Dietary Intake and Risk of Developing Inflammatory Bowel Disease: A Systematic Review of the Literature

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OBJECTIVES: **The incidence of inflammatory bowel disease (IBD) is increasing. Dietary factors such as the spread of the "Western" diet, high in fat and protein but low in fruits and vegetables, may be associated with the increase. Although many studies have evaluated the association between diet and IBD risk, there has been no systematic review.**

METHODS: **We performed a systematic review using guideline-recommended methodology to evaluate the association between pre-illness intake of nutrients (fats, carbohydrates, protein) and food groups (fruits, vegetables, meats) and the risk of subsequent IBD diagnosis. Eligible studies were identified via structured keyword searches in PubMed and Google Scholar and manual searches.**

RESULTS: **Nineteen studies were included, encompassing 2,609 IBD patients (1,269 Crohn's disease (CD) and 1,340 ulcerative colitis (UC) patients) and over 4,000 controls. Studies reported a positive association between high intake of saturated fats, monounsaturated fatty acids, total polyunsaturated fatty acids (PUFAs), total omega-3 fatty acids, omega-6 fatty acids, mono- and disaccharides, and meat and increased subsequent CD risk. Studies reported a negative association between dietary fiber and fruits and subsequent CD risk. High intakes of total fats, total PUFAs, omega-6 fatty acids, and meat were associated with an increased risk of UC. High vegetable intake was associated with a decreased risk of UC.**

CONCLUSIONS: **High dietary intakes of total fats, PUFAs, omega-6 fatty acids, and meat were associated with an increased risk of CD and UC. High fiber and fruit intakes were associated with decreased CD risk, and high vegetable intake was associated with decreased UC risk.**

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INTRODUCTION

The incidence of inflammatory bowel disease (IBD) is rising in Europe and North America, as well as in areas where IBD was previously thought to be uncommon (e.g., China, South Korea, Puerto Rico) (1–3). The spread of the "Western" diet, high in fat and protein but low in fruits and vegetables, has been proposed as a possible explanation for the recent increase in IBD incidence (4).

Diet may influence gut inflammation through several biologically plausible mechanisms, including antigen presentation, change in prostaglandin balance, and alteration of the microflora (5,6). However, the association between pre-illness diet and IBD risk has not been clearly demonstrated (7–12).

There had been no systematic review of the association between dietary intake and the risk of development of IBD. We therefore performed a systematic review of studies on the influence of pre-illness intake of nutrients (fats, carbohydrates, and protein) and food groups (fruits, vegetables, and meats) on the risk of developing IBD.

METHODS

Search strategy

Two investigators (J.K.H. and B.A.) independently conducted structured searches of PubMed and Google Scholar from 1966 to August 2010, using the medical subject heading (MeSH) terms "causality" and "etiology," using the explode function for subgroup

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Table 1. Characteristics of 19 studies included in the systematic review of diet and risk of developing inflammatory bowel disease

Study	Year	Country	Design	Method	Recruitment: cases
Miller (7)	1976	Germany	CC	Diet history (questionnaire and interview)	Clinic Single center
Kasper (16)	1979	Germany	CC	Diet history (interview)	Unspecified Single center
Thornton (17)	1979	UK	CC	Diet history (interview)	Unspecified Single center
Thornton (31)	1980	UK	CC	Diet history (interview)	Unspecified Single center
Jarnerot (24)	1983	Sweden	CC	Diet history (interview)	Unspecified Single center
Gilat (25)	1987	US, Denmark, Italy, Netherlands, UK, Sweden, Israel, Canada	CC	Diet history (questionnaire and interview)	Hospital and clinic Multicenter
Higashi (27)	1991	Japan	CC	Diet history (interview)	Hospital and clinic Multicenter
Kurata (28)	1994	Japan	CC	Diet history (questionnaire and interview)	Hospital Multicenter
Tragnone (18)	1995	Italy	CC	Diet history (interview)	Unspecified Multicenter
Reif (21)	1997	Israel	CC	Diet history (interview)	Referral Single center
Geerling (22)	2000	Netherlands	CC	Diet history (interview) and FFQ	Clinic Multicenter
Sakamoto (14)	2005	Japan	CC	FFQ	Hospital Multicenter
Bernstein (29)	2006	Canada	CC	Diet history (questionnaire)	Registry
Halfvarson (26)	2006	Sweden, Denmark	CC	Diet history (questionnaire)	Registry
Amre (4)	2007	Canada	CC	FFQ (YAQ)	Referral Multicenter
Hart (19)	2008	EPIC	Nested CC	FFQ	Multicenter
Hart (23)	2009	EPIC	Nested CC	FFQ	Multicenter
Jantchou (15)	2010	France	Cohort	Diet history (questionnaire)	Multicenter
John (20)	2010	EPIC: Norfolk, UK	Nested CC	7-day food diary	Multicenter

