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ORIGINAL PAPER

Macronutrient intake and stomach cancer

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Abstract
Purpose This study examines the association between intake of selected macronutrients and the risk of stomach cancer in a Northern American population.
Methods Mailed questionnaires were completed between 1994 and 1997 in eight Canadian provinces by 1,181 incident, histologically confirmed cases of stomach cancer and 5,039 population controls. Information on nutrient intake was obtained using a food frequency questionnaire. Odds ratios (ORs) and the corresponding 95 % confidence intervals (CIs) were derived through unconditional logistic regression to adjust for potential confounders, including an estimate of total energy intake.
Results Intakes of total fat, saturated fat, and cholesterol were significantly associated with the risk of stomach cancer: The ORs for the highest versus the lowest quartile were 1.58 (95 % CI 1.13–2.20), 1.86 (95 % CI 1.37–2.52), and 1.75 (95 % CI 1.36–2.25), respectively. Total fiber was inversely associated with stomach cancer ($p = 0.03$). The positive associations with intake of total fat and saturated fat were apparently stronger in women, overweight or obese subjects, and ever smokers. Saturated fat was specifically associated with increased risk of gastric cardia cancer, with an OR of 3.31 (95 % CI 1.48–7.43).
Conclusions A diet high in saturated fat appears to increase the risk of stomach cancer, particularly among obese subjects and for gastric cardia cancer.

Keywords Logistic regression · Odds ratio · Fat · Obesity

Abbreviations

BMI	Body mass index
CI	Confidence interval
FFQ	Food frequency questionnaire
ICD-O-2	International Classification of Diseases for Oncology, 2nd edition
OR	Odds ratio

Introduction

Although incidence and mortality rates have been declining worldwide, stomach cancer remains the fifth most common cancer and the third leading cause of cancer death in both sexes in the world [1]. Similarly, incidence and mortality rates of stomach cancer have been declining for several decades in Canada; however, stomach cancer remains the eleventh most common cancer among men and the ninth and tenth cause of death from cancer among men and women, respectively [2].

Development of gastric cancer is a complex and multifactorial process [3]. Gastric cancer is associated with genetic factors [4], *Helicobacter pylori* [5], tobacco smoking [6], heavy alcohol drinking [7, 8], obesity [9], a diet rich in

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salt [10], and a low intake of fresh fruit and vegetables [11] and fiber [12]. It is also now clear that two anatomic locations, cardia and non-cardia, present distinct and sometimes opposite epidemiological characteristics [13].

Diet has been identified as an important factor in the etiology of stomach cancer, but the role of various dietary factors is still an open question [14, 15]. Some case–control studies reported direct associations between intake of total protein [16–20], total fat [21–23] and saturated fat [17, 22, 24, 25], and gastric cancer. However, other studies [26–30] found no such associations and some found negative associations with total protein [23, 26, 31], monounsaturated and polyunsaturated fat [2, 17, 22], and especially with vegetable protein [26, 29] and vegetable fat [16, 29, 30]. A US cohort study of the elderly reported that total fat and selected fat subtypes were not related to the risk of gastric cancer [32].

Some studies reported that intake of fat and saturated fat was positively associated with non-cardia cancer [19], or distal stomach cancer [25], but O'Doherty et al. [32] found no association with either subtype of gastric cancer. Likewise, a few case–control studies reported an association between cholesterol intake and increased risk of gastric cancer [17, 19, 21] or with distal gastric cancer only [33]. However, most of studies found no such association with cholesterol [16, 18, 27, 28, 30].

Findings were inconsistent for carbohydrate intake, since both positive [26, 31, 34] and negative [22, 26, 27, 35] associations with stomach cancer have been reported. Further, other case–control [16–19, 23, 28, 30] and cohort studies [36] found no consistent associations.

A number of case–control studies reported that total fiber and vegetable fiber were inversely associated with the risk of stomach cancer [17, 21, 25–27, 31, 33, 37, 38], but results from other case–control [28] and cohort studies [39, 40] did not support those findings.

