Calcium and Vitamin D and Risk of Colorectal Cancer: Results From a Large Population-based Case-control Study in Newfoundland and Labrador and Ontario

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ABSTRACT

Background: Previous epidemiological studies have been suggestive but inconclusive in demonstrating inverse associations of calcium, vitamin D, dairy product intakes with risk of colorectal cancer (CRC). We conducted a large population-based comparison of such associations in Newfoundland and Labrador (NL) and Ontario (ON).

Methods: A case control study design was used. Colorectal cancer cases were new CRC patients aged 20-74 years. Controls were a sex and age-group matched random sample of the population in each province. 1760 cases and 2481 controls from NL and ON were analyzed. Information on dietary intake and lifestyle was collected using self-administered food frequency and personal history questionnaires.

Results: Controls reported higher mean daily intakes of total calcium and total vitamin D than cases in both provinces. In ON, significant reduced CRC risk was associated with intakes of total calcium (OR of highest vs. lowest quintiles was 0.57, 95% CI 0.42-0.77, p_{trend}=0.03), total vitamin D (OR=0.73, 95% CI 0.54-1.00), dietary calcium (OR=0.76, 95% CI 0.60-0.97), dietary vitamin D (OR=0.77, 95% CI 0.61-0.99), total dairy products and milk (OR=0.78, 95% CI 0.60-1.00), calcium-containing supplements use (OR=0.76). In NL, the inverse associations of calcium, vitamin D with CRC risk were most pronounced among calcium- or vitamin D-containing supplement users (OR=0.67, 0.68, respectively).

Conclusions: Results of this study add to the evidence that total calcium, dietary calcium, total vitamin D, dietary vitamin D, calcium- or vitamin D-containing supplement use may reduce the risk of CRC. The inverse associations of CRC risk with intakes of total dairy products and milk may be largely due to calcium and vitamin D.

Key words: Calcium; vitamin D; dairy products; colorectal cancer

La traduction du résumé se trouve à la fin de l'article.

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Diet has long been regarded as one of the most important environmental factors associated with colorectal cancer (CRC).[1] Since 1980 when Garland and Garland proposed that the inverse association between ultraviolet-B and colon cancer risk was mediated through vitamin D,[2] numerous studies have been done to explore the relationships among calcium, vitamin D and CRC risk.[3-18] Calcium has been hypothesized to protect against CRC by binding secondary bile acids and ionized fatty acids in the colon lumen to form insoluble calcium soaps, thereby reducing their proliferative effects on the colonic mucosa.[19] The roles of dietary calcium and vitamin D are correlated since vitamin D regulates the absorption of calcium.[20] In addition to its indirect role in maintaining calcium homeostasis, the direct genomic action of vitamin D is linked to a multitude of biological responses, including the synthesis of DNA and prevention of double-strand breaks by exogenous or endogenous sources.[20]

Dairy products contain large amounts of calcium and vitamin D through fortification. It has been shown that calcium, especially in combinations as found in milk, effectively precipitates luminal cytotoxic surfactants and thus inhibits colonic cytotoxicity.[21,22] Jarvinen et al.[23] indicated that individuals with a high consumption of milk have a potentially reduced risk of colon cancer; however, the association did not appear to be due to intake of calcium, vitamin D, or to specific effects of fermented milk. Recent research indicates that calcium and vitamin D might act together, rather than separately, to reduce risk of CRC.[24] Results from a multicentre, placebo-controlled randomized clinical trial found that calcium supplementation was inversely associated with adenoma recurrence only when vitamin D levels were above the median (29.1 ng/ml).[25]

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Despite the biological plausibility, epidemiological studies have been suggestive but inconclusive for a protective role of dietary calcium and vitamin D in CRC prevention. The World Cancer Research Fund/American Institute for Cancer Research expert report in 2007[24] summarized 11 cohort studies regarding dietary and serum vitamin D intake and colorectal cancer risk. Six of these have reported non-significant decreased risk;[5,26-30] two have shown no impact on CRC;[27,31] and three other studies have indicated non-significant increased risk.[23,32,33] The expert report also indicated that increased milk and dietary calcium intake are associated with reduced CRC risk.[24]

We investigated these possible associations among persons in both NL and ON. NL is geographically isolated, culturally distinct, and relatively economically disadvantaged, thus fresh fruits and vegetables are less often available. Consequently, people may consume more preserved and salted traditional foods. Our interdisciplinary CRC research team tried to explore whether and how the high incidence of CRC in NL can be partly explained by the unique dietary habits of the NL population. Squire et al. recently found that in NL, higher intakes of red pickled meat were associated with increased risk of CRC.[34] In contrast, ON is a centrally located, culturally diverse, and economically advantaged province. It is hypothesized that consistent results of the protective effects of calcium and vitamin D in two diverse provinces would provide support to the argument that calcium and vitamin D have chemo-preventive effects on CRC. To our knowledge, little has been done in this area in Canada. Therefore, the purpose of this report is to assess the effects of dietary calcium, vitamin D and dairy products on the occurrence of CRC and to compare these possible associations between the two provinces.

SUBJECTS AND METHODS

Selection of cases and controls

Data for this case-control study were obtained from the Ontario Familial Colorectal Cancer Registries (OFCCR) and Newfoundland Familial Colorectal Cancer Registries (NFCCR). In ON, incident cases diagnosed during 1997-2000 were identified through the population-based Ontario Cancer Registry (Phase one). In NL, incident cases diagnosed during 1999-2003 were identified through the population tumour registry maintained by the Newfoundland Cancer Registry. Both registries were used to identify newly diagnosed cases of colon or rectal cancer (pathology confirmed ICD 9th revision codes: 153.0-153.9, 154.1-154.3, and 154.8 or ICD-10 codes: 18.0-18.7, 19.9, 20.9) among those aged 20-74 years. Phase two of the OFCCR enrolled cases diagnosed in ON during 2003-2006.[35,36]

Initial contact was with the surgeon/physician identified on the pathology report. Once physician consent was obtained, cases were then contacted to inform them of the study. Participants who indicated their willingness to participate in the study were sent, in sequence, a written consent form, family history questionnaire (FHQ), personal history questionnaire (PHQ), and food frequency questionnaire (FFQ). Non-responders were sent postcard reminders and wre phoned several weeks after initial contact to remind them of the mailing. Controls were a random sample of residents in each province aged 20-74 years. In ON, controls were identified through a list of residential phone numbers or from population-based property assessment rolls (owners and occupants). In NL, controls were identified through random digit dialing.[34] Both registries frequency matched controls to cases on sex and five-year age strata. Once verbal consent for participation was obtained from controls during the phone contact, the same survey package as sent to cases was forwarded to each potential participant.

