 43 Joos S, Wildau N, Kohnen R, Szecsenyi J, Schuppan D, Willich SN, et al. Acupuncture and moxibustion in the treatment of ulcerative colitis: a randomized controlled study. *Scand J Gastroenterol* 2006; 41:1056–1063.
- 44 Oxelmark L, Magnusson A, Löfberg R, Hillerås P. Group-based intervention program in inflammatory bowel disease patients: effects on quality of life. *Inflamm Bowel Dis* 2007; 13:182–190.
- 45 Timmer A, Preiss JC, Motschall E, Rücker G, Jantschek G, Moser G. Psychological interventions for treatment of inflammatory bowel disease. *Cochrane Database Syst Rev* 2011; 2:CD006913.
- 46 Neilson K, Ftanou M, Monshat K, Salzberg M, Bell S, Kamm MA, et al. A controlled study of a group mindfulness intervention for individuals living with inflammatory bowel disease. *Inflamm Bowel Dis* 2016; 22:694–701.
- 47 Esters P, Dignass A. Complementary therapies in inflammatory bowel diseases. *Curr Drug Targets* 2014; 15:1079–1088.
- 48 Posadzki P, Watson L, Ernst E. Herb-drug interactions: an overview of systematic reviews. Br J Clin Pharmacol 2013; 75:603–618.
- 49 Yang HY, Chen PC, Wang JD. Chinese herbs containing aristolochic acid associated with renal failure and urothelial carcinoma: a review from epidemiologic observations to causal inference. *Biomed Res Int* 2014; 2014:569325.
- 50 Falkenberg T, Hök J, Sundberg T. Research group integrative care. Department of Neurobiology, Care Sciences and Society, Web site: Karolinska Institutet; 2008. Available at: http://ki.se/en/nvs/researchgroup-integrative-care. [Accessed 30 June 2016].

- 51 Joos S, Rosemann T, Szecsenyi J, Hahn EG, Willich SN, Brinkhaus B. Use of complementary and alternative medicine in Germany – A survey of patients with inflammatory bowel disease. *BMC Complement Altern Med* 2006; 6:19.
- 52 Gangl A. Alternative and complementary therapies for inflammatory bowel disease. Nat Clin Pract Gastroenterol Hepatol 2006; 3:180–181.
- 53 Hilsden RJ, Verhoef MJ, Best A, Pocobelli G. Complementary and alternative medicine use by Canadian patients with inflammatory bowel disease: results from a national survey. *Am J Gastroenterol* 2003; 98:1563–1568.
- 54 Rawsthorne P, Clara I, Graff LA, Bernstein KI, Carr R, Walker JR, et al. The Manitoba Inflammatory Bowel Disease Cohort Study: a prospective longitudinal evaluation of the use of complementary and alternative medicine services and products. *Gut* 2012; 61:521–527.
- 55 Lindberg A, Fossum B, Karlen P, Oxelmark L. Experiences of complementary and alternative medicine in patients with inflammatory bowel disease – a qualitative study. *BMC Complement Altern Med* 2014; 14:407.
- 56 Siegel CA. Review article: explaining risks of inflammatory bowel disease therapy to patients. *Aliment Pharmacol Ther* 2011; 33:23–32.
- 57 lijima H, Shinzaki S, Takehara T. The importance of vitamins D and K for the bone health and immune function in inflammatory bowel disease. *Curr Opin Clin Nutr Metab Care* 2012; 15:635–640.

- 58 Barbalho SM, Goulart Rde A, Quesada K, Bechara MD, de Carvalho Ade C. Inflammatory bowel disease: can omega-3 fatty acids really help? *Ann Gastroenterol* 2016; 29:37–43.
- 59 Ghouri YA, Richards DM, Rahimi EF, Krill JT, Jelinek KA, DuPont AW. Systematic review of randomized controlled trials of probiotics, prebiotics, and synbiotics in inflammatory bowel disease. *Clin Exp Gastroenterol* 2014; 7:473–487.
- 60 Ng SC, Lam YT, Tsoi KK, Chan FK, Sung JJ, Wu JC. Systematic review: the efficacy of herbal therapy in inflammatory bowel disease. *Aliment Pharmacol Ther* 2013; 38:854–863.
- 61 Mrzljak A, Kosuta I, Skrtic A, Kanizaj TF, Vrhovac R. Drug-induced liver injury associated with Noni (*Morinda citrifolia*) juice and phenobarbital. *Case Rep Gastroenterol* 2013; 7:19–24.
- 62 Stadlbauer V, Fickert P, Lackner C, Schmerlaib J, Krisper P, Trauner M, Stauber RE. Hepatotoxicity of NONI juice: report of two cases. *World J Gastroenterol* 2005; 11:4758–4760.
- 63 Swedish Medical Products Agency. Herbal medicinal products, traditional herbal medicinal products and natural remedies; 2016. Available at: https:// lakemedelsverket.se/malgrupp/Foretag/Vaxtbaserade-lakemedel-traditionellavaxtbaserade-lakemedel-och-naturlakemedel/. [Accessed 30 June 2016].
- 64 Knox KE, Fønnebø V, Falkenberg T. Emerging complementary and alternative medicine policy initiatives and the need for dialogue. J Altern Complement Med 2009; 15:959–962.