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Dairy products, calcium and phosphorus intake, and the risk of prostate cancer: results of the French prospective SU.VI.MAX (Supplémentation en Vitamines et Minéraux Antioxydants) study

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Although dairy products have been found to be associated with an elevated risk of prostate cancer, studies investigating the potential effect of Ca are limited, and findings are inconsistent. The objective of the present study was to test the relationship between the risk of prostate cancer and consumption of dairy products and Ca. The analysis included 2776 men from the French SU.VI.MAX (Supplementation en Vitamines et Minéraux Antioxydants) prospective study, among whom sixty-nine developed prostate cancer during the follow-up period (median: 7·7 years). Food consumption was assessed at inclusion from repeated 24 h records and nutrient intake was calculated using a food composition table. A higher risk of prostate cancer was observed among subjects with higher dairy product (relative risk (RR; 95 % CI), 4th quartile *v*. 1st: 1·35 (1·02, 1·78), $P=0·04$) and Ca intake (RR (95 % CI), 4th quartile *v*. 1st: 2·43 (1·05, 5·62), $P=0·04$). Nevertheless, we identified a harmful effect of yoghurt consumption upon the risk of prostate cancer (RR (95 % CI), increment 125 g/d: 1·61 (1·07, 2·43), $P=0·02$) independently of the Ca content. Our data support the hypothesis that dairy products have a harmful effect with respect to the risk of prostate cancer, largely related to Ca content. The higher risk of prostate cancer with linear increasing yoghurt consumption seems to be independent of Ca and may be related to some other component.

Prostate cancer: Dietary calcium: Dietary phosphorus: Dairy products: Yoghurt

Prostate cancer is the most common cancer among men in France (Remontet *et al.* 2003). Many epidemiological studies have suggested that dietary factors play a role in prostate cancer development (Bostwick *et al.* 2004). High consumption of dairy foods has been associated with an increased risk of prostate cancer in both prospective and case–control studies (Chan & Giovannucci, 2001; Dagnelie *et al.* 2004; Tseng *et al.* 2005). Fat from dairy products has long been suspected to be responsible for this association but recently published studies have suggested an effect of other nutrients in dairy products, such as Ca and possibly P (Chan *et al.* 2001). High Ca intake may increase the risk of prostate cancer through down-regulation of the production of 1,25-hydroxyvitamin D (Chen & Holick, 2003).

Epidemiological studies have investigated the relationship between Ca intake and the risk of prostate cancer (Giovannucci *et al.* 1998; Schuurman *et al.* 1999; Chan *et al.* 2000, 2001; Tavani *et al.* 2001, 2005; Kristal *et al.* 2002; Rodriguez *et al.* 2003; Tseng *et al.* 2005). Some of these suggested an increase in the risk of prostate cancer with high levels of Ca intake, but statistical significance was reached in only four studies (Giovannucci *et al.* 1998; Chan *et al.* 2001; Rodriguez *et al.* 2003; Tseng *et al.* 2005). Furthermore, most studies were conducted in the USA or Northern Europe, where dairy food consumption habits are different from those of the French. Thus, in the present study, we investigated the association between dairy food consumption, dairy-related nutrients (i.e. Ca and P) and the risk of prostate cancer in a healthy population of middle-aged participants in the SU.VI.MAX (Supplémentation en Vitamines et Minéraux Antioxydants) prospective study.

Materials and methods

Study population

Subjects were participants in the SU.VI.MAX study, a randomized, double-blind, placebo-controlled, primary prevention trial designed to assess the potential effect of daily supplementation with nutritional doses of antioxidants (vitamins C and E and β-carotene) and minerals (Se and Zn) on the incidence of cancers and IHD. Details of the study design have been described elsewhere (Hercberg *et al.* 2004). Briefly, 12 741 eligible subjects were enrolled in 1994–1995 for a planned follow-up of 8 years. The cohort consisted of 7713 women aged 35–60 years and 5028 men aged 45–60 years at baseline. Participants were invited yearly to either a clinical or a biological examination. Subjects also regularly provided information on health events and dietary habits by filling out computerized questionnaires using the Minitel Telematic Network through a processing unit loaded with specific software.

The SU.VI.MAX study was approved by the Ethical Committee for Studies with Human Subjects of Paris-Cochin Hospital

Abbreviations: RR, relative risk; SU.VI.MAX, Supplémentation en Vitamines et Minéraux Antioxydants.

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Dietary assessment methods

Subjects were invited to complete a 24 h record every 2 months. The six records were distributed randomly throughout the days of the week, thereby including all days of the week and all seasons for mean intake. Dietary data were collected using the Minitel Telematic Network. At baseline, participants received a manual containing a guide for codification of foods and photographs of portion sizes in order to more easily estimate portion size. A pilot study had previously been conducted to validate the photographs.

In the present analysis, we included 2805 men who had completed at least five dietary records over the first 18 months of the study, as we had previously reported that five 24 h records were necessary to take into account seasonal and weekly variations in the estimate of Ca intake (Mennen *et al.* 2002). We randomly selected five records for subjects who had completed more than five 24 h records during the recording period of 18 months.

Total dairy products were considered along with specific products (yoghurt, fresh cheese, milk and cheese). The dietary intake of nutrients, especially Ca and P, were calculated using a food composition table (Hercberg, 2005).

