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Glycemic index, glycemic load and cancer risk

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Background: Dietary glycemic index (GI) and glycemic load (GL) have been related to the risk of selected cancers, but the issue remains open.

Patients and methods: Mailed questionnaires were completed between 1994 and 1997 in eight Canadian provinces for incident, histologically confirmed cases of the stomach ($n = 1182$), colon ($n = 1727$), rectum ($n = 1447$), liver ($n = 309$), pancreas ($n = 628$), lung ($n = 3341$), breast ($n = 2362$), ovary ($n = 442$), prostate ($n = 1799$), testis ($n = 686$), kidney ($n = 1345$), bladder ($n = 1029$), brain ($n = 1009$), non-Hodgkin's lymphomas (NHL, $n = 1666$), leukemias ($n = 1069$), multiple myelomas ($n = 343$), and 5039 population controls. Dietary information on eating habits 2 years before participants' enrollment in the study was obtained using a validated food frequency questionnaire (FFQ). Odds ratios (ORs) and 95% confidence intervals (CI) were derived by unconditional logistic regression including recognized confounding factors.

Results: Dietary GI was positively associated with the risk of prostate cancer (OR, 1.26 for the highest versus the lowest quartile). A higher dietary GL significantly increased the risk of colorectal (OR, 1.28), rectal (OR, 1.44) and pancreatic (OR, 1.41) cancers. No other significant associations were found.

Conclusions: Our findings suggest that a diet high in GI and GL is associated with increased risk of selected cancers.

Key words: Canada, glycemic index, glycemic load, logistic regression, odds ratio

introduction

Several lines of evidence suggest a potential role of glucose and insulin in promoting tumor growth [1, 2]. Hence, it has been suggested that the nature of the carbohydrates consumed may play a role in carcinogenesis [3]. The glycemic index (GI) is a classification of carbohydrate-rich foods based on postprandial blood glucose responses, dependent upon the nature of the carbohydrate and the type and extent of food processing [4]. Compared with low GI foods, high GI foods result in larger fluctuations of blood glucose and insulin for the same amount of carbohydrate ingested. Low GI diets compared with high GI diets may improve glycemic control, leading to lower insulin output and inflammatory responses as well as lower the risk of several chronic diseases, including cancer [5, 6]. In a recent meta-analysis of prospective studies, Dong et al. found a direct relationship between the dietary GI and breast cancer risk [7], but this was not confirmed by Mulholland et al. [8]. Likewise, other meta-analyses of several cancer sites found no association of either GI or GL with colorectal or pancreatic cancer risk [9], but found a positive association of GL with endometrial cancer risk [10], while two comprehensive meta-analyses of all major cancer sites found direct associations of GI with breast cancer [6] and with colorectal and endometrial cancers [11].

Only one study [12] was able to address the risk of several cancer sites in relation to GI and GL in the same dataset. The present study, therefore, assessed the association of the dietary GI and GL with the risk of cancers from a Canadian nationwide population-based case–control study, the National Enhanced Cancer Surveillance System (NECSS). This is, therefore, one of the few available datasets addressing the role of GI and GL in several cancer sites.

methods

The NECSS collected individual data from a population-based sample that covered 19 types of cancers (most common cancers were included) and

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population controls in the Canadian provinces of British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Prince Edward Island, Nova Scotia and Newfoundland. The present study did not include cases of colon, rectum and bladder cancers from Ontario as the use of data for this province was restricted. The decision was made before the project started.