Dietary and epidemiologic data collection

Information on dietary intake was collected using a self-administered FFQ. The FFQ administered in ON was the well-known Hawaii FFQ.[37,38] The FFQ administered in NL was modified based on the ON questionnaire and adapted to include regional foods in NL.[34] The FFQ was used to assess diet over the 1-2 years prior to diagnosis or interview in each province. Participants were questioned about their intake of almost 170 foods which were believed to be important to the contribution of most nutrients in the diet. For each food item, subjects were asked to estimate the frequency of food intake and their usual portion size: 'Regular', 'Small' or 'Large'. Food photographs were provided that showed regular, small and large portion sizes for vegetables, meat and chicken. Participants were also questioned on their use of any individual or multivitamin supplements, including the usual brand name, the amounts taken and the duration of consumption. Nutrient intakes were computed by multiplying the frequency of consumption of each food item by the nutrient content of the portion size.

Possible associations between CRC risk and the consumption of five groups of dairy foods (total dairy products, milk, non-milk dairy products (e.g., cream), yogurt, cheese) were also investigated. Total dairy food consumption was computed by adding the daily servings of all foods in the dairy categories. Total milk consumption was calculated by adding the daily servings of non-fat milk or skim milk, low-fat milk (2%), and whole milk. Non-milk dairy product consumption was calculated by adding the daily servings of yogurt, cheese and cream.

The self-administered personal history questionnaire included many close-ended questions about medical history, bowel screening history, medication use, diet, physical activity, alcohol and tobacco use and socio-demographic measures such as education and income. Identifying information such as sex, age, date of birth, and marital status was collected. For female participants, there were additional questions relating to reproductive factors.

For analyses, we excluded those who did not provide sufficient dietary information, those who failed to provide information on potential risk factors, those who reported energy intake in the upper or lower 2.5% of intake (lower and upper cutoff: in NL, 925 and 4700 kcal for men, 1100 and 4900 kcal for women, respectively; in ON, 1040 and 5200 kcal for men, 835 and 4100 kcal for women, respectively), and patients who had familial adenomatous polyposis (FAP) and/or an in-situ tumour. In ON, 896 subjects were excluded; in NL, 281 subjects were excluded. After these exclusions, based on those who completed both the PHQ and FFQ, 3,102 subjects (1,272 cases and 1,830 controls) from ON and 1,139 subjects (488 cases and 651 controls) from NL remained. Data collected from these subjects were used for the analysis. Since one of the main objectives of this study was an interprovincial comparison, a province-stratified rather than pooled analysis was performed.

Statistical analyses

Descriptive statistics stratified by case-control status were used to describe the demographic/ health-related characteristics and dietary

Table 1. Selected Characteristics of Cases and Controls, Stratified by Province, CRC Case-control Study in NL and ON

Characteristics	NL		ON	
	Cases (n=488)	Controls (n=651)	Cases (n=1272)	Controls (n=1830)
Age (years)†	62.7*±9.0	60.5±9.5	58.4*±10.9	61.5±9.7
BMI§ (kg/m^2)†	27.8*±4.8	27.2±4.4	26.7*±4.7	26.3±4.5
Physical activity (METs/week§)†	58.0±74.7	50.2±73.2	43.8±58.6	41.4±59.2
First-degree relatives with CRC (%)‡	163* (33.4)	114 (17.5)	341* (26.8)	223 (12.2)
Reported any colon screening (%)‡	60* (12.3)	145 (22.3)	198* (15.6)	476 (26.0)
Regular use of NSAID§ (%)‡	164 (33.5)	252 (38.7)	433* (34.0)	787 (43.0)
Regular use of multivitamin supplements (%)‡	66* (13.5)	145 (22.3)	436* (34.3)	701 (38.3)
Reported HRT§ (%)‡	132* (27.1)	251 (38.6)	440* (34.6)	827 (45.2)
Smokers, current and/or past (%)‡	353* (72.3)	401 (61.6)	733 (57.6)	1078 (58.9)
Heavy drinkers§ (%)‡	54 (11.0)	68 (10.4)	154 (12.1)	205 (11.2)
High level of education§ (%)‡	181* (37.0)	351 (53.9)	700 (55.0)	1087 (59.4)
High household income§ (%)‡	102* (20.9)	229 (35.1)	506 (39.8)	758 (41.4)

* Significant difference between cases and controls (p<0.05).
† Continuous variables presented as mean±SD (standard deviation), differences between cases and controls based on t-test.
‡ Categorical variables presented as number (%), differences between cases and controls based on chi-square test.
§ BMI, body mass index; METs/week, metabolic equivalent hours per week; NSAID, nonsteroidal anti-inflammatory drugs; HRT, hormone replacement therapy, female only; heavy drinkers, average drinks >14 times/week; high level of education, included some college, university or post-secondary school; high household income, average household income >$50,000/year.

Table 2. Mean Intakes of Foods and Nutrients Among Cases and Controls, Stratified by Province, CRC Case-control Study

Intakes of Foods and Nutrients†	NL Subjects		ON Subjects	
	Cases (n=488)	Controls (n=651)	Cases (n=1272)	Controls (n=1830)
Fruit (servings/week)	9.6±8.1	10.5±8.2	11.3±8.1	11.0±8.2
Vegetables (servings/week)	11.1±7.6	11.9±8.3	13.8±9.0	13.2±8.5
Red meat (servings/week)	3.5±3.3	3.6±3.4	4.6*±4.4	4.0±3.8
Total energy (kcal/day)	2441.5*±838.2	2293.6±744.9	2266.0*±796.1	2161.5±757.7
Calcium (mg/day)				
Total calcium	989.6*±402.6	1108.3±500.9	1137.1*±509.2	1231.6±544.1
Calcium from food	933.4*±354.1	989.0±394.9	956.0*±302.0	1009.5±314.9
Calcium from supplements	56.2*±160.2	119.3±249.1	181.1*±404.7	222.1±440.6
Vitamin D (IU/day)				
Total vitamin D	332.2*±242.5	393.5±299.5	319.8*±218.4	352.7±236.4
Vitamin D from food	244.9±124.1	251.0±130.0	202.1*±104.5	220.8±111.0
Vitamin D from supplements	87.3*±201.0	142.5±260.3	117.7*±186.8	131.9±203.6
Dairy products (servings/week)				
Total dairy products	12.8±10.2	13.4±10.4	12.2*±8.6	13.0±9.9
Milk	8.2±8.0	8.3±8.0	7.2*±6.6	8.1±8.1
Non-milk products	5.0±5.7	5.2±5.9	5.6±5.1	5.5±5.2
Yogurt	2.0±3.7	2.2±3.9	1.3±1.9	1.3±1.7
Cheese	3.0±3.7	3.0±4.1	3.8±4.2	3.8±4.3

* Significant difference between cases and controls (p<0.05).
† Continuous variables presented as mean±SD (standard deviation), differences between cases and controls based on t-test.

intakes of subjects. Intakes of calcium and vitamin D were energy-adjusted by using residuals calculated from the linear regression of the log of nutrient intake versus the log of energy intake.[39] Intakes of total calcium and total vitamin D were calculated by adding energy-adjusted nutrients from food and unadjusted nutrients from supplements. Intakes of calcium, vitamin D and dairy products were categorized into quintiles based on the distribution among the study population without missing endpoints and were entered into models as indicator variables with the lowest quintile as the referent group.