Relatively few North American etiological studies of stomach cancer have been published. Given the notable different results in the various studies, the present study examined the role of selected macronutrients in the etiology of stomach cancer using data from a nationwide Canadian population-based case–control study, the National Enhanced Cancer Surveillance System (NECSS).

Materials and methods

Between 1994 and 1997, the NECSS collected individual data from a population-based sample that covered 19 types of cancer and population controls in the Canadian provinces of British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Prince Edward Island, Nova Scotia, and Newfoundland and Labrador.

Cases

Participating provincial cancer registries ascertained a total of 2,425 (816 women and 1,609 men) incident, histologically confirmed stomach cancer cases aged 20–76 years. Of these, 393 (14.0 %; 141 women and 252 men) had died by the time of physician contact, and 223 (7.9 %; 91 females and 132 males) were not contacted because the attending physician refused consent (generally because the patient was too ill). Of 1,809 questionnaires sent by provincial cancer registries, 1,181 were completed, yielding a response rate of 65.3 %. Our study therefore included a total of 1,181 (379 women and 802 men) cases of stomach cancer as defined by the second edition of the International Classification of Diseases for Oncology (ICD-O-2) [41]. The topography codes were as follows: C16 stomach, cardia cancer C16.0 and non-cardia cancer from C16.1 to C16.9. Cases (544) from Ontario had the ICD code C16 stomach only.

Controls

Individuals without cancer and with age and sex distributions similar to those of all cancer cases in the NECSS were selected from a random sample within each province. Provincial cancer registries collected information from controls at the same time as for the cancer cases, using the same protocol. The strategies for selecting population controls varied by province and depended on data availability and accessibility. In British Columbia, Saskatchewan, Manitoba, Prince Edward Island, and Nova Scotia, age group- and sex-stratified random samples of population were obtained through the provincial health insurance plans. In Ontario, Ministry of Finance data were used to obtain a stratified random sample. Population samples in Alberta and Newfoundland and Labrador were obtained using random digit dialing.

Of 8,117 questionnaires sent to potential controls, 573 were returned because they were incorrectly addressed; of the remaining 7,544, 5,039 (2,547 men and 2,492 women) were completed, corresponding to 66.8 % of controls contacted.

Data collection

The provincial cancer registries identified most stomach cancer cases within 1–3 months of diagnosis through pathology reports. After obtaining the attending physician's consent, the provincial cancer registries mailed questionnaires to cases and controls. If the questionnaire was not returned within 14 days, a reminder postcard was sent out and, if necessary, a second copy of the questionnaire at 4 weeks. After 6 weeks, telephone follow-up was

used to complete the questionnaire, if required. Information was collected on socioeconomic status, height, weight, smoking history, alcohol drinking, physical activity, and dietary history.

We collected information on how much each subject weighed "about 2 years ago" and classified body mass index (BMI) according to the World Health Organization standards for adults [42]: underweight (<18.50 kg/m^2), normal weight (18.50–24.99 kg/m^2), overweight (25.00–29.99 kg/m^2), and obese (≥30.00 kg/m^2).

We defined ever smokers as people who smoked at least 100 cigarettes in their entire life and current smokers as those who were still smoking during the year preceding the interview.

We derived data on macronutrients from a food frequency questionnaire (FFQ) based on two validated instruments, the short Block questionnaire [43] and the Willett questionnaire [44], with minor modifications to account for differences between Canadian and American diets. The FFQ was used to determine usual dietary intake 2 years before participants' enrollment in the study. The FFQ lists 69 foods and beverages grouped into eight sections: (1) breads and cereals; (2) meat, poultry, fish, eggs, and cheese; (3) vegetables; (4) fruit; (5) sweets; (6) miscellaneous; (7) beverages made with water; and (8) other beverages. For each food item, cases and controls were asked to describe how often (per day, per week, per month), on average, they ate the specified serving size. We used a nutrient database based on the 2005 version of the Canadian Nutrient File to estimate nutrient and total energy intake [45].