cases

Between 1994 and 1997, participating cancer registries ascertained a total of 34 861 (15 361 females and 19 500 males) histologically confirmed incident cancer cases aged 20–76 years. Of these, 3924 patients (11.3%; 1553 females and 2371 males) had died by the time of physician contact, and 2611 (7.5%; 1300 females and 1311 males) were not contacted because the attending physician refused consent (generally because the patient was too ill). Of 28 326 questionnaires sent, 20 384 were completed, yielding a response rate of 58.5% of cases ascertained or 71.9% of patients contacted. The present analysis included therefore 20 384 (11 101 males and 9283 females) histologically confirmed cases as defined by the second edition of the International Classification of Diseases for Oncology (ICDO-2) [13]. The cancer sites considered include stomach (803 men and 379 women), colon (959 men and 768 women), rectum (858 men and 589 women), liver (225 men and 84 women), pancreas (353 men and 275 women), lung (1736 men and 1605 women), female breast (2362), ovary (442), prostate (1799), testis (686), kidney (727 men and 618 women), bladder (670 men and 359 women), brain (617 men and 392 women), non-Hodgkin's lymphomas (NHL) (877 men and 789 women), leukemia (640 men and 429 women) and multiple myeloma (151 men and 192 women).

controls

Individuals without cancer were selected from a random sample within each province, with an age/sex distribution similar to that of all cancer cases in the NECSS. The strategies for selecting population controls varied by province, depending on data availability and accessibility. In Prince Edward Island, Nova Scotia, Manitoba, Saskatchewan and British Columbia, age group- and sex-stratified random samples of the population were obtained through the provincial health insurance plans. In Ontario, Ministry of Finance data were used to obtain stratified random samples. Newfoundland and Alberta used random digit dialing to obtain population samples.

Of 8117 questionnaires sent to potential controls, 573 were returned because of wrong address; of the remainder, 5039 (2547 men and 2492 women) were completed, corresponding to 62.1% of controls ascertained and 66.8% of controls contacted.

data collection

The cancer registries identified most cases within 1–3 months of diagnosis through pathology reports. After obtaining physician's consent, questionnaires were mailed to cancer cases and controls by the cancer registries. If a questionnaire was not completed and returned, a reminder postcard was sent after 14 days, and a second copy of the questionnaire was sent at 4 weeks. After 6 weeks, telephone follow-up was used, if required, to complete the questionnaire. Information was collected on the socioeconomic status, height, weight, smoking history, alcohol drinking, physical activity, menstrual and reproductive history, and diet. For weight, we collected information on how much each subject weighed 'about 2 years ago'. For cigarette smoking, we defined ever smokers as people who smoked at least 100 cigarettes in their entire life. Information on recreational physical activity 2 years before the study included session frequency, season of participation and average time per session for each of 12 categories of the most common types of moderate and strenuous leisure-time physical activities.

Dietary information was derived from a food frequency questionnaire (FFQ), based on two validated instruments: the short block questionnaire [14] and the Willett questionnaire [15], with minor modifications to account for differences in Canadian and American diets. The FFQ was used to ascertain usual dietary intakes 2 years before participants' enrollment in the study. The FFQ included 69 specific foods and beverages, and was grouped into eight sections: (i) breads and cereals; (ii) meat, poultry, fish, eggs and cheese; (iii) vegetables; (iv) fruits; (v) sweets; (vi) miscellaneous such as peanut butter and nuts; (vii) beverages made with water such as coffee, tea and juices and (viii) other beverages, for example, soft drinks, beer, wine and liquor. For each food item, cases and controls were asked to describe how often (per day, per week, per month), on average, they consumed the specified serving size. A nutrient database based on the 2005 version of the Canadian nutrient file was used to estimate nutrient and total energy intake [16].

To compute the average daily GI and glycemic load (GL), we assigned GI values to the 45 carbohydrate-containing foods or food groups from the FFQ. These were based on the recent international tables of GI and GL [17], and the GI values of foods typically found on the Canadian market were preferentially chosen from the international tables. The GI was expressed as a percentage of the glycemic response elicited by white bread as a standard food with a GI of 100. The average daily GI for a subject's diet was computed by summing the products of the GI value of each food times the amount of available carbohydrate; then divided by the total amount of available carbohydrates consumed per day. The average daily GL (g) was calculated by summing the products of the GI value of each food times the amount of available carbohydrates consumed per day divided by 100. Each GL unit represents the equivalent of 1 g of carbohydrate from white bread.