CC, case control; CD, Crohn's disease; EPIC, European Prospective Investigation into Cancer and Nutrition: UK, Denmark, Germany, Sweden, and Italy; FFQ, food frequency questionnaire; ht, height; IBD, inflammatory bowel disease; NA, not available; SES, socioeconomic status; UC, ulcerative colitis; wt, weight; YAQ, Youth Adolescent Questionnaire.

Table 1. Continued

Recruitment: controls	UC	CD	Controls	Adjustment	Mean age of cases at time of study (y)	Sex (% female)	Time from IBD diagnosis to study
Clinic Orthopedic	0	34	34	Age, sex, ht, wt, occupation	33	NA	NA
Unspecified	0	35	70	Age, sex, SES	30	57.1	1–2 y
Clinic Orthopedic	0	30	30	Age, sex, SES, marital status	33	67	5 mo
Clinic Orthopedic	30	0	30	Age, sex, SES, marital status	NA	43	2 mo
Clinic Orthopedic	30	30	30	Age, sex	CD 21 UC 19	CD 56.7 UC 36.7	<3 y
Population-based registry	196	302	996	Age, sex	20–25	Unspecified	Unspecified
Hospital and clinic Multicenter	50	0	50	Age, sex	39.3	52	0–20 y
Hospital Multicenter	101	0	143	Age, sex, inpatient status	20–29 (median)	44.5	<3 y
Unspecified Multicenter	53	51	208	Age, sex, geography	UC 39.5 CD 32	UC 45 CD 35	<6 mo
Population-based registry	54	33	144	Age, sex, geography, SES	UC 30.1 CD 29.1	UC 45 CD 39	<1 y
General practice registry	43	0	43	Age, sex	37.8	46.5	<6 mo
Hospital Multicenter	111	128	219	Age, sex	20–29 (median)	UC 48 CD 27.8	<3 y
Population-based registry	217	364	433	Age, sex, geography	18–50	UC 54.6 CD 62.6	NA
Population-based registry	125	102	227	Twin	UC 27 (median) CD 25 (median)	UC 50 CD60	17 y
Orthopedic and population-based registry	0	130	202	Age, sex, geography, time of diagnosis	14.2	40.8	<1 mo
EPIC	139	0	556	Age, sex, center, time of recruitment	58.8 (median)	UC 51.1	NA
EPIC	126	0	504	Age, sex, center, time of recruitment	60 (median)	47	NA
NA	43	30	NA	NA	CD 55.6 UC 56.7	100	NA
EPIC	22	0	91	Age, sex, center, time of recruitment	72.1 (median)	45.5	NA

Table 2. Dietary fat intake and odds of developing inflammatory bowel disease

Study	Year	IBD type[2]	Intake level	Odds ratio adjustment	Total fats	Saturated	MUFAs
Sakamoto	2005	CD	Highest quartile	Adjusted for energy intake, age, sex, geography, education, smoking	2.86 (1.39–5.90)	1.46 (0.71–2.99)	2.49 (1.23–5.03)
			Cut point (g/d)		65.5	19	24.4
Amre	2007	CD	Highest quartile	Crude OR	2.25 (1.18–4.27)	2.15 (1.13–4.07)	2.24 (1.17–4.29)
				Adjusted for total energy intake, age, sex, BMI	2.3 (0.67–7.69)	1.81 (0.59–5.61)	2.41 (0.72–8.07)
			Cut point (g/d)		96.5	35.4	35.9
Jantchou	2010	CD	Highest tertile	Adjusted HR for energy	0.98 (0.25–3.88)	–	–
			Cut point (g/d)		NA	–	–
Reif	1997	UC	"High" intake	Adjusted for energy intake	3.94 (0.92–16.89)	2.98 (0.92–9.62)	3.66 (1.06–12.58)
			Cut point (g/d)		119	66	55
Geerling	2000	UC	"High" intake	Adjusted for energy intake	4.1 (0.6–28.4)	3.7 (0.4–30.9)	33.9 (2.6–443.1)
			Cut point (g/d)		NA	NA	NA
Sakamoto	2005	UC	Highest quartile	Adjusted for energy intake, age, sex, geography, education, smoking	2.34 (1.02–5.39)	1.56 (0.69–3.52)	2.61 (1.10–6.22)
			Cut point (g/d)		65.5	19	24.4
Hart	2008	UC	Highest quartile	Nutrient as % of total intake	1.13 (0.65–1.99)	0.95 (0.46–1.98)	1.10 (0.57–2.14)
			Cut point (% of daily energy)		Women 37 Men 39	Women 15.5 Men 15.5	Women 13.6 Men 13.6
Hart	2009	UC	Highest quartile	Crude OR	–	–	(Oleic) 1.01 (0.55–1.89)
				Adjusted for age at recruitment, sex, center, smoking, total energy intake	–	–	1.21 (0.48–3.01)
				Adjusted for age at recruitment, sex, center, smoking, total energy intake, and other fatty acids	–	–	0.78 (0.26–2.4)
			Cut point (g/d)		–	–	Women 28.3 Men 33.5
Jantchou	2010	UC	Highest tertile	Adjusted HR for energy	1.47 (0.56–3.84)	–	–
			Cut point (g/d)		NA	–	–
John	2010	UC	Highest tertile	Adjusted for age at recruitment, sex, center, smoking, total energy intake	–	–	–
				Adjusted for age at recruitment, sex, center, smoking, total energy intake, and other fatty acids	–	–	–
			Cut point (g/d)		–	–	–