Age and total energy intake-adjusted odds ratios (OR) and their corresponding 95% confidence intervals (95% CI) were calculated from maximum-likelihood estimates in unconditional logistic regression to assess the association of the outcome with dietary intakes. Multivariate unconditional logistic regression was used to evaluate the association of intakes of calcium, vitamin D and dairy products with CRC risk after adjusting for a set of potential confounders or covariates. Tests for trend were used to assess dose-response relationships based on the median of each category of dietary intake.

Potential confounding factors include age (18-49, 50-59, 60-69 and 70+ years); sex; body mass index (BMI<18.5, 18.5-24.9, 25-29.9, and ≥30 kg/m^2); physical activity (<7.4, 7.4-22.4, 22.4-53.0, and >53.0 metabolic equivalent hours/week, METs/week); first-degree relatives with CRC (yes, no); polyps (yes, no); diabetes (yes, no); history of colon screening procedure (yes, no); cigarette smoking (ever smoke, never smoke); alcohol drinking (<14, ≥14 drinks/week); education attainment (high school graduate or less, technical school/some college/university, and bachelor's degree/graduate degree); household income (<$12,000; $12,000-29,999, $30,000-49,999, and ≥$50,000); marital status (married, single/never married, and separated/divorced/widowed); regular use of medication and supplements: non-steroid anti-inflammatory drug (NSAID)(yes, no), multivitamin supplements (yes, no), folate supplement (yes, no); reported hormone replacement therapy (HRT, females only)(yes, no); dietary intakes: total energy intake (quintiles), fruits (0-6, 6-7, 7-14, and >14 servings/week), vegetables (0-6, 6-7, 7-14, and >14 servings/week), red meat (0-2, 2-3, 3-5, and >5 servings/week); and province of residence (NL, ON). The basis for the assessment of confounding factors included: 1) literature and previous studies, 2) biological plausibility, 3) whether the regression coefficient of the primary dependent variable changed by 10% or more after addition of the potentially confounding variable, or 4) whether the covariate entered the model at p<0.05. The final list of potential confounding factors included in the model was based on both backwards-stepwise procedure and the literature. Statistical tests were two-sided, and p values less than 0.05

Table 3. Associations (Adjusted OR† 95% CI†) of Calcium and Vitamin D Intakes With CRC Risk Among Cases and Controls, Stratified by Province, CRC Case-control Study

Intakes of Calcium and Vitamin D	NL Subjects (n=1139)				ON Subjects (n=3102)			
	No. of Cases/ Controls	Median Intake‖	OR‡ (95% CI)	OR§ (95% CI)	No. of Cases/ Controls	Median Intake‖	OR‡ (95% CI)	OR§ (95% CI)
Total calcium								
Q1	109/119	580.0	1.00	1.00	301/320	708.5	1.00	1.00
Q2	107/121	798.1	1.04 (0.71,1.51)	1.30 (0.85,1.98)	265/356	898.1	0.84 (0.67,1.06)	0.89 (0.67,1.20)
Q3	106/121	963.5	1.01 (0.70,1.48)	1.17 (0.76,1.78)	264/356	1071.7	0.84 (0.67,1.06)	0.97 (0.72,1.31)
Q4	93/135	1190.0	0.77 (0.53,1.13)	0.94 (0.61,1.44)	231/390	1308.4	0.68* (0.54,0.86)	0.66* (0.49,0.90)
Q5	73/155	1653.4	0.50* (0.34,0.74)	0.68 (0.44,1.07)	211/408	1834.0	0.61* (0.48,0.77)	0.57* (0.42,0.77)
P for trend¶			0.02	0.15			0.02	0.03
Calcium from food								
Q1	105/123	573.3	1.00	1.00	283/338	656.3	1.00	1.00
Q2	102/126	764.3	1.04 (0.71,1.52)	1.33 (0.87,2.03)	267/354	816.7	0.97 (0.77,1.22)	0.95 (0.75,1.21)
Q3	96/131	902.4	0.92 (0.63,1.35)	1.11 (0.72,1.72)	261/359	946.5	0.98 (0.78,1.23)	1.03 (0.82,1.31)
Q4	103/125	1089.7	1.02 (0.70,1.49)	1.26 (0.82,1.94)	237/384	1094.5	0.79* (0.63,1.00)	0.83 (0.66,1.05)
Q5	82/146	1405.7	0.66* (0.45,0.96)	0.94 (0.61,1.45)	224/395	1382.9	0.71* (0.56,0.90)	0.76* (0.60,0.97)
P for trend¶			0.11	0.67			0.02	0.06
Calcium from supplements								
Non-users	407/471	0	1.00	1.00	761/1002	0	1.00	1.00
Users	81/180	>0	0.51* (0.38,0.68)	0.67* (0.47,0.94)	511/828	>0	0.87* (0.75,1.00)	0.76* (0.63,0.93)
Total vitamin D								
Q1	102/126	124.2	1.00	1.00	285/336	107.7	1.00	1.00
Q2	106/122	199.4	1.11 (0.76,1.62)	1.36 (0.85,2.15)	247/374	179.9	0.86 (0.68,1.08)	0.89 (0.66,1.20)
Q3	115/112	261.4	1.28 (0.88,1.86)	1.40 (0.90,2.65)	275/345	265.8	1.06 (0.84,1.33)	1.15 (0.85,1.54)
Q4	87/141	407.5	0.71* (0.48,1.03)	0.78 (0.49,1.24)	236/385	464.0	0.76* (0.61,0.96)	0.79 (0.58,1.07)
Q5	78/150	754.3	0.60* (0.41,0.88)	0.85 (0.53,1.37)	229/390	645.4	0.79* (0.63,0.99)	0.73* (0.54,1.00)
P for trend¶			0.12	0.39			0.19	0.18
Vitamin D from food								
Q1	97/131	110.7	1.00	1.00	284/337	95.5	1.00	1.00
Q2	101/127	179.8	1.17 (0.80,1.71)	1.30 (0.85,1.98)	251/370	148.5	0.91 (0.72,1.14)	0.92 (0.72,1.16)
Q3	94/133	228.7	1.01 (0.69,1.48)	1.26 (0.82,1.92)	262/358	198.9	1.02 (0.81,1.28)	1.09 (0.86,1.38)
Q4	108/120	285.3	1.24 (0.85,1.81)	1.51 (0.98,2.31)	263/358	253.9	1.03 (0.82,1.30)	1.07 (0.84,1.36)
Q5	88/140	404.0	0.81 (0.55,1.18)	0.95 (0.62,1.47)	212/407	359.0	0.71* (0.56,0.89)	0.77* (0.61,0.99)
P for trend¶			0.49	0.90			0.22	0.38
Vitamin D from supplements								
Non-users	402/474	0	1.00	1.00	874/1212	0	1.00	1.00
Users	86/177	>0	0.55* (0.41,0.73)	0.68* (0.48,0.97)	398/618	>0	0.91 (0.78,1.06)	1.11 (0.76,1.61)