Statistical analysis

We used unconditional multiple logistic regression to estimate the odds ratios (ORs) of stomach cancer and the corresponding 95 % confidence intervals (CI). We included the following potential confounding variables: sex, age (years), province, education (≤8, 9–13, ≥14 years), BMI (<25.0, 25.0–29.9, ≥30 kg/m^2), alcohol consumption (g/day), pack-years of smoking, total of fruit and vegetable consumption (servings/week) as general indicators of healthy diet, and total energy intake. Tests for trend were made for each study variable by substituting the variable in the model in continuous form. Nutrient intake amounts were categorized by quartiles, based on the distributions among the controls. All analyses were performed using SAS software [46].

Results

Table 1 shows the distribution of 1,181 cases of stomach cancer and 5,039 controls according to selected covariates. Stomach cancer cases were somewhat older than controls and tended to be less educated; they were more frequently overweight and reported using more tobacco and alcohol.

Table 1 Distribution of 1,181 stomach cancer cases and 5,039 population-based controls, according to selected covariates, NECSS, Canada, 1994–1997

	Cases		Controls	
	Number	Percent	Number	Percent
Sex				
Men	802	67.9	2,547	50.5
Women	379	32.1	2,492	49.5
Age (years)				
Mean (SD)	61.9 (9.8)		56.8 (13.6)	
20–49	154	13.0	1,471	29.2
50–59	255	21.6	923	18.4
60–69	436	36.9	1,646	32.7
≥70	336	28.5	989	19.7
Race/ethnicity				
White	916	93.1	4,257	95.6
Others	68	6.9	194	4.4
Education (years)				
≤8	315	26.7	796	16.0
9–13	571	48.4	2,536	51.2
≥14	263	22.3	1,624	32.8
Body mass index (kg/m^2)				
< 25	492	41.7	2,419	48.3
25–<30	464	39.3	1,884	37.6
≥30	213	18.0	702	14.0
Smoking status				
Never smokers	311	27.2	1,923	39.0
Ever smokers	832	72.8	3,009	61.0
Pack-year smoking				
Never smokers	311	26.3	1,923	38.2
≤10	194	16.4	1,105	22.0
11–20	203	17.2	744	14.8
21–30	155	13.1	482	9.6
>30	280	23.7	678	13.5
Alcohol drinking (g/d)				
Never drinkers	430	36.4	1,779	35.4
≤7.65	273	23.1	1,482	29.5
7.66–22.28	224	19.0	1,038	20.6
≥22.29	236	20.0	624	12.4
Total fruit and vegetables (servings/week)				
≤4.47	325	27.5	1,272	25.3
4.47–9.46	289	24.5	1,300	25.9
9.47–14.9	303	25.7	1,266	25.2
≥15	264	22.4	1,187	23.6

Totals may vary due to missing values

SD standard deviation, *NECSS* National Enhanced Cancer Surveillance System

Table 2 presents the ORs, and the corresponding 95 % CIs, of various types of fats, proteins, cholesterol, carbohydrate, sugars, and fiber. Total fat intake was positively associated with stomach cancer (OR 1.58, 95 % CI 1.13–2.20) for the highest versus the lowest quartile, p for trend = 0.007. The OR for saturated fat was 1.86 (95 % CI 1.37–2.52) for the highest versus the lowest quartile, p for trend = 0.0002. There was no association with monounsaturated or polyunsaturated fatty acids or with trans fats. Cholesterol intake was also associated with stomach cancer (OR 1.75, 95 % CI 1.36–2.25, p for trend <0.0001). Total fiber intake was inversely associated with stomach cancer (OR 0.76, 95 % CI 0.57–1.00) for the highest versus the lowest quartile, p for trend = 0.03. We found no significant association with intake of total protein, total carbohydrates and sugars.