statistical analysis

The dietary GI and GL were categorized by quartiles based on the distributions among the controls. Unconditional logistic regression was used to estimate odds ratios (ORs), and the corresponding 95% confidence intervals (CI), including terms for sex (excluding sex-specific cancers), age group (20–49, 50–59, 60–69, ≥70), province, education (≤8, 9–13, ≥14 years), body mass index (BMI, <25, 25–29.99, ≥30 kg/m^2), total alcohol consumption (g/day), pack-years smoking and energy intake (non-carbohydrate and alcohol), and number of live births and years of menstruation for ovarian cancer, and age at menarche, number of live births and age at first pregnancy for breast cancer. The analyses for colon and rectal cancers were also adjusted for physical activity. Confounding variables, except for the age group, province, BMI and sex, were treated as continuous variables.

results

Table 1 shows the mean daily GI and GL and the corresponding standard deviations for cases, by cancer sites, and controls, stratified by sex.

Table 2 presents the ORs and the corresponding 95% CI of selected cancers according to quartiles of dietary GI and GL. The GI was positively associated with prostate cancer: the OR was 1.26 (95% CI 1.03–1.54) for the highest versus the lowest quartile. The GL was significantly associated with colorectal cancer (CRC), the OR for the highest versus the lowest quartile being 1.28 (95% CI 1.05–1.57). When the analyses were separated by subsite, the GL was significantly associated with the risk of rectal cancer only; the OR for the highest versus the lowest quartile was 1.44 (95% CI 1.12–1.85). For pancreatic

Table 1. Mean intake (standard deviation) of glycemic index and glycemic load by types of Cancer and controls, National Enhanced Cancer Surveillance System (NECSS), Canada, 1994–1997

Types of cancer	Cases (*n*)			Median	Mean (standard deviation)	
	Total	Men	Women	Age (years)	Glycemic index	Glycemic load (g/day)
Total Controls	5039			60	82.1 (6.2)	184.6 (92.5)
Men	2547			63	82.8 (6.3)	190.8 (95.1)
Women	2492			57	81.4 (5.9)	178.2 (89.4)
Stomach	1182	803	379	64	82.3 (6.2)	200.1 (94.8)
Colon	1727	959	768	65	82.4 (5.8)	193.9 (84.7)
Rectum	1447	858	589	64	82.4 (5.8)	192.2 (83.9)
Liver	309	225	84	63	80.9 (6.7)	191.1 (97.6)
Pancreas	628	353	275	64	82.4 (5.8)	192.2 (93.9)
Lung	3341	1736	1605	65	83.3 (6.5)	181.6 (88.9)
Breast (women)	2362		2362	56	81.1 (5.8)	177.1 (80.8)
Premenopausal women	913		913	46	80.8 (5.9)	173.9 (76.2)
Postmenopausal women	1449		1449	63	81.4 (5.7)	179.2 (83.6)
Ovary	442		442	55	81.1 (5.4)	184.3 (80.4)
Prostate	1799	1799		67	82.9 (5.7)	192.6 (83.2)
Testis	686	686		35	82.1 (5.4)	205.1 (102.3)
Kidney	1345	727	618	60	82.6 (5.8)	190.9 (93.9)
Bladder	1029	670	359	65	83.1 (6.2)	183.6 (83.4)
Brain	1009	617	392	50	81.6 (5.8)	193.7 (86.1)
Non-Hodgkin's lymphoma (NHL)	1666	877	798	60	81.8 (5.7)	193.0 (86.7)
Leukemia	1069	640	429	60	82.2 (5.4)	193.4 (83.5)
Multiple myeloma	343	151	192	65	81.8 (5.6)	188.6 (80.3)

cancer, the OR for the highest versus the lowest quartile of GL was 1.41 (95% CI 1.02–1.95). No significant associations were found with cancers of the stomach, liver, lung, breast, ovary, testis, kidney, bladder, brain, NHL, leukemia and multiple myeloma. When we added total vegetable and fruit intake to the models, the results did not appreciably change (data not shown). No significant association was observed with carbohydrate intake.