* Significant difference from reference category, p<0.05.
† OR, Odds ratio; 95% CI, 95% confidence interval.
‡ Adjusted for age and total energy intake.
§ Adjusted for total energy intake, age, sex, BMI, physical activity (METs/week), first-degree relatives with CRC, polyps, diabetes, reported colon screening procedure, cigarette smoking, alcohol drinking, education attainment, household income, marital status, regular use of NSAID, regular use of multivitamin supplements, reported HRT (females only), and intakes of fruits, vegetables and red meat. Variables were included in the final model based on a ≥10% alternation in the parameter coefficient of interest.
‖ Units of mg/day for calcium, and IU/day for vitamin D.
¶ Two-sided p-value for test of linear trend was calculated by using median values for each quintile of intake.

were considered statistically significant. Statistical analyses were performed using SAS statistical software.[40]

RESULTS

Demographic and lifestyle characteristics of the study participants, stratified by province and case-control status, are shown in Table 1. The study participants included 1,760 cases (488 from NL, 1,272 from ON) and 2,481 controls (651 from NL, 1,830 from ON) with average response rates of 65.0% and 53.5% in cases and controls, respectively. NL cases were slightly older than controls (mean, 62.7 for cases, 60.5 for controls), while ON cases were slightly younger than controls (mean, 58.4 for cases, 61.5 for controls). In both provinces, cases had higher BMI than controls; more often had first-degree relatives with CRC; were less likely to report any colon screening procedure, to report use of multivitamin supplements, and to have taken HRT over the previous 1-2 years (females only). Physical activity (METs/week) or heavy alcohol drinking history did not vary significantly between cases and controls in the two provinces. NL cases tended to be smokers and less likely to have acquired higher education or to obtain a high income during the previous year (all p<0.05). ON CRC cases less often used NSAID during the previous year (all p<0.05).

Table 2 gives the mean intakes of food, selected nutrients and dairy products by the cases and controls in both provinces. Both provinces' cases reported higher intakes of total energy than controls. There was higher red meat consumption among ON cases, but no marked differences in the fruit and vegetable consumption between cases and controls were found in either province. Controls generally reported higher levels of mean daily intake of calcium and vitamin D, however, the extent of the differences varied by province. Specifically, both provinces' controls reported significantly higher intakes of total calcium, calcium from food, calcium from supplements, total vitamin D and vitamin D from supplements compared to their respective cases (all p<0.05). In ON, controls also reported significantly higher consumption of vitamin D from food, total dairy products and milk than did cases (all p<0.05).

The OR and 95% CI of CRC according to intakes of calcium and vitamin D from food and supplements, stratified by province, are shown in Table 3. Inverse associations with CRC risk were observed for high intakes of age-energy-adjusted total calcium, calcium from food and total vitamin D in both provinces; however, after other potential covariates were taken into account, the inverse associations were no longer significant in NL, while the protective effect of these nutrients remained significant in ON. The multivariate-

Table 4. Associations (Adjusted OR†, 95% CI†) of Dairy Product Intakes With CRC Risk Among Cases and Controls, Stratified by Province, CRC Case-control Study

Dairy Products	NL Subjects (n=1139)				ON Subjects (n=3102)			
	No. of Cases/ Controls	Median Intake‖	OR‡ (95% CI)	OR§ (95% CI)	No. of Cases/ Controls	Median Intake‖	OR‡ (95% CI)	OR§ (95% CI)
Total Dairy Products								
Q1	110/133	2.4	1.00	1.00	271/385	3.1	1.00	1.00
Q2	87/127	7.2	0.85 (0.59,1.23)	0.89 (0.57,1.41)	239/353	6.9	0.97 (0.77,1.22)	1.03 (0.81,1.31)
Q3	103/126	10.5	0.79 (0.54,1.14)	1.07 (0.68,1.70)	267/354	10.4	1.05 (0.84,1.33)	1.12 (0.88,1.42)
Q4	97/129	16.1	0.75 (0.51,1.09)	0.90 (0.56,1.45)	263/352	15.6	1.01 (0.80,1.28)	1.07 (0.84,1.37)
Q5	91/136	25.9	0.69* (0.46,1.01)	0.89 (0.55,1.45)	232/386	25.5	0.74* (0.58,0.94)	0.78* (0.60,1.00)
P for trend¶			0.03	0.42			0.12	0.21
Milk								
Q1	115/138	0	1.00	1.00	333/475	0.6	1.00	1.00
Q2	101/145	3.5	0.85 (0.60,1.22)	1.06 (0.69,1.64)	240/345	3.0	1.03 (0.83,1.28)	1.09 (0.87,1.36)
Q3	93/122	6.9	0.89 (0.62,1.28)	1.27 (0.81,1.98)	296/392	6.9	1.09 (0.88,1.34)	1.12 (0.90,1.39)
Q4	112/140	8.9	0.85 (0.60,1.22)	1.14 (0.73,1.77)	254/346	7.9	1.06 (0.85,1.32)	1.09 (0.87,1.37)
Q5	67/106	17.0	0.67* (0.45,0.99)	0.96 (0.58,1.57)	149/272	14.9	0.73* (0.56,0.94)	0.78* (0.60,1.00)
P for trend¶			0.02	0.81			0.18	0.23
Non-milk								
Q1	97/143	0.3	1.00	1.00	255/402	1.1	1.00	1.00
Q2	98/129	2.0	1.35 (0.94,1.95)	1.40 (0.89,2.20)	243/375	2.5	1.02 (0.81,1.28)	1.04 (0.82,1.32)
Q3	105/117	3.6	0.94 (0.64,1.38)	0.98 (0.61,1.59)	270/356	4.1	1.15 (0.92,1.45)	1.14 (0.90,1.45)
Q4	103/124	6.0	1.16 (0.80,1.69)	1.43 (0.89,2.29)	255/341	6.5	1.11 (0.88,1.40)	1.13 (0.88,1.44)
Q5	85/138	11.4	0.91 (0.61,1.37)	1.12 (0.67,1.89)	249/356	11.5	0.96 (0.75,1.22)	0.98 (0.76,1.26)
P for trend¶			0.51	0.88			0.69	0.79
Yogurt**								
Q1	157/229	0	1.00	1.00	553/766	0	1.00	1.00
Q2	165/214	1.1	1.15 (0.86, 1.53)	1.27 (0.87,1.85)	230/320	0.3	0.95 (0.77,1.16)	0.98 (0.79,1.21)
Q3	112/171	5.0	0.91 (0.66, 1.25)	1.02 (0.75,1.39)	130/196	0.5	0.85 (0.66,1.09)	0.92 (0.71,1.20)
Q4	–	–	–	–	168/266	1.3	0.81 (0.65,1.02)	0.88 (0.69,1.11)
Q5	–	–	–	–	191/282	3.5	0.83 (0.66,1.03)	0.85 (0.68,1.07)
P for trend¶			0.56	0.85			0.23	0.06
Cheese								
Q1	104/158	0	1.00	1.00	303/444	0.5	1.00	1.00
Q2	103/108	1.0	1.26 (0.87,1.81)	1.53 (0.97,2.43)	230/359	1.3	0.94 (0.75,1.18)	0.98 (0.78,1.23)
Q3	101/144	2.0	1.12 (0.78,1.61)	1.34 (0.85,2.12)	244/349	2.5	0.99 (0.79,1.24)	1.00 (0.79,1.25)
Q4	87/110	5.3	1.00 (0.68,1.46)	1.26 (0.78,2.02)	259/322	5.0	1.10 (0.87,1.37)	1.12 (0.89,1.42)
Q5	93/131	7.0	0.97 (0.66,1.44)	1.25 (0.76,2.05)	236/356	10.0	0.87 (0.69,1.10)	0.90 (0.70,1.14)
P for trend¶			0.34	0.94			0.51	0.56