Table 3 shows results stratified by sex, BMI, smoking status, and subsite of stomach cancer. The association between intake of total fat, and specifically saturated fat, and stomach cancer appeared to be stronger in overweight and obese subjects (OR 1.77 and 2.35, respectively), and that with saturated fat was apparently stronger in smokers (OR 1.79). These interactions, however, were not significant. The inverse association between total fiber and stomach

Table 2 Odds ratios (ORs)[a] and 95 % confidence intervals (CIs) of fat, cholesterol, protein, and carbohydrate intake for stomach cancer, NECSS, Canada, 1994–1997

Nutrients (g/week)	Quartiles				p value for trend
	I (low)	II	III	IV (high)	
Total fat					
OR (95 % CI)	1.0 (ref.)	1.14 (0.90–1.44)	1.22 (0.93–1.62)	1.58 (1.13–2.20)	0.007
Saturated fat					
OR (95 % CI)	1.0 (ref.)	1.39 (1.10–1.75)	1.41 (1.08–1.83)	1.86 (1.37–2.52)	0.0002
Monounsaturated fat					
OR (95 % CI)	1.0 (ref.)	0.93 (0.74–1.17)	1.05 (0.80–1.36)	1.17 (0.85–1.61)	0.23
Polyunsaturated fat					
OR (95 % CI)	1.0 (ref.)	1.06 (0.85–1.33)	0.84 (0.64–1.10)	1.00 (0.74–1.36)	0.73
Trans fat					
OR (95 % CI)	1.0 (ref.)	1.03 (0.83–1.28)	1.15 (0.92–1.43)	1.08 (0.85–1.37)	0.42
Cholesterol (mg/week)					
OR (95 % CI)	1.0 (ref.)	1.15 (0.92–1.45)	1.48 (1.18–1.87)	1.75 (1.36–2.25)	<0.0001
Total protein					
OR (95 % CI)	1.0 (ref.)	0.92 (0.72–1.17)	1.09 (0.82–1.44)	1.04 (0.73–1.48)	0.61
Total carbohydrate					
OR (95 % CI)	1.0 (ref.)	0.90 (0.71–1.15)	0.87 (0.64–1.19)	0.77 (0.52–1.14)	0.20
Sucrose					
OR (95 % CI)	1.0 (ref.)	1.04 (0.84–1.28)	0.99 (0.78–1.23)	1.19 (0.93–1.52)	0.19
Lactose					
OR (95 % CI)	1.0 (ref.)	1.17 (0.96–1.43)	1.00 (0.82–1.24)	1.04 (0.84–1.29)	0.89
Maltose					
OR (95 % CI)	1.0 (ref.)	0.91 (0.73–1.12)	0.94 (0.75–1.17)	0.85 (0.67–1.10)	0.28
Glucose					
OR (95 % CI)	1.0 (ref.)	0.78 (0.64–0.96)	0.88 (0.71–1.08)	0.82 (0.66–1.03)	0.20
Fructose					
OR (95 % CI)	1.0 (ref.)	0.88 (0.72–1.08)	0.88 (0.71–1.08)	0.85 (0.69–1.07)	0.19
Galactose					
OR (95 % CI)	1.0 (ref.)	1.23 (1.10–1.52)	0.98 (0.79–1.22)	1.25 (0.99–1.57)	0.24
Total fiber					
OR (95 % CI)	1.0 (ref.)	0.92 (0.74–1.14)	0.77 (0.60–0.98)	0.76 (0.57–1.00)	0.03

[a] Adjusted for age (years), sex, province, race/ethnicity, education, body mass index (<25, 25–29.9, ≥30), alcohol drinking (g/day), pack-year smoking, total of fruit and vegetables (servings/week) for fat, protein, and cholesterol, and total energy intake

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cancer was stronger in women (OR 0.64, interaction test, $p = 0.04$).