BMI, body mass index; CD, Crohn's disease; DHA, docosahexonenoic acid; EPA, eicosapentaenoic acid; HR, hazard ratio; IBD, inflammatory bowel disease; NA, not available; OR, odds ratio; UC, ulcerative colitis.

Table 2. Continued

PUFA				
Total PUFAs	Total omega-3	DHA	EPA	Omega-6
2.31 (1.12–5.03)	3.24 (1.52–6.88)	–	–	2.57 (1.24–5.32)
16.3	3.2	–	–	12.9
2.53 (1.32–4.82)	1.76 (0.91–3.40)	(Long-chain omega-3) 0.66 (0.33–1.3)		2.22 (1.16–2.4)
2.38 (0.84–6.71)	1.42 (0.51–3.92)	0.44 (0.19–1)		1.9 (0.7–5.21)
18.1	205.5 (mg)	130 (mg)		17.1
–	–	–	–	–
–	–	–	–	–
6.54 (1.45–29.68)	–	–	–	–
30	–	–	–	–
5.1 (1–26.7)	–	–	–	1.9 (0.4–8.6)
NA				NA
1.66 (0.68–4.04)	1.72 (0.75–3.96)	–	–	1.62 (0.68–3.84)
16.3	3.2	–	–	12.9
1.56 (0.87–2.77)	–	–	–	–
Women 6.5	–	–	–	–
Men 6.6				
–	(α-linoleic) 1.11 (0.62–1.99)	0.7 (0.3–1.37)	1 (0.52–1.91)	1.85 (1.03–3.32)
–	1.46 (0.67–3.14)	0.64 (0.32–1.3)	0.96 (0.49–1.88)	2.49 (1.23–5.07)
–	1.28 (0.46–3.58)	0.23 (0.06–0.97)	2.58 (0.66 –10.05)	2.31 (0.99–5.36)
–	Women 1.7	Women 0.33	Women 0.17	Women 12.6
	Men 2.1	Men 0.41	Men 0.19	Men 14.9
–	–	–	–	–
–	–	–	–	–
–	0.28 (0.07–1.11)	0.21 (0.05–0.83)	0.31 (0.08–1.22)	–
–	0.31 (0.07–1.27)	0.17 (0.04–0.78)	0.25 (0.06–1.07)	–
–	1.6	0.13	0.09	–

terms with operators ("and," "or") for "inflammatory bowel disease," "ulcerative colitis," "Crohn's," "diet," and "nutrition." There were no language restrictions. Eligible studies and relevant review articles were hand-searched to identify additional studies missed by database searches.

Eligibility criteria

Fully published case-control and cohort studies of the association between pre-illness diet and IBD risk were eligible for inclusion. Titles and abstracts were screened to identify relevant articles, which were subsequently assessed for the following criteria: pre-diagnosis diet evaluation in IBD cases, description of patient inclusion or exclusion criteria, and adjustment of risk estimates for a minimum of age and sex. Studies were excluded if they investigated diet as therapy for IBD or were ecological studies. Both investigators independently reviewed all identified citations to determine their eligibility. Discrepancies were resolved by consensus of the study team.