* Significant difference from reference category, p<0.05.
† OR, Odds ratio; 95% CI, 95% confidence interval.
‡ Adjusted for age and total energy intake.
§ Adjusted for total energy intake, age, sex, BMI, physical activity (METs/week), first-degree relatives with CRC, polyps, diabetes, reported colon screening procedure, cigarette smoking, alcohol drinking, education attainment, household income, marital status, regular use of NSAID, regular use of multivitamin supplements, reported HRT (females only), and intakes of fruits, vegetables and red meat. Variables were included in the final model based on a ≥10% alternation in the parameter coefficient of interest.
‖ Units of servings/week for each dairy product.
¶ Two-sided p-value for test of linear trend was calculated by using median values for each quintile of intake.
** Due to small sample size in NL, yogurt intake was only divided into 3 groups.

adjusted OR of CRC in ON for individuals in the highest quintile of intake compared with those in the lowest quintile was 0.57 for total calcium (95% CI 0.42-0.77, p-trend=0.03), 0.76 for dietary calcium (95% CI 0.60-0.97, p-trend=0.06), and 0.73 for total vitamin D (95% CI 0.54-1.00, p-trend=0.18). In addition, a higher intake of dietary vitamin D in ON subjects was also significantly and inversely associated with CRC risk (OR=0.77, 95% CI 0.61-0.99, p-trend=0.38). The observed reductions in risk among participants consuming calcium-containing supplements were 33% (NL) and 24% (ON). In NL, a 32% reduced risk emerged for consuming vitamin D-containing supplements.

In addition, we evaluated the consumption of total dairy foods and specific dairy foods in relation to the risk of CRC (Table 4). In ON, the risk of CRC was significantly reduced for those who consumed total dairy food >25.5 servings/week compared to those who consumed <3.1 servings/week (OR=0.78, 95% CI 0.60-1.00) in both age-energy-adjusted models and multivariate-adjusted models. In particular, those who consumed ≥14.9 cups/week of milk had a 22% lower risk of CRC compared to those who consumed <0.6 cups/week. A non-significant inverse association was found in yogurt intake. In NL, inverse associations were observed for age-energy-adjusted total dairy foods and milk; however, after adjusting for multi-variables, the inverse relationships were no longer significant.

When the combined effect of total calcium and total vitamin D was considered, the inverse association was most pronounced among subjects reporting high calcium and high vitamin D intakes compared to those reporting a low intake of both nutrients (Table 5).

DISCUSSION

In this large population case-control study, significant inverse associations were observed among the ON population for intakes of total calcium, dietary calcium, supplemental calcium, total vitamin D, dietary vitamin D, total dairy products and milk. In the NL population, inverse associations of supplemental calcium and supplemental vitamin D intakes with CRC risk were found. Our findings support a number of studies in other populations that have reported inverse associations between intakes of calcium and vitamin D and CRC risk.[4,41-45]

It is a little surprising that we did not observe meaningful associations of calcium and vitamin D intakes from food with CRC risk

Table 5. Adjusted OR†, 95% CI† of CRC Risk According to Level of Total Calcium and Total Vitamin D Intake in the ON Population

Total Vitamin D Intake (IU/day)	Total Calcium Intake (mg/day)		
	T1§ (≤835.2)	**T2§ (835.3-1064.2)**	**T3§ (>1064.2)**
T1§ (≤157.3)			
No. of cases/controls	343/420	99/127	15/30
OR† (95% CI)	1.00	0.94 (0.69,1.29)	0.84 (0.65,1.14)
T2† (157.4-241.5)			
No. of cases/controls	115/120	230/322	86/141
OR† (95% CI)	1.10 (0.80,1.86)	1.06 (0.84,1.34)	0.81 (0.59,1.11)
T3§ (>241.5)			
No. of cases/controls	15/20	94/162	275/488
OR† (95% CI)	1.00 (0.50,2.02)	0.86 (0.63,1.17)	0.75* (0.49,0.99)

* Significant difference from reference category, $p<0.05$.
† OR, Odds ratio; 95% CI, 95% confidence interval.
‡ Adjusted for total energy intake, age, sex, BMI, physical activity (METs/week), first-degree relatives with CRC, polyps, diabetes, reported colon screening procedure, cigarette smoking, alcohol drinking, education attainment, household income, marital status, regular use of NSAID, regular use of multivitamin supplements, reported HRT (females only), and intakes of fruits, vegetables and red meat. Variables were included in the final model based on a ≥10% alternation in the parameter coefficient of interest.
§ Intakes of total calcium and vitamin D were categorized into tertiles based on the distribution among subjects, T1 for tertile 1, T2 for tertile 2, and T3 for tertile 3.

in NL after adjusting for multi-variables. We did observe these inverse associations in NL after adjusting for age and total energy intake only. One possibility is that intakes of these nutrients in NL were too low, even in the highest quintiles, for us to observe significant associations. This may be the case with calcium, for which intakes in ON subjects were found to be considerably higher than in NL subjects (Table 2). Other researchers have also found lower intakes of dietary calcium by NL adults as compared to those resident in ON.[46-48] It is also possible that the findings in this study may be due in part to collinearity between nutrients and foods of which they are constituents. For instance, dietary fat, phosphorous and dietary fibre may limit the intestinal absorption of calcium due to increased production of insoluble calcium complexes.[49-51] However, the inverse associations of calcium and vitamin D with CRC risk were most pronounced among NL subjects who use calcium- or vitamin D-containing supplements. NL controls were more likely than cases to consume calcium- or vitamin D-containing supplements (Table 2). Yet it is also likely that supplement users may be more conscious about health and therefore may have healthier dietary and physical activity habits as compared to non-supplement users. However, we did attempt to control for the effects of other physiologic, behavioural, and dietary factors in these analyses. Another possibility is that calcium- or vitamin D-containing supplements may have independent effects on cancer risk. Discussion of such potential biological mechanisms is beyond the scope of the present paper.

Results from this study, however, found that inverse associations did exist for total dairy products and milk in ON. It has been shown that calcium, especially in combinations as found in milk, effectively precipitates luminal cytolytic substances and reduces cytotoxicity of fecal water, an accepted risk marker for colon cancer.[21,22] Besides calcium and vitamin D through fortification, many other components of dairy foods have been shown experimentally to protect against CRC. Dairy foods contain conjugated linoleic acid and lactoferrin, which inhibit colonic carcinogenesis in animal models,[52,53] and it has been suggested that the milk protein casein has antimutagenic activity on the digestive tract.[54] Certain micro-organisms in fermented dairy foods have also been hypothesized to reduce the risk of CRC.[55] In this study, fermented dairy foods, such as cheese and yogurt, did not appear to be related to CRC risk. A possible reason is that cheese fats, particularly saturated fats, might increase risk.[56] However, the intakes of cheese and yogurt were too low to expect significant associations to emerge with analysis of the dietary intake data.