We had information on subtype of gastric cancer in 631 cases. Of these, 189 were cardia and 442 non-cardia cancers. The association with saturated fat (OR 3.31, 95 % CI 1.48–7.43) was stronger, on restricted to, cardia cancers, whereas that with cholesterol or total fiber were similar for both subsites.

Discussion

In this large nationwide population-based case–control study, intakes of total fat, saturated fat, and cholesterol were positively associated with risk of stomach cancer. Intake of saturated fat, in particular, was associated with the risk of stomach cancer in overweight and obese people. The association was stronger in people with cancer of the gastric cardia. Fiber was inversely associated with stomach cancer. No significant associations were found with total proteins, monounsaturated fat, polyunsaturated fats, trans fats, total carbohydrates, and sugars.

Different types of fat appear to play different roles in the etiology of stomach cancer [47, 48]. Similar to our study, several studies reported that high intake of total fat, specifically saturated fat, was positively associated with the risk of stomach cancer [17, 19, 22–25], although other studies did not [30, 32]. Our results are also consistent with our previous findings indicating that intake of meat, specifically processed meat and red meat, one of the main sources of fat in this population, was associated with an increased risk of stomach cancer [49]. We did not include meat in our regression analyses, since this would have represented an over adjustment for fat-related variables.

Obesity, an important and growing public health problem worldwide [50], has been linked to a variety of chronic diseases, including several neoplasms [51, 52]. A number of cohort studies found obesity related to increased incidence and mortality from gastric cancer [53–57], and specifically with cancer of the gastric cardia [58–60]. Some case–control studies also reported that obesity was associated with the risk of gastric cardia cancer [61–63], which was in agreement with our findings. We also found that high intake of total fat and saturated fat was associated with high risk of stomach cancer among overweight and obese subjects.

Increased cancer risk in obese subjects points to the role of adipose tissue-related inflammation in addition to energy metabolism in cancer [64], since inflammation may affect several phases of the process of carcinogenesis [64]. An increased fat intake was also associated with a high risk of gastric stump carcinoma in rats [65].

Our study found that dietary cholesterol was associated with stomach cancer. This is in agreement with some [17, 19, 20, 33], but not other [16, 18, 21, 27, 28, 30] studies on the issue. The mechanisms linking cholesterol to cancer risk are unclear. Alterations in lipid and apolipoprotein levels, potentially associated with high cholesterol intake, may also contribute to inflammation [66].

We conducted additional analyses on the combined effect of saturated fat intake and obesity by subtype of stomach cancer. The risk of cardia gastric cancer rose with increasing intake of saturated fat and with increasing BMI. The highest risk of cardia gastric cancer was observed among obese subjects who reported a high intake of saturated fat (i.e., tertile III). Compared with normal-weight subjects who reported a low intake of saturated fat (i.e., tertile I), the OR of gastric cardia cancer was 7.08 (95 % CI 2.58–19.46) for high intake of saturated fat (tertile III) in obese subjects; this was not apparent in subjects with non-cardia gastric cancer. However, the sample size was small to adequately address interactions for cardia cancer only.

Although some cohort studies reported that intake of total fibers was not associated with stomach cancer [39, 40], the source of fibers may play different roles in development of gastric cancer [67]. A meta-analysis indicated that dietary fiber intake is inversely associated with stomach cancer [12]. This is consistent with our findings, specifically in women. High-fiber foods tend to have a higher content of antioxidants and phytochemicals [68, 69] and can help normalize blood glucose and insulin levels [69].

This large population-based study involved eight of the ten Canadian provinces and was based on a widely used and validated FFQ [43]. Nevertheless, the possibility of misclassification of diet as a result of recall bias cannot be ruled out. However, non-differential misclassification between cases and controls would likely bias the ORs toward unity in most instances [70]. Cases might report their food intake differently than controls. However, the recall of FFQ data by controls is satisfactorily reproducible in different settings [71].