Data extraction

With the use of standardized forms, the following data points were collected for each study: location and design, sampling frame, method of case and control recruitment, method of diet evaluation, number of patients with ulcerative colitis (UC) or Crohn's disease (CD) and of controls, age at IBD diagnosis, sex distribution, length of time from IBD diagnosis to study recruitment, and the variables adjusted for in the calculation of diet–risk estimates.

Dietary data were collected for nutrients (dietary fats, carbohydrates, and proteins) and food groups (fruits, vegetables, fiber, meat, fish, dairy, and eggs). Dietary fat intake was further categorized as total fat intake, saturated fat, monounsaturated fatty acids (MUFAs), total polyunsaturated fatty acids (PUFAs), omega-3 fatty acids, long-chain omega-3 fatty acids, and omega-6 fatty acids. Carbohydrate intake was categorized as total carbohydrates, mono- and disaccharides, and polysaccharides. Protein intake was categorized as total protein, animal protein, and vegetable protein.

Risk estimates were reported for highest level of intake, with daily-intake cutoffs included where data were available. In studies that reported on overlapping study populations, only the largest report was included (4,13). For risk estimates, we report crude and adjusted odds ratios (ORs) with factors for risk-estimate adjustment. Given the heterogeneity among studies, quantitative summaries and pooling of the data were not performed.

RESULTS

Search results

A total of 1,085 publications were identified. Of these 68 articles reviewed in English, Spanish, German, Japanese, or Slovak, 19 met the review inclusion criteria (**Table 1**). Case-control study design was used in 18 studies, and cohort design was used in one study. A total of 2,609 patients with IBD were described in these studies (1,340 UC and 1,269 CD patients). Eighteen studies included adult patients, and one included only pediatric patients. Twelve studies reported time from diet ascertainment to IBD diagnosis, with five studies report-

Table 3. Dietary carbohydrate intake and odds of developing inflammatory bowel disease

Study	Year	IBD type	Level of intake	Odds ratio adjustment	Total carbohydrates	Mono- and disaccharides	Polysaccharides
Tragnone	1995	CD	High	Crude RR	4.1 (1.8–9.4)	(Sugar)	(Starch)
						3.5 (1.5–8.1)	5.5 (2.1–14.2)
			Cut point (g/d)		300	100	200
Reif	1997	CD	"High" intake	Adjusted for energy intake	–	1.37 (0.37–5.09)	–
			Cut point (g/d)		–	163	–
Sakamoto	2005	CD	Highest quartile	Adjusted for energy intake	0.53 (0.27–1.03)	–	–
			Cut point (g/d)		300	–	–
Amre	2007	CD	Highest quartile	Crude OR	1.42 (0.77–2.61)	–	–
				Adjusted for total energy intake, age, sex, BMI	0.38 (0.09–1.63)	–	–
			Cut point (g/d)		369.8	–	–
Jantchou	2010	CD	Highest tertile	Adjusted HR for energy	1.31 (0.42–4.14)	–	–
				Cut point (g/d)	NA	–	–
Tragnone	1995	UC	High	Crude RR	8.1 (3.6–18.4)	(Sugar)	(Starch)
						3.2 (1.5–6.9)	6 (2.5–14.7)
			Cut point (g/d)		300	100	200
Reif	1997	UC	"High" intake	Adjusted for energy intake	–	3.98 (1.02–15.52)	–
			Cut point (g/d)		–	163	–
Geerling	2000	UC	"High" intake	Adjusted for energy intake	2.2 (0.4–11.8)	3 (0.7–13.4)	0.9 (0.1–6.4)
			Cut point (g/d)		NA	NA	NA
Sakamoto	2005	UC	Highest quartile	Adjusted for energy intake	0.66 (0.31–1.41)	–	–
			Cut point (g/d)		300	–	–
Hart	2008	UC	Highest quartile	Nutrient as % of total intake	1.12 (0.63–1.97)	(Sugars)	(Starch)
						0.95 (0.46–1.98)	0.52 (0.19–1.46)
			Cut point (% of daily energy)		Women 51.7 Men 48.8	Women 23.2 Men 23.2	Women 25.1 Men 25.1
Jantchou	2010	UC	Highest tertile	Adjusted HR for energy	0.51 (0.24–1.08)	–	–
				Cut point (g/d)	NA	–	–

BMI, body mass index; CD, Crohn's disease; HR, hazard ratio; IBD, inflammatory bowel disease; NA, not available; OR, odds ratio; RR, relative risk; UC, ulcerative colitis.

ing a mean of less than one year from IBD diagnosis. Four studies, including one cohort study, used prospective diet ascertainment (dietary evaluation performed before IBD diagnosis).