This study had a number of strengths. The large sample size allowed the identification of associations that might not be detectable in smaller studies. More importantly, previous findings by other researchers about the protective effects of these nutrients on CRC risk were confined to specific study populations, and this makes it difficult to generalize the results. In this study, we examined the effects of calcium, vitamin D and dairy product intake on the occurrence of CRC in two Canadian provinces with different rates of CRC incidence. We compared differences of these associations between the two provinces. Furthermore, nutrient intakes were adjusted for total energy intake. The use of calorie-adjusted values in multivariate models will often overcome the problem of high collinearity frequently observed between nutritional factors.[39] This adjustment also reduces between-person variation due to over- or under-reporting of food intakes.[39] The relationships of calcium, vitamin D, dairy products and CRC risk may differ appreciably by several factors, so we controlled for a wide range of potential confounding factors using multivariate logistic regression models. Although some random misclassification of dietary components is likely, non-differential misclassification generally tends to bias the risk estimates toward the null.

Consideration must be given to the potential limitations in the present study that may have influenced the observed associations. First, as in most case-control studies, potential recall and selection biases are possible. Since exposure information was collected after diagnosis, differential recall between cases and controls could bias results. In particular, cases may recall dietary exposures differently from controls because of the presence of illness or symptoms. Controls may have agreed to join this study because of an interest in health and may therefore have healthier dietary and physical activity habits, a pattern that may exaggerate differences with the cases beyond what might have been seen with truly comparable controls.

Second, by design, cases and controls had similar sex distribution; however, cases and controls were not well matched according to age group. Estimates of nutrient intakes from a FFQ are not precise and there is always the potential for measurement error. Although the original FFQ used in this study has been validated,[37,38] this questionnaire requires further evaluation. Third, these findings may reflect problems of collinearity between various nutrients, between selected foods, and between multivitamin supplements, thus this possibility cannot be completely eliminated.

Another potential limitation of this study may be the absence of information on sun exposure. As we know, it is difficult to accu-

rately measure vitamin D exposure in humans.[43] We did not have information on sunshine exposure at baseline. Finally, it is also possible that the 1-2 year referent period on which dietary data were based is insufficient if more remote dietary practices (e.g., 5-10 yrs) have stronger influence on CRC risk.

In conclusion, in Canada the results of our case-control study add to the evidence that dietary calcium and vitamin D are associated with a lower risk of CRC. Furthermore, dairy products, milk, supplemental calcium and vitamin D are inversely related with CRC risk. More specifically, the present data support a joint action of calcium and vitamin D in the prevention of colorectal carcinogenesis.