About 14 % of the cancer cases were not included in this study, either because they were too ill or had died. However, the overall response rate was satisfactory and similar (about two-thirds) to that of controls. Our results are, therefore, unlikely to be substantially influenced by information or selection bias. With reference to confounding, we were able to adjust the analyses for a large number of relevant covariates, including an estimate of total energy intake. Heavy, though not moderate, alcohol drinking is related to some excess gastric cancer risk [7, 8]. In addition, heavy alcohol drinking is related to poorer diet. For

Table 3 Odds ratios (ORs)[a] and 95 % confidence intervals (CIs) of stomach cancer for total fat, saturated, cholesterol, and total fiber for subjects in the highest versus the lowest quartile in separate strata of sex, BMI, smoking status, and subtype of stomach cancer, NECSS, Canada, 1994–1997

Types of nutrients	Sex		Body mass index (kg/m^2)		Smoking status		Subsite of stomach cancer[b]	
	Men ($n = 802$)	Women ($n = 379$)	<25 ($n = 492$)	≥25 ($n = 677$)	Never ($n = 311$)	Ever ($n = 832$)	Cardia ($n = 189$)	Non-cardia ($n = 442$)
Total fat								
I	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
II	1.10 (0.80–1.50)	1.24 (0.87–1.78)	1.08 (0.76–1.52)	1.23 (0.89–1.70)	0.87 (0.57–1.32)	1.29 (0.97–1.73)	1.80 (0.94–3.43)	0.99 (0.69–1.42)
III	1.11 (0.77–1.60)	1.45 (0.94–2.25)	1.25 (0.83–1.88)	1.24 (0.85–1.82)	0.97 (0.59–1.61)	1.32 (0.94–1.86)	1.46 (0.71–3.04)	0.95 (0.62–1.46)
IV	1.41 (0.92–2.17)	1.95 (1.11–3.41)	1.46 (0.88–2.42)	1.77 (1.13–2.79)	1.04 (0.56–1.96)	1.73 (1.15–2.61)	1.93 (0.84–4.45)	1.03 (0.62–1.72)
p value for trend	0.10	0.02	0.12	0.01	0.77	0.009	0.27	0.90
Saturated fat								
I	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
II	1.38 (1.01–1.89)	1.45 (1.02–2.05)	1.28 (0.92–1.79)	1.53 (1.10–2.13)	1.30 (0.87–1.93)	1.47 (1.10–1.97)	2.44 (1.23–4.85)	1.17 (0.82–1.66)
III	1.42 (1.01–1.99)	1.48 (0.98–2.26)	1.20 (0.82–1.77)	1.68 (1.17–2.41)	1.27 (0.79–2.05)	1.51 (1.09–2.09)	2.15 (1.03–4.46)	1.02 (0.69–1.50)
IV	1.80 (1.21–2.67)	2.05 (1.23–3.40)	1.47 (0.93–2.32)	2.35 (1.55–3.57)	1.58 (0.88–2.83)	1.79 (1.24–2.61)	3.31 (1.48–7.43)	1.13 (0.71–1.79)
p value for trend	0.005	0.01	0.14	0.0001	0.17	0.0004	0.01	0.79
Cholesterol (mg/week)								
I	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
II	1.11 (0.82–1.50)	1.21 (0.84–1.73)	1.18 (0.84–1.65)	1.15 (0.84–1.58)	1.09 (0.72–1.66)	1.16 (0.88–1.53)	1.13 (0.63–2.03)	1.15 (0.80–1.64)
III	1.22 (0.90–1.65)	2.04 (1.43–2.92)	1.61 (1.15–2.25)	1.44 (1.05–1.97)	1.80 (1.20–2.71)	1.37 (1.03–1.81)	1.14 (0.64–2.03)	1.51 (1.06–2.16)
IV	1.48 (1.07–2.06)	2.26 (1.48–3.45)	1.87 (1.28–2.72)	1.72 (1.22–2.43)	2.10 (1.31–3.35)	1.55 (1.13–2.13)	1.80 (0.99–3.29)	1.89 (1.28–2.79)
p value for trend	0.01	<0.0001	0.0003	0.0007	0.0004	0.002	0.03	0.0005
Total fibers								
I	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
II	0.86 (0.66–1.13)	1.05 (0.74–1.51)	1.07 (0.77–1.48)	0.82 (0.61–1.10)	0.83 (0.55–1.26)	0.90 (0.70–1.17)	0.66 (0.40–1.10)	0.87 (0.62–1.23)
III	0.73 (0.54–0.99)	0.85 (0.56–1.27)	0.81 (0.56–1.17)	0.73 (0.53–1.01)	0.82 (0.52–1.29)	0.69 (0.51–0.93)	0.60 (0.35–1.04)	0.79 (0.54–1.14)
IV	0.89 (0.63–1.27)	0.64 (0.39–1.04)	0.74 (0.48–1.13)	0.76 (0.53–1.12)	0.64 (0.37–1.11)	0.72 (0.52–1.01)	0.54 (0.29–1.00)	0.66 (0.43–1.02)
p value for trend	0.51	0.04	0.07	0.17	0.13	0.03	0.07	0.06