Dietary fats

Crohn's disease. Three studies reported on dietary fats and CD risk (4,14,15) (**Table 2**); two reported an association between high total fat intake and increased CD risk, with one statistically significant (4,14,15). However, the only study with prospective diet ascertainment showed no significant association (15).

Two studies reported that high MUFA intake was associated with increased risk of CD (OR range 2.41–2.49), with one statistically significant (4,14). High total PUFA intake and total omega-3 fatty acid intake were also associated with increased CD risk in two studies, one statistically significant (4). High omega-6 fatty acid intake was associated with increased CD risk in two studies, with one statistically significant (4,14). However, three other studies (16–18) evaluated the association of total fat, saturated fat, MUFAs, and total PUFAs and reported no significant differences in pre-illness intake between CD patients and controls.

Ulcerative colitis. Seven studies reported on dietary fats and risk of UC (14,15,19–23). All five studies evaluating total fat reported an association between high intake and increased risk of UC (OR range 1.13–4.1), with one study statistically significant (14,15,19,22). Two studies with prospective diet ascertainment

Table 4. Dietary protein intake and odds of developing inflammatory bowel disease

Study	Year	IBD type	Level of intake	Odds ratio adjustment	Total protein	Animal protein	Vegetable protein
Tragnone	1995	CD	High	Crude RR	1.6 (NA)	–	–
			Cut point (g/d)		100	–	–
Reif	1997	CD	"High" intake	Adjusted for energy intake	1.47 (0.28–7.72)	–	–
			Cut point (g/d)		98	–	–
Sakamoto	2005	CD	Highest quartile	Adjusted for energy intake	2.06 (0.99–4.28)	–	–
			Cut point (g/d)		74.2	–	–
Amre	2007	CD	Highest quartile	Crude OR	1.38 (0.75–2.56)	–	–
				Adjusted for total energy intake, age, sex, BMI	0.45 (0.13–1.5)	–	–
			Cut point (g/d)		106.9	–	–
Jantchou	2010	CD	Highest tertile	Adjusted HR for energy	3.34 (0.90–12.4)	2.70 (0.69–10.52)	1.04 (0.28–3.80)
			Cut point (g/kg)		1.72	NA	NA
Tragnone	1995	UC	High	Crude RR	3.7 (1.6–8.6)	–	–
			Cut point (g/d)		100	–	–
Reif	1997	UC	"High" intake	Adjusted for energy intake	1.47 (0.28–7.72)	–	–
			Cut point (g/d)		120	–	–
Geerling	2000	UC	"High" intake	Adjusted for energy intake	0.2 (0.02–1.5)	0.2 (0.04–1.1)	2.4 (0.6–10.4)
			Cut point (g/d)		NA	NA	NA
Sakamoto	2005	UC	Highest quartile	Adjusted for energy intake	1.36 (0.58– 3.2)	–	–
			Cut point (g/d)		74.2	–	–
Hart	2008	UC	Highest quartile	Nutrient as % of total intake	1.13 (0.65–1.99)	–	–
			Cut point (% of daily energy)		Women 17.6 Men 48.8	–	–
Jantchou	2010	UC	Highest tertile	Adjusted HR for energy intake, body weight	3.24 (1.07–9.84)	3.29 (1.34–8.04)	1.70 (0.59–4.81)
			Cut point (g/kg)		1.72	NA	NA

BMI, body mass index; CD, Crohn's disease; HR, hazard ratio; IBD, inflammatory bowel disease; NA, not available; OR, odds ratio; RR, relative risk; UC, ulcerative colitis.

were not statistically significant. Four studies reported a positive association between MUFAs and UC, with three statistically significant (OR range 1.1–33.9) (14,19,21,22). High total PUFA intake was associated with increased UC risk in all four studies, two statistically significant (OR range 1.56–6.54). Total omega-3 fatty acids were associated with increased UC risk in two studies and decreased risk in one study, but the difference was not statistically significant in any of the studies. Two studies reported that high intake of docosahexonenoic acid was associated with decreased risk of UC; both were statistically significant (OR range 0.17–0.23). High omega-6 fatty acid intake was associated with increased risk of UC in three studies, but none was statistically significant (OR range 1.62–2.31). Two additional studies evaluated total fat, saturated fat, MUFAs, and total PUFAs and did not observe any difference in pre-illness intake between UC patients and controls (6,18).