REFERENCES

1. Doll R, Peto R. The causes of cancer: Quantitative estimates of avoidable risks of cancer in the United States today. *J Natl Cancer Inst* 1981;66(6):1191-308.
2. Garland C, Garland F. Do sunlight and vitamin D reduce the likelihood of colon cancer? *Int J Epidemiol* 1980;9:227-31.
3. Lamprecht SA, Lipkin M. Chemoprevention of colon cancer by calcium, vitamin D and folate: Molecular mechanisms. *Nat Rev Cancer* 2003;3(8):601-14.
4. Ishihara J, Inoue M, Iwasaki M, Sasazuki S, Tsugane S. Dietary calcium, vitamin D, and the risk of colorectal cancer. *Am J Clin Nutr* 2008;88(6):1576-83.
5. Garland C, Shekelle RB, Barrett-Connor E, Criqui MH, Rossof AH, Paul O. Dietary vitamin D and calcium and risk of colorectal cancer: A 19-year prospective study in men. *Lancet* 1985;1(8424):307-9.
6. Garland CF, Garland FC, Gorham ED, Lipkin M, Newmark H, Mohr SB, et al. The role of vitamin D in cancer prevention. *Am J Public Health* 2006;96(2):252-61.
7. Giovannucci E, Liu Y, Rimm EB, Hollis BW, Fuchs CS, Stampfer MJ, et al. Prospective study of predictors of vitamin D status and cancer incidence and mortality in men. *J Natl Cancer Inst* 2006;98(7):451-59.
8. Wei MY, Garland CF, Gorham ED, Mohr SB, Giovannucci E. Vitamin D and prevention of colorectal adenoma: A meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2008;17(11):2958-69.
9. Garland CF, Gorham ED, Mohr SB, Garland FC. Vitamin D for cancer prevention: Global perspective. *Ann Epidemiol* 2009;19(7):468-83.
10. Yin L, Grandi N, Raum E, Haug U, Arndt V, Brenner H. Meta-analysis: Longitudinal studies of serum vitamin D and colorectal cancer risk. *Aliment Pharmacol Ther* 2009;30(2):113-25.
11. Woolcott CG, Wilkens LR, Nomura AM, Horst RL, Goodman MT, Murphy SP, et al. Plasma 25-hydroxyvitamin D levels and the risk of colorectal cancer: The multiethnic cohort study. *Cancer Epidemiol Biomarkers Prev* 2010;19(1):130-34.
12. Grant WB. Relation between prediagnostic serum 25-hydroxyvitamin D level and incidence of breast, colorectal, and other cancers. *J Photochem Photobiol B* 2010;101(2):130-36.
13. Grau MV, Baron JA, Sandler RS, Wallace K, Haile RW, Church TR, et al. Prolonged effect of calcium supplementation on risk of colorectal adenomas in a randomized trial. *J Natl Cancer Inst* 2007;99(2):129-36.
14. Lappe JM, Travers-Gustafson D, Davies KM, Recker RR, Heaney RP. Vitamin D and calcium supplementation reduces cancer risk: Results of a randomized trial. *Am J Clin Nutr* 2007;85(6):1586-91.
15. Wactawski-Wende J, Kotchen JM, Anderson GL, Assaf AR, Brunner RL, O'Sullivan MJ, et al. Calcium plus vitamin D supplementation and the risk of colorectal cancer. *N Engl J Med* 2006;354(7):684-96.
16. Carroll C, Cooper K, Papaioannou D, Hind D, Pilgrim H, Tappenden P. Supplemental calcium in the chemoprevention of colorectal cancer: A systematic review and meta-analysis. *Clin Ther* 2010;32(5):789-803.
17. Weingarten MA, Zalmanovici A, Yaphe J. Dietary calcium supplementation for preventing colorectal cancer and adenomatous polyps. *Cochrane Database Syst Rev* 2008;1:CD003548.
18. Shaukat A, Scouras N, Schünemann HJ. Role of supplemental calcium in the recurrence of colorectal adenomas: A metaanalysis of randomized controlled trials. *Am J Gastroenterol* 2005;100(2):390-94.
19. Newmark HL, Wargovich MJ, Bruce WR. Colon cancer and dietary fat, phosphate, and calcium: A hypothesis. *J Natl Cancer Inst* 1984;72(6):1323-25.
20. Jacobs ET, Jurutka PW, Martinez ME, Alberts DS. Vitamin D, calcium, and colorectal neoplasia: New insights on mechanisms of action. *Cancer Prev Res (Phila Pa)* 2009;2(3):197-99.
21. Glinghammar B, Venturi M, Rowland IR, Rafter JJ. Shift from a dairy product-rich to a dairy product-free diet: Influence on cytotoxicity and genotoxicity of fecal water—potential risk factors for colon cancer. *Am J Clin Nutr* 1997;66(5):1277-82.
22. Govers MJ, Termont DS, Lapre JA, Kleibeuker JH, Vonk RJ, Van der Meer R. Calcium in milk products precipitates intestinal fatty acids and secondary bile acids and thus inhibits colonic cytotoxicity in humans. *Cancer Res* 1996;56(14):3270-75.
23. Jarvinen R, Knekt P, Hakulinen T, Aromaa A. Prospective study on milk products, calcium and cancers of the colon and rectum. *Eur J Clin Nutr* 2001;55(11):1000-7.
24. World Cancer Research Fund/American institute for Cancer Research. Food, nutrition, physical activity, and the prevention of cancer: A global perspective. Washington, DC: AICR, 2007.
25. Grau MV, Baron JA, Sandler RS, Haile RW, Beach ML, Church TR, et al. Vitamin D, calcium supplementation, and colorectal adenomas: Results of a randomized trial. *J Natl Cancer Inst* 2003;95(23):1765-71.
26. Bostick RM, Potter JD, Sellers TA, McKenzie DR, Kushi LH, Folsom AR. Relation of calcium, vitamin D, and dairy food intake to incidence of colon cancer among older women. The Iowa Women's Health Study. *Am J Epidemiol* 1993;137(12):1302-17.
27. McCullough ML, Robertson AS, Rodriguez C, Jacobs EJ, Chao A, Carolyn J, et al. Calcium, vitamin D, dairy products, and risk of colorectal cancer in the Cancer Prevention Study II Nutrition Cohort (United States). *Cancer Causes Control* 2003;14(1):1-12.
28. Zheng W, Anderson KE, Kushi LH, Sellers TA, Greenstein J, Hong CP, et al. A prospective cohort study of intake of calcium, vitamin D, and other micronutrients in relation to incidence of rectal cancer among postmenopausal women. *Cancer Epidemiol Biomarkers Prev* 1998;7(3):221-25.
29. Martinez ME, Giovannucci EL, Colditz GA, Stampfer MJ, Hunter DJ, Speizer FE, et al. Calcium, vitamin D, and the occurrence of colorectal cancer among women. *J Natl Cancer Inst* 1996;88(19):1375-82.
30. Kearney J, Giovannucci E, Rimm EB, Ascherio A, Stampfer MJ, Colditz GA, et al. Calcium, vitamin D, and dairy foods and the occurrence of colon cancer in men. *Am J Epidemiol* 1996;143(9):907-17.
31. Pietinen P, Malila N, Virtanen M, Hartman TJ, Tangrea JA, Albanes D, et al. Diet and risk of colorectal cancer in a cohort of Finnish men. *Cancer Causes Control* 1999;10(5):387-96.
32. Terry P, Baron JA, Bergkvist L, Holmberg L, Wolk A. Dietary calcium and vitamin D intake and risk of colorectal cancer: A prospective cohort study in women. *Nutr Cancer* 2002;43(1):39-46.
33. Lin J, Zhang SM, Cook NR, Manson JE, Lee IM, Buring JE. Intakes of calcium and vitamin D and risk of colorectal cancer in women. *Am J Epidemiol* 2005;161(8):755-64.
34. Wang PP, Dicks E, Gong X, Buehler S, Zhao J, Squires J, et al. Validity of random-digit-dialing in recruiting controls in a case-control study. *Am J Health Behav* 2009;33(5):513-20.
35. Squires J, Roebothan B, Buehler S, Sun Z, Cotterchio M, Younghusband B, et al. Pickled meat consumption and colorectal cancer (CRC): A case-control study in Newfoundland and Labrador, Canada. *Cancer Causes Control* 2010;21(9):1513-21.
36. Zhao J, Halfyard B, West R, Buehler S, Sun Z, Squires J, et al. Tobacco smoking and colorectal cancer: A population-based case-control study in Newfoundland and Labrador. *Can J Public Health* 2010;101(4):281-89.
37. Stram DO, Hankin JH, Wilkens LR, Pike MC, Monroe KR, Park S, et al. Calibration of the dietary questionnaire for a multiethnic cohort in Hawaii and Los Angeles. *Am J Epidemiol* 2000;151(4):358-70.
38. Kolonel LN, Henderson BE, Hankin JH, Nomura AM, Wilkens LR, Pike MC, et al. A multiethnic cohort in Hawaii and Los Angeles: Baseline characteristics. *Am J Epidemiol* 2000;151(4):346-57.
39. Willett W, Stampfer MJ. Total energy intake: Implications for epidemiologic analyses. *Am J Epidemiol* 1986;124(1):17-27.
40. Nilsen TI, Vatten LJ. Prospective study of colorectal cancer risk and physical activity, diabetes, blood glucose and BMI: Exploring the hyperinsulinaemia hypothesis. *Br J Cancer* 2001;84(3):417-22.
41. Mizoue T, Kimura Y, Toyomura K, Nagano J, Kono S, Mibu R, et al. Calcium, dairy foods, vitamin D, and colorectal cancer risk: The Fukuoka Colorectal Cancer Study. *Cancer Epidemiol Biomarkers Prev* 2008;17(10):2800-7.
42. Ryan-Harshman M, Aldoori W. Diet and colorectal cancer: Review of the evidence. *Can Fam Phys* 2007;53(11):1913-20.
43. Grant WB, Garland CF. A critical review of studies on vitamin D in relation to colorectal cancer. *Nutr Cancer* 2004;48(2):115-23.
44. Huncharek M, Muscat J, Kupelnick B. Colorectal cancer risk and dietary intake of calcium, vitamin D, and dairy products: A meta-analysis of 26,335 cases from 60 observational studies. *Nutr Cancer* 2009;61(1):47-69.
45. Lipworth L, Bender TJ, Rossi M, Bosetti C, Negri E, Talamini R, et al. Dietary vitamin D intake and cancers of the colon and rectum: A case-control study in Italy. *Nutr Cancer* 2009;61(1):70-75.
46. Roebothan BV. Nutrition Newfoundland and Labrador. 2003. Available at: http://www.hc-sc.gc.ca/fn-an/surveill/nutrition/prov/index-eng.php#2 (Accessed May 2010).
47. Mendelson R. Report of the Ontario Food Survey, 2003. Available at: http://www.hc-sc.gc.ca/fn-an/surveill/nutrition/prov/index-eng.php#2 (Accessed May 2010).
48. Thun MJ, Calle EE, Namboodiri MM, Flanders WD, Coates RJ, Byers T, et al. Risk factors for fatal colon cancer in a large prospective study. *J Natl Cancer Inst* 1992;84(19):1491-500.
49. Wu K, Willett WC, Fuchs CS, Colditz GA, Giovannucci EL. Calcium intake and risk of colon cancer in women and men. *J Natl Cancer Inst* 2002;94(6):437-46.