Interaction test Chi square ($df = 3$): total fat interaction with sex (0.779, $p = 0.85$), BMI kg/m^2 (2.972, $p = 0.36$), and smoking status (6.552, $p = 0.09$); saturated fat interaction with BMI kg/m^2 (5.238, $p = 0.14$) and smoking status (3.104, $p = 0.38$); cholesterol interaction with smoking status (1.198, $p = 0.75$); and total fiber interaction with sex (13.633, $p = 0.03$) and smoking status (2.940, $p = 0.40$)

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[a] Adjusted for age (years), sex, province, race/ethnicity, education, body mass index (<25, 25–29.9, ≥30), alcohol drinking (g/day), pack-year smoking, total of fruit and vegetables (servings/week) (not adjusted for fiber), and total energy intake

[b] Data did not include cases and controls in Ontario province; cases had topography codes, C16 stomach only, but not had codes: cardia cancer C16.0 and non-cardia cancer from C16.1 to C16.9

this reason, we included a term for alcohol in multivariate analysis.

Helicobacter pylori is associated with the risk of non-cardia gastric cancers [72]. In fact, chronic *H. pylori* infection plays a key role in gastric cancer development, and essentially all non-cardia gastric cancer have—or had been—infected with *H. pylori* [73–76], but diet may still play a relevant role in the development of stomach cancer [77, 78]. We did not have information on history of *H. pylori* infection, but since most, if not all, cases of (non-cardia) gastric cancer had been likely infected with *H. pylori* [73], this cannot be treated as a confounding or modifying factor.

In conclusion, our findings add to the evidence that selected types of fat, and specifically saturated fat, play a role in the etiology of stomach cancer. They indicate, therefore, that a low-fat diet, and specifically one low in saturated fats, may be an effective strategy for preventing stomach cancer in the Canadian population, particularly in overweight and obese subjects.

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Appendix

The Canadian Cancer Registries Epidemiology Research Group comprises a principal investigator from each of the provincial cancer registries involved in the National Enhanced Cancer Surveillance System: Bertha Paulse, MSc, BN, Newfoundland Cancer Foundation; Ron Dewar, MA, Nova Scotia Cancer Registry; Dagny Dryer, MD, Prince Edward Island Cancer Registry; Nancy Kreiger, PhD, Cancer Care Ontario; Heather Whittaker, Manitoba Cancer Treatment and Research Foundation; Diane Robson, BA, Saskatchewan Cancer Foundation; Shirley Fincham, PhD, Alberta Cancer Board; and Nhu Le, PhD, British Columbia Cancer Agency.

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