When the analyses for cancers with positive results were stratified by age, sex, BMI and smoking status (supplementary Table S1, available at *Annals of Oncology* online for online presentation), the risk of both colon and rectal cancers for dietary GL were apparently stronger in men. The risk of colon cancer was apparently stronger in ever smokers, whereas the risk of rectal cancer was apparently stronger in subjects aged <65 years, normal weight and never smokers. However, the interactions with age, sex, BMI and smoking status were not significant ($P > 0.05$). The risk of pancreatic cancer was apparently stronger in women for GI, and in subjects with overweight and obesity for GL (P for interaction for both sex and BMI, >0.05). The associations of the GI and prostate cancer was more pronounced in subjects <65 years of age and ever smokers, again in the absence of significant heterogeneity. We also looked at strata of GI and GL by physical activity and BMI combined, i.e. overweight/obese individuals with low physical activity (<1 h/week), as a proxy of higher insulin resistance states. We found no relevant effect modification for colon and rectal cancers, although the number of cases in each category was small (311 colon cancer cases and 249 rectal cancer cases).

discussion

In this large, nationwide population-based case–control study, a high GI was positively associated with the risk of prostate cancer. The GL was associated with the risk of colorectal (mainly rectum) and pancreatic cancers. No significant associations were found with cancers of the stomach, liver, lung, breast, ovary, testis, kidney, bladder, brain, NHL, leukemia and multiple myeloma.

Numerous studies have investigated the dietary GI and GL as potential risk factors in several cancers, but only a cohort study [12] considered a large number of malignant neoplasms in the same dataset. Most attention has been focused on cancers of the colorectum. A case–control study from Italy reported that GI and GL were positively associated with CRC [18]. The women's health study also found that a higher dietary GL was positively related to CRC in women [19]. However, no associations between GI, GL and CRC were found in other cohort studies [12, 20–22]. A recent meta-analysis suggested that dietary GI and GL were associated with increased risk of CRC [11], but this was not confirmed by two other meta-analyses [6, 9].

A multicenter case–control study from Italy reported that high GI diets were positively associated with pancreatic cancer; the association was more pronounced in women, under the age of 65 years, and ever smokers [23]. Similarly, our study showed a positive association in women, but not in men, though in the absence of significant difference between sexes. We also found that the GL was positively associated with the risk of pancreatic cancer, mainly in overweight and obese subjects. A cohort

Table 2. Odds ratio[a] (OR) and 95% confidence interval (CI) of dietary glycemic index (GI) and glycemic load (GL) for selected cancer sites, National Enhanced Cancer Surveillance System (NECSS), Canada, 1994–1997