50. Chan JM, Giovannucci E, Andersson SO, Yuen J, Adami HO, Wolk A. Dairy products, calcium, phosphorous, vitamin D, and risk of prostate cancer (Sweden). *Cancer Causes Control* 1998;9(6):559-66.
51. Wolf RL, Cauley JA, Baker CE, Ferrell RE, Charron M, Caggiula AW, et al. Factors associated with calcium absorption efficiency in pre- and perimenopausal women. *Am J Clin Nutr* 2000;72(2):466-71.
52. MacDonald HB. Conjugated linoleic acid and disease prevention: A review of current knowledge. *J Am Coll Nutr* 2000;19(Suppl 1):111S-118S.
53. Tsuda H, Sekine K, Ushida Y, Kuhara T, Takasuka N, Iigo M, et al. Milk and dairy products in cancer prevention: Focus on bovine lactoferrin. *Mutat Res* 2000;462(2-3):227-33.
54. van Boekel MA, Goeptar AR, Alink GM. Antimutagenic activity of casein against MNNG in the E. coli DNA repair host-mediated assay. *Cancer Lett* 1997;114(1-2):85-87.
55. Kampman E, Goldbohm RA, van den Brandt PA, van 't Veer P. Fermented dairy products, calcium, and colorectal cancer in The Netherlands Cohort Study. *Cancer Res* 1994;54(12):3186-90.
56. Norat T, Riboli E. Dairy products and colorectal cancer. A review of possible mechanisms and epidemiological evidence. *Eur J Clin Nutr* 2003;57(1):1-17.

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RÉSUMÉ

Contexte : Des études épidémiologiques antérieures, bien que peu concluantes, donnent à penser que les apports en calcium, en vitamine D et en produits laitiers sont inversement associés au risque de cancer colorectal (CCR). Nous avons mené une vaste comparaison populationnelle de telles associations à Terre-Neuve-et-Labrador (T.-N.-L.) et en Ontario.

Méthode : Nous avons utilisé un plan d'étude cas/témoins. Nos cas de cancer colorectal étaient des patients nouvellement atteints de CCR âgés de 20 à 74 ans. Nos témoins étaient un échantillon aléatoire de la population de chaque province, assortis selon le sexe et le groupe d'âge. Nous avons analysé 1 760 cas et 2 481 témoins de T.-N.-L. et de l'Ontario. Des renseignements sur leurs apports alimentaires et leurs modes de vie ont été recueillis au moyen de questionnaires auto-administrés sur la fréquence de consommation des produits alimentaires et les antécédents personnels.

Résultats : Dans les deux provinces, les témoins ont déclaré des apports moyens quotidiens plus élevés en calcium total et en vitamine D totale. En Ontario, un risque de CCR significativement réduit était associé aux apports en calcium total (RC des quintiles supérieur et inférieur = 0,57, IC de 95 % = 0,42-0,77, P=0,03), en vitamine D totale (RC=0,73, IC de 95 % = 0,54-1,00), en calcium alimentaire (RC=0,76, IC de 95 % = 0,60-0,97), en vitamine D alimentaire (RC=0,77, IC de 95 % = 0,61-0,99), en lait et produits laitiers totaux (RC=0,78, IC de 95 % = 0,60-1,00) et à la consommation de suppléments contenant du calcium (RC=0,76). À T.-N.-L., les associations inverses entre le calcium, la vitamine D et le risque de CCR étaient plus prononcées chez les consommateurs de suppléments contenant du calcium ou de la vitamine D (RC=0,67, 0,68, respectivement).

Conclusion : Les résultats de cette étude tendent à confirmer que le calcium total, le calcium alimentaire, la vitamine D totale, la vitamine D alimentaire et la consommation de suppléments contenant du calcium ou de la vitamine D peuvent réduire le risque de CCR. Les associations inverses entre le risque de CCR et les apports en lait et produits laitiers totaux pourraient s'expliquer dans une large mesure par le calcium et la vitamine D.

Mots clés : calcium; vitamine D; produits laitiers; tumeurs colorectales

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New Conversations on Suicidality
3-5 October 2011 — Vancouver, BC
Contact:
www.casp2011.ca

Engaging Priority Populations
A joint initiative of the Ontario Public Health Association and Health Promotion Ontario
5-6 October 2011 — Toronto, ON
Contact:
www.ophafallforum.ca — E-mail: admin@opha.on.ca

Action on Wellness
An International Symposium
11-13 October 2011 — Banff, AB
Contact:
www.actiononwellness.ca

The Art and Science of Knowledge Exchange
19-20 October 2011 — Toronto, Ontario
Contact:
www.catie.ca/eng/GetInvolved/ASKE2011.shtml

42nd Union World Conference on Lung Health
Partnerships for Scaling-up and Care
26-30 October 2011 — Lille, France
Contact:
www.worldlunghealth.org/

HealthAchieve 2011
7-9 November 2011 — Toronto, ON
Contact:
www.healthachieve.com/

Canadian Injury Prevention and Safety Promotion Conference/Conférence canadienne sur la prévention des traumatismes et la promotion de la santé
Be Visible/Sois visible
16-18 November/novembre 2011 — Vancouver, BC
Contact/contacter :
www.injurypreventionconference.ca

CDPAC Fourth Pan-Canadian Conference
Integrated Chronic Disease Prevention: It Works!
8-10 February 2012 — Ottawa, Ontario
Contact:
www.cdpac.ca/content.php?doc=196

15th World Conference on Tobacco or Health
International Epidemiology Association
20-24 March 2012 — Singapore
Contact:
wctoh2012.org/

21st Annual Canadian Conference on HIV/AIDS Research
21e Congrès canadien annuel de recherche sur le VIH/sida
19-22 April/avril 2012 — Montreal, QC
Contact/contacter :
info@cahr-conference-acrv.ca — www.cahr-conference-acrv.ca

CALL FOR ABSTRACTS
13th World Congress on Public Health
Moving Towards Global Health Equity: Opportunities and Threats
21-29 April 2012 — Addis Ababa, Ethiopia
Contact:
www.etpha.org/2012/
Deadline for Abstracts: October 21, 2011

CPHA 2012 Annual Conference
2012 Conférence annuelle de l'ACSP
11-14 June/juin 2012 — Edmonton, AB
Contact/contacter :
www.conference.cpha.ca — conference@cpha.ca
* Note: the conference will be held from Monday to Thursday
* N.B. : la conférence aura lieu du lundi au jeudi

22nd Biennial Meeting of the International Society for the Study of Behavioural Development
8-12 July 2012 — Edmonton, AB
Contact:
www.issbd2012.com