Carbohydrates

Crohn's disease. Five studies reported on carbohydrates and CD (**Table 3**), and no consistent associations were observed (4,14,15,18). Two studies reported that high intake of monosaccharides and disaccharides was associated with an increased risk of CD (OR range 1.37–3.5) (18,21), with one study statistically significant. A single study reported an association between high polysaccharide intake and increased risk of CD (OR 5.5, 95% confidence interval (CI) 2.1–14.2). Three additional studies reporting only frequencies observed that CD patients consumed more mono- and disaccharides before illness than controls, all statistically significant (7,16,24).

Ulcerative colitis. Of six studies, none observed a consistent association between total carbohydrate intake and UC risk (14,15,18,19,21,22). Three of four studies reported an association

Table 5. Dietary intake of fruits, vegetables, and fiber and odds of developing inflammatory bowel disease

Study	Year	IBD type	Intake level	Odds adjustment ratio	Fruit		Vegetables	Dietary fiber
Gilat	1987	CD	High	Crude OR		0.65 (0.43–0.99)		–
				Adjusted for familiy history, recurrent infections, eczema		0.58 (0.37–0.91)		–
			Frequency			>4/day		–
Reif	1997	CD	"High" intake	Adjusted for energy intake	0.65 (0.25–1.65)		1.28 (0.55–2.95)	0.4 (0.10–1.65)
			Cut point (g/d)		295		329	26
Sakamoto	2005	CD	Highest quartile	Adjusted for energy intake	0.8 (0.38–1.66)		1.55 (0.76–3.17)	0.9 (0.43–1.86)
			Cut point (g/d)		136.3		197.2	12.6
Halfvarson	2006	CD	High	Crude OR	0.2 (0.1–0.9)		–	–
			Frequency		Daily		–	–
Amre	2007	CD	Highest quartile	Crude OR	0.49 (0.25–0.96)		0.71 (0.37–1.34)	0.51 (0.26–0)
				Adjusted for total energy intake, age, sex, BMI	0.37 (0.16–0.86)		0.69 (0.33–1.44)	0.12 (0.04–0.37)
			Cut point (g/d)		30		47	22.1
Gilat	1987	UC	High	Crude OR		0.67 (0.4–1.11)		–
				Adjusted for family history, recurrent infections, eczema		0.77 (0.45–1.35)		–
			Frequency			>4/day		–
Higashi	1991	UC	High	Crude RR	1.22 (0.47–3.20)		Fresh 0.42 (0.17–1.01)	–
							Cooked 2.00 (0.76–5.46)	
			Frequency		Daily		Daily	–
Kurata	1994	UC	Highest tertile	RR adjusted for sex, age, geography, inpatient status		0.6 (0.3–1.3)		–
			Cut point (g/d)			NA		–
Reif	1997	UC	High	Adjusted for energy intake	0.42 (0.13–1.38)		0.32 (0.09–1.12)	0.81 (0.27–2.47)
			Cut point (g/d)		295		329	26
Geerling	2000	UC	"High" intake	Adjusted for energy intake				0.7 (0.2–3.4)
			Cut point (g/d)					NA
Sakamoto	2005	UC	Highest quartile	Adjusted for energy intake	0.62 (0.29–1.32)		0.75 (0.35–1.62)	0.53 (0.24–1.01)
			Cut point (g/d)		136.3		197.2	12.6
Halfvarson	2006	UC	High	Crude OR	2.9 (0.9–9.4)		–	–
			Frequency		Daily		–	–
Hart	2008	UC			–	–	–	1.12 (0.59–2.11)
			Cut point (% of daily energy)		–	–	–	Women 23.3
								Men 23.9

BMI, body mass index; CD, Crohn's disease; HR, hazard ratio; IBD, inflammatory bowel disease; NA, not available; OR, odds ratio; RR, relative risk; UC, ulcerative colitis.

of high mono- and disaccharides and increased UC risk, with two statistically significant (OR range 0.95–3.98) (14,18,21,22). No consistent association was observed between polysaccharides and UC risk (18,19,22).

Protein

Crohn's disease. Of five studies that reported data on the association of protein intake and the development of CD (**Table 4**), four showed that high total protein was associated with increased risk of CD, whereas one reported a decreased risk of CD, with none statistically significant (OR range 0.45–3.34) (4,14,15,18,21). One study with prospective diet ascertainment reported a significant trend of increased risk of CD with increasing intake of protein ($P = 0.04$) (15).

Ulcerative colitis. Five of six studies reported an association of high total protein intake and increased risk of UC (OR range 0.2–3.7) (14,15,18,19,21,22); this was statistically significant in two studies (18,15). Both studies with prospective diet ascertainment reported an association of total protein with increased UC risk, with one statistically significant (15,19).