Types of cancer	Quartiles				*P* value for trend
	I (Low)	II	III	IV (High)	
Controls (quartile cut points)					
GI (men and women combined)	≤78.05	78.06–81.91	81.92–85.97	≥85.98	
GL (men and women combined)	≤129.89	129.90–170.75	170.76–221.52	≥221.53	
GI (men)	≤78.78	78.79–82.63	82.64–86.63	≥86.64	
GL (men)	≤131.97	131.98–175.53	175.54–231.66	≥231.67	
GI (women)	≤77.49	77.50–81.16	81.17–85.25	≥85.26	
GL (women)	≤127.16	127.17–166.46	166.47–212.05	≥212.06	
Stomach (*n* = 1182)					
GI	1.0 (ref.)	1.22 (1.00–1.49)	1.07 (0.88–1.31)	0.90 (0.74–1.11)	0.16
GL	1.0 (ref.)	0.88 (0.70–1.11)	0.97 (0.74–1.26)	0.93 (0.67–1.29)	0.84
Colorectum (*n* = 3174)					
GI	1.0 (ref.)	1.33 (1.14–1.55)	1.26 (1.08–1.47)	1.05 (0.90–1.24)	0.67
GL	1.0 (ref.)	1.15 (0.98–1.36)	1.16 (0.97–1.38)	1.28 (1.05–1.57)	0.03
Colon (*n* = 1727)					
GI	1.0 (ref.)	1.25 (1.04–1.50)	1.24 (1.03–1.48)	1.05 (0.87–1.28)	0.62
GL	1.0 (ref.)	1.03 (0.84–1.25)	1.11 (0.90–1.37)	1.18 (0.93–1.50)	0.13
Rectum (*n* = 1447)					
GI	1.0 (ref.)	1.45 (1.20–1.75)	1.31 (1.08–1.59)	1.07 (0.87–1.32)	0.73
GL	1.0 (ref.)	1.32 (1.07–1.62)	1.22 (0.97–1.52)	1.44 (1.12–1.85)	0.02
Liver (*n* = 309)					
GI	1.0 (ref.)	0.77 (0.54–1.09)	0.80 (0.56–1.13)	0.71 (0.49–1.01)	0.08
GL	1.0 (ref.)	0.99 (0.68–1.45)	1.06 (0.70–1.59)	1.17 (0.75–1.84)	0.46
Pancreas (*n* = 628)					
GI	1.0 (ref.)	1.28 (0.99–1.65)	1.11 (0.86–1.44)	1.09 (0.84–1.42)	0.80
GL	1.0 (ref.)	1.14 (0.86–1.49)	1.29 (0.97–1.73)	1.41 (1.02–1.95)	0.03
Lung (*n* = 3341)					
GI	1.0 (ref.)	1.27 (1.07–1.50)	1.10 (0.94–1.30)	1.04 (0.89–1.23)	0.82
GL	1.0 (ref.)	0.93 (0.79–1.10)	1.00 (0.84–1.20)	0.98 (0.80–1.21)	0.94
Breast (women) (*n* = 2362)					
GI	1.0 (ref.)	1.18 (0.99–1.39)	1.10 (0.93–1.30)	0.94 (0.78–1.12)	0.40
GL	1.0 (ref.)	0.90 (0.75–1.09)	0.83 (0.65–1.05)	0.83 (0.61–1.12)	0.20
Premenopausal women (*n* = 913)					
GI	1.0 (ref.)	1.08 (0.84–1.40)	1.11 (0.84–1.46)	0.93 (0.69–1.24)	0.73
GL	1.0 (ref.)	1.01 (0.75–1.37)	0.95 (0.65–1.38)	0.87 (0.54–1.41)	0.54
Postmenopausal women (*n* = 1449)					
GI	1.0 (ref.)	1.22 (0.98–1.53)	1.09 (0.88–1.36)	0.93 (0.74–1.17)	0.36
GL	1.0 (ref.)	0.83 (0.65–1.06)	0.74 (0.54–1.01)	0.79 (0.54–1.19)	0.24
Ovary (*n* = 442)					
GI	1.0 (ref.)	1.15 (0.85–1.56)	1.05 (0.77–1.44)	0.84 (0.61–1.17)	0.27
GL	1.0 (ref.)	1.02 (0.71–1.48)	1.15 (0.74–1.80)	1.10 (0.62–1.95)	0.66
Prostate (*n* = 1799)					
GI	1.0 (ref.)	1.32 (1.09–1.61)	1.28 (1.05–1.56)	1.26 (1.03–1.54)	0.05
GL	1.0 (ref.)	1.23 (0.99–1.52)	1.40 (1.07–1.82)	1.29 (0.92–1.81)	0.10
Testis (*n* = 686)					
GI	1.0 (ref.)	1.21 (0.91–1.61)	1.14 (0.85–1.53)	0.98 (0.72–1.35)	0.91
GL	1.0 (ref.)	0.99 (0.71–1.39)	0.89 (0.60–1.34)	0.72 (0.44–1.19)	0.17
Kidney (*n* = 1345)					
GI	1.0 (ref.)	1.24 (1.03–1.50)	1.21 (1.01–1.46)	1.18 (0.98–1.43)	0.13
GL	1.0 (ref.)	1.09 (0.90–1.33)	1.06 (0.86–1.31)	1.09 (0.86–1.38)	0.60
Bladder (*n* = 1029)					
GI	1.0 (ref.)	1.24 (0.99–1.55)	1.11 (0.88–1.39)	1.26 (1.01–1.58)	0.11
GL	1.0 (ref.)	0.94 (0.75–1.18)	0.93 (0.73–1.19)	0.92 (0.69–1.22)	0.59
Brain (*n* = 1009)					
GI	1.0 (ref.)	1.14 (0.93–1.39)	1.02 (0.83–1.26)	0.95 (0.76–1.18)	0.44