Two studies differentiated animal from vegetable sources of protein; one reported an increased risk of UC (OR 3.29, 95% CI 1.34–8.04) with high intake of animal protein, and the other showed no statistically significant association (15,22). Both studies reported a non-significant positive association of high vegetable protein with increased UC risk.

Fruits, vegetables, and fiber

Crohn's disease. Five studies reported data on fruit, vegetable, and fiber intake and CD risk (**Table 5**). All five reported that high fruit intake was associated with a decreased risk of CD, and the association was statistically significant in two—in those who consumed fruit more than once daily compared with less than weekly (OR 0.2, 95% CI 0.1–0.9) and in those who consumed fruit more than four times a day compared with those who consumed fruit less than once a day (OR 0.58, 95% CI 0.37–0.91) (4,14,21,25,26). Studies conflicted regarding vegetables, with no studies being statistically significant (4,14,21,25,26). All three studies providing data on dietary fiber and CD showed that high fiber intake decreased CD risk, with one study statistically significant in those consuming more than 22.1 g/d compared with less than 13.8 g/d (OR 0.12, 95% CI 0.04–0.37) (4,14,21).

Ulcerative colitis. Eight studies reported data on fruit, vegetable, and fiber intake and UC risk (14,19,21,22,25–28). None of those on fruit intake and UC was statistically significant (OR range 0.42–2.9) (14,21,25–28). High vegetable intake was associated with decreased CD risk in three studies, but none was statistically significant (OR range 0.32–0.75) (14,21,27). Of four studies reporting on dietary fiber and UC, three reported a decreased UC risk, but none was statistically significant (14,19,21,22). One study reported that UC patients had higher fiber intake before diagnosis compared with controls (mean 26.6 g daily vs. 22.3 g daily) (24).

Meat

Crohn's disease. Of five studies (**Table 6**), two reported an association between high meat intake and increased risk of CD, with one statistically significant (OR range 1.9–2.48) (14,29). Conflicting data were found regarding the association of fish (OR range 0.46–2.41) and eggs (OR range 0.4–1.76) with CD risk (4,14,21,26).

Ulcerative colitis. Of seven studies, five reported an association between high meat intake and increased risk of UC, with two studies statistically significant (OR range 1.30–2.62) (14,24,27–29). Three of four studies reported that high consumption of fish and seafood was associated with an increased risk of UC, with one statistically significant (OR 1.83, 95% CI 1.00–3.36) (14,21,24,27). Four of the five studies reported that a high consumption of eggs increased UC risk (14,15,21,26,27). No associations between dairy and UC were statistically significant (OR range 0.79–2.67) (14,15,27,28).

DISCUSSION

We performed a systematic review of the possible association between pre-diagnosis dietary intake and the risk of developing IBD and identified 19 studies (18 case-control and only one cohort) with 2,609 patients with IBD (1,340 UC and 1,269 CD patients). Studies reported increased risk of developing UC with high intake of total fat, PUFAs, omega-6 fatty acids, and meats, and increased risk of CD with high intake of PUFAs, omega-6 fatty acids, saturated fats, and meat. Decreased risk of CD, but not UC, was associated with high intake of dietary fiber and fruits. Lastly, there was no consistent association between total carbohydrate intake and IBD risk, even in studies reporting intake greater than double the recommended daily intake (130 mg total carbohydrates per day) (30).

Our review indicated a consistent association between high dietary fiber and decreased risk of CD, with the protective effect observed to be statistically significant in those consuming more than 22.1 g/d (30). Our review also observed that high intake of fruits is associated with a 73–80% decreased risk of CD. This association was confounded by dietary fiber intake and the fact that a diet high in fruits may conversely be low in fats and meats.

The association between high meat intake and IBD is unclear. The majority of studies also showed a positive association of total protein intake and IBD (87% to 148% increased risk), but it was statistically significant in only two. Moreover, the one study of total protein and CD that adjusted for age, sex, and body mass index in addition to energy reported a crude OR greater than 1, but this decreased to 0.45 with adjustment.

This systematic review has limitations. Pooling of data from different studies was not possible because of heterogeneity in study design, nutrient cutoffs, and study populations. Our decision to use full articles and not abstracts may have excluded studies in progress. This review is affected primarily by the limitations of the individual studies and potential publication bias against negative studies. IBD diagnosis could not be independently verified in the studies. The retrospective nature of the majority of studies

Table 6. Dietary intake of meat, fish, dairy, and eggs and odds of developing inflammatory bowel disease

Study	Year	IBD type	Intake level	Odds ratio adjustment	Meat		Fish	Dairy	Eggs
Reif	1997	CD	"High" intake	Adjusted for energy intake	–	–	0.57 (0.16–2.03)	–	1.76 (0.58–5.39)
			Cut point (g/d)		–	–	20	–	20
Sakamoto	2005	CD	Highest quartile	Adjusted for energy intake	1.90 (0.95–3.78)		2.41 (1.18–4.89)	0.50 (0.24–1.05)	1.42 (0.72–2.83)
			Cut point (g/d)		94.6		64.8	259.8	43
Bernstein	2006	CD	High	Adjusted for age and sex	(Chicken) 1.42 (0.92–2.19)	(Pork) 2.48 (1.4–4.4)	–	–	–
			Frequency		>3 times/week	>3 times/week	–	–	–
Halfvarson	2006	CD	High	Crude OR	–	–	–	–	0.4 (0.1–2.6)
			Frequency		–	–	–	–	Daily
Amre	2007	CD	Highest quartile	Crude OR	–	–	0.64 (0.31–1.28)	–	–
				Adjusted for total energy intake, age, sex, BMI	–	–	0.46 (0.20–1.06)	–	–
			Cut point (g/d)		–	–	8	–	
Higashi	1991	UC	High	Crude RR	1.4 (0.4–5.06)		2.00 (0.45–10.06)	2.67 (0.65–12.65)	2.00 (0.76–5.46)
			Frequency		Daily		Daily	>3 times/week	Daily
Kurata	1994	UC	Highest tertile	RR adjusted for sex, age, geography, inpatient status	1.3 (0.6–3.0)		–	(Cheese) 1.3 (0.5–3.4)	–
			Cut point (g/d)		NA		–	–	–
Reif	1997	UC	High	Adjusted for energy intake	–	–	0.65 (0.26–1.65)	–	4.45 (1.74–11.34)
			Cut point (g/d)		–	–	20	–	20
Sakamoto	2005	UC	Highest quartile	Adjusted for energy intake	1.35 (0.66–2.74)		1.21 (0.57–2.56)	0.79 (0.36–1.73)	1.22 (0.56–2.56)
			Cut point (g/d)		94.6		64.8	259.8	43
Bernstein	2006	UC	High	Adjusted for age and sex	(Chicken) 1.58 (0.97–2.59)	(Pork) 2.62 (1.37–5.03)	–	–	–
			Frequency		>3 times/week	>3 times/week	–	–	–
Halfvarson	2006	UC	High	Crude OR	–	–	–	–	3.3 (1.3–8.5)
			Frequency		–	–	–	–	Daily
Jantchou	2010	UC	Highest tertile	Adjusted HR for energy	1.87 (1.00–3.49)		1.83 (1.00–3.36)	0.94 (0.53–1.67)	0.97 (0.52–1.78)
			Mean value (g/d)		144.4		59.1	511.4	46.1

BMI, body mass index; CD, Crohn's disease; HR, hazard ratio; IBD, inflammatory bowel disease; NA, not available; OR, odds ratio; RR, relative risk; UC, ulcerative colitis.

may have resulted in recall bias involving IBD cases. However, several associations reported by studies with prospectively collected diet data agreed with the studies with retrospective data (15,19,20,23). There was heterogeneity among studies in time from IBD diagnosis to diet-pattern ascertainment. However, there were no obvious differences in the findings of studies with less than one year compared with those with more than one year between IBD diagnosis and diet ascertainment. The studies with prospective data ascertainment (15,19,20,23) from the European Prospective Investigation into Cancer and Nutrition used a middle-aged population (mean age at UC diagnosis, 58.8 years) and may reflect different dietary patterns or subsets of IBD. Lastly, the aim of our systematic review was to evaluate pre-illness dietary patterns, and therefore our observations cannot be extrapolated to the influence of diet on current disease activity.

In conclusion, in a systematic review of studies on pre-illness diet and the risk of development of IBD, we made several important observations. High intakes of total fats, PUFAs, omega-6 fatty acids, and meat were consistently associated with increased risk of developing UC as well as CD. High vegetable intake was consistently associated with decreased risk of UC, whereas fiber and fruit intake was consistently associated with reduced risk of CD. Further studies using prospectively collected data will be required to confirm these observations.

CONFLICT OF INTEREST

Guarantor of the article: Hashem El-Serag, MD, MPH.

Specific author contributions: Jason K. Hou: study design, literature search, data abstraction, and primary authorship; Bincy Abraham: study design, literature search and review, and editorial input; Hashem El-Serag: study design, data interpretation, and editorial input. All authors approved the final draft submitted.

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