Continued

Table 2. *Continued*

Types of cancer	Quartiles				*P* value for trend
	I (Low)	II	III	IV (High)	
GL	1.0 (ref.)	0.94 (0.75–1.17)	0.99 (0.78–1.26)	0.98 (0.75–1.28)	0.87
Non-Hodgkin's lymphoma (NHL, *n* = 1666)					
GI	1.0 (ref.)	1.15 (0.98–1.36)	1.12 (0.95–1.32)	0.91 (0.76–1.08)	0.30
GL	1.0 (ref.)	1.02 (0.86–1.23)	1.20 (0.99–1.45)	1.09 (0.88–1.35)	0.27
Leukemia (*n* = 1069)					
GI	1.0 (ref.)	1.36 (1.12–1.66)	1.24 (1.01–1.51)	1.12 (0.91–1.38)	0.53
GL	1.0 (ref.)	1.09 (0.88–1.35)	1.11 (0.88–1.40)	1.23 (0.95–1.58)	0.13
Multiple myeloma (*n* = 343)					
GI	1.0 (ref.)	1.60 (1.15–2.22)	1.34 (0.95–1.91)	1.31 (0.91–1.88)	0.28
GL	1.0 (ref.)	1.01 (0.70–1.46)	1.18 (0.80–1.75)	1.15 (0.73–1.79)	0.44

[a]Adjusted for 10-year age group (20–49, 50–59, 60–69, 70–76), province, education, body mass index (BMI, <25, 25–29.9, ≥30), alcohol consumption (grams/day), pack-year smoking and energy intake (non-carbohydrate and alcohol); adjusted for strenuous and moderate activity for colon and rectal cancers; adjusted for number of live births and years of menstruation for ovarian cancer, number of live births and age at first menstruation for premenopausal breast cancer and number of live births and age at the end of first pregnancy for postmenopausal breast cancer.
Note: The GI was expressed as a percentage of the glycemic response elicited by white bread as a standard food with a GI of 100.

study found that the GL was directly related to pancreatic cancer, particularly among women with both BMI >25 kg/m^2 and low physical activity [24]. However, the prostate, lung, colorectal and ovarian cancer screening study observed an elevated risk of pancreatic cancer for available carbohydrate intake during the first 4 years of follow-up, but not subsequently [25]. Most cohort studies did not find dietary GI and GL related to pancreatic cancer [12, 24, 26].

Direct associations of dietary GI and GL with risk of breast cancer were observed in some case–control [27] and cohort studies [28]. However, other case–control and cohort studies found no association [12, 29, 30], in agreement with the present one. Recently, two meta-analysis found that GI, but not GL, significantly increased the risk of breast cancer [6, 7], but this was not observed in other meta-analyses [8, 11]. Cohort studies indicated that the dietary GL was directly related to the risk of breast cancer in pre- [28, 31] and postmenopausal women, but such associations were not reproduced in other cohort studies [30, 32]. At least two reasons could explain some of the inconsistent results between GI and/or GL and breast cancer risk: most studies were not designed to assess GI and GL, and correlates of GI and GL in various populations may differ.

A case–control study from Italy reported that GI and GL were positively associated with the risk of prostate cancer [33], in agreement with our study. However, similar associations were not observed in three US cohort studies [6, 34, 35].

A case–control study reported that diets with a high GI and GL were associated with ovarian cancer [36]. Other case–control and cohort studies found that the GL was related to an increased risk of ovarian cancer only in overweight or obese women [37, 38]. However, such an association was not observed in another cohort study [12], in agreement with the present investigation.

Two case–control studies from Italy reported that GI and GL were positively related to stomach cancer [39, 40]. However, these findings were not supported by cohort [41] and case–control studies [42], in broad agreement with the present results. Italian and Greek case–control studies reported that a higher dietary GL was associated with an increased risk of liver cancer, and the association was stronger in the presence of hepatitis B virus and/or hepatitis C virus markers [43, 44]. A case–control study from Italy also found that diets with higher GI and GL were positively associated with the risk of renal cell carcinoma [45]. However, this was not supported by other studies [12], including ours. In addition, our results did not show any associations with several other cancers, consistently with another cohort study from North America [12].

Our data did not show any material associations of GI with any of the cancers considered, with the exception of a moderate association with prostate cancer. This implies that more than the type of carbohydrate (GI) it is the amount plus type (GL) that counts.

Diets high in GI or GL result in higher levels of blood glucose and insulin, which can promote glucose intolerance, insulin resistance and hyperinsulinemia [46]. Insulin may affect cancer development by exerting mitogenic effects, directly and indirectly by affecting insulin-like growth factors (IGF) binding proteins (IGFBPs) and increasing the bioactivity of IGF-I [47]. Insulin and IGF-I also inhibit apoptosis [48]. Some, but not all, epidemiological studies [49, 50] showed that circulating levels of glucose, insulin and IGF-I or plasma C-peptide were positively associated with the risk of colorectal, breast, pancreas and prostate cancers [51–54]. A collaborative analysis of 17 prospective studies from 12 countries found that plasma concentrations of IGF-I were positively associated with breast cancer risk [55]. Four meta-analyses indicated that high circulating IGF-I concentrations were associated with the risk of premenopausal breast cancer, colorectal [56] and prostate cancers [56–58]. Another meta-analysis indicated that increased pre-diagnostic serum levels of insulin and glucose were related to the development of colorectal and pancreatic cancers [59]. Wang et al. (2009) reported that a high sucrose diet play a role in intestinal epithelial cell proliferation and tumorigenesis [60], by increasing circulating levels of insulin and IGF-I in mice. Diabetes, a condition preceded by long-

term hyperinsulinemia, has been associated with increased risk of colorectal, liver, pancreas, endometrium and perhaps postmenopausal breast cancers [61, 62].

The NECSS is a large population-based study from 8 of 10 Canadian provinces, based on a widely used and validated FFQ [14, 15]. The possibility recall bias cannot be excluded. However, nondifferential misclassification between cases and controls in most instances would bias the ORs towards unity [63]. Cases might report their food intake differently than controls. However, knowledge of this possible relation between carbohydrate intake and cancer risk was limited in the general Canadian public at the time of data collection. Furthermore, it has been shown that recall of FFQ data by controls is satisfactorily reproducible [64]. Selection bias might also have been introduced into our data. About 10% of the cancer cases (who were too ill or had died) were not included in this study. However, 71% of cases and 67% of controls participated. This response rate is satisfactory for a population-based case–control study. The present results are, therefore, unlikely to be substantially influenced by selection bias.

A possible limitation of this study is that the GI and GL values were derived from a limited variety of food items listed in the FFQs, and this may limit the corresponding detectable range. Although our FFQ was not specifically designed to study the dietary GI, it included 45 carbohydrate food categories with different GIs (i.e. not overlapping). For example, rice, a high GI food, was a separate item from pasta, a medium–low GI food, and from combined beans and lentils, both low GI foods. In addition, we were unable to allow total fiber as a possible confounder in the analysis, which was inversely correlated with the GL.

In addition, considering the main analyses for a total of 38 tests for trends, we found four results to be significant at $p < 0.05$, which is higher than the expected 2 out of 38 associations. However, the possibility of chance findings must be borne in mind when interpreting our results.

In conclusion, this investigation suggests that diets high in GI and GL may be associated with an increased risk of selected digestive tract and prostate cancers.

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disclosure

The authors have declared no conflicts of interest.

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