Identification of prostate cancer cases

Confirmed or suspected events were self-declared by subjects during the yearly follow-up process or were identified by the official death certificate. Investigations were conducted in all cases to obtain medical data from participants, physicians and/or hospitals. All information was reviewed by an independent expert committee and cases were validated by pathological report and classified using the *International Chronic Diseases Classification, 10th Revision, Clinical Modification*. Prostate cancer cases were identified as C61.

For the present study, we excluded subjects who had reported a cancer diagnosis (except for basal cell skin cancer or *in situ* tumours) before the start of follow-up (*n* 20), subjects lost to follow-up during the dietary data assessment period (*n* 9) and subjects with cancer other than prostate cancer (*n* 119). Our final analysis included 2776 subjects, among whom sixty-nine developed prostate cancer during the follow-up period (median follow-up: 7·7 years).

Statistical analysis

To examine the relationships between dairy food, dietary Ca, P and the risk of prostate cancer, we used Cox proportional hazards models to estimate relative risk (RR) and 95 % CI. Age at the beginning of the follow-up period was used as the primary time variable. Age at diagnosis of prostate cancer or at the censoring date (date of the last follow-up questionnaire, date of death or December 2004, whichever occurred first) was used as the end-of-study time variable (Korn *et al.* 1997).

We adjusted for total dietary energy intake by use of the energy-adjusted nutrient intake method (Willett & Stampfer, 1986), considering residuals of nutrient intakes over total energy (other than from alcohol), and then including in the model the quartiles of energy from fat and energy from other sources (proteins and carbohydrates). For dairy food consumption, adjustment for energy was performed by including the quartile of energy from fat and energy from other sources (proteins and carbohydrates) in the Cox model alone.

Quartiles of nutrients and some dairy foods (i.e. total dairy products, milk and cheese) were calculated based on distribution of non-cases. For yoghurt and fresh cheese, we considered a non-consumer category and we classified consumers into tertiles according to the distribution of non-cases. Tests for linear trend were performed using the ordinal score. We also tested for a potential interaction between Ca and P.

We controlled for the following baseline factors: BMI at recruitment ($<18{\cdot}5$, $18{\cdot}5–25{\cdot}0$, $25{\cdot}0–30{\cdot}0$, $\geq 30{\cdot}0\,kg/m^2$), total daily alcohol intake (0, 0–16, 16–32, >32 g), family history of prostate cancer (yes/no), overall physical activity level (low, moderate, high), occupation (retired, white collar, inactive, self-employed, worker/farmer, employees as reference), group of treatment (antioxidants/placebo) and smoking status at baseline (smoker, former smoker, never-smoker). We also tested other potential confounders such as saturated fatty acids, vegetable consumption and meat consumption in order to test potential changes in associations with the risk of prostate cancer.

All analyses were performed using SAS software, version 8·2 (SAS Institute, Cary, NC, USA).

Results

Characteristics of the studied population

Baseline characteristics of men with or without prostate cancer are presented in Table 1.

BMI, level of physical activity, smoking status, alcohol consumption, energy intake from food, energy-adjusted total Ca intake, energy-adjusted non-dairy Ca intake and total dairy product consumption were not statistically different between cases and non-cases. In contrast, men who developed prostate cancer were significantly older (mean 57·1 (SD) 4·7 years) than non-cases (mean 53·3 (SD) 4·7 years; $P<0{\cdot}001$). A family history of prostate cancer was more frequent ($P=0{\cdot}05$) among cases (10·1 %) than non-cases (4·8 %). Daily mean energy-adjusted intake of Ca from dairy products ($P=0{\cdot}05$) and P ($P=0{\cdot}03$) were higher among cases than non-cases.

The correlation coefficient between Ca intake and *P* intake was 0·81. Dairy food was the major source of Ca, accounting for 59·8 % of total Ca intake.

Nutrient intake and prostate cancer

The crude (age- and energy-adjusted) and multivariate RR of prostate cancer with respect to Ca and P intake are presented in Table 2.

An increase in the risk of prostate cancer was observed with increasing intake of Ca ($P=0{\cdot}04$), with a multivariate RR (95 % CI) for the upper quartile compared with the lowest of 2·43 (1·05, 5·62). This effect was significant only for Ca from dairy sources, with a multivariate RR (95 % CI) of 2·94 (1·16, 7·51) for subjects in the 4th quartile compared with those in the 1st quartile. Non-dairy Ca intake was not associated with the risk of prostate cancer. The risk of prostate cancer seemed to be modified by P intake ($P=0{\cdot}04$), although RR were not significant (RR (95 % CI), highest quartile *v.* lowest: 1·83 (0·89, 3·73)).

Table 1. Baseline characteristics of the studied population (invasive cancer) according to status (Means and standard deviations or percentages)

	Cases		Non-cases		
	Mean	SD	Mean	SD	*P* for test*
n	69	2588			
Supplementation group (%)	50·72		50·81		NS
Age (years)†	57·1	4·7	53·3	4·7	$<0·0001$
Occupation (%)					
Employees	27·5		35·1		0·02
White collar	24·6		33·7		
Self-employed	10·1		5·1		
Worker/farmer	0·0		6·4		
Retired	30·4		13·9		
Inactive	7·3		5·7		
Smoking habits (%)					
Smoker	13·2		13·3		NS
Ex-smoker	51·5		51·1		
Never-smoker	35·3		35·6		
Overall physical activity (%)					
High	49·3		52·5		NS
Moderate	26·9		24·0		
Low	23·9		23·5		
BMI (kg/m^2)					
$<18·5$	1·5		0·5		NS
18·5–25·0	50·8		51·5		
25·0–30·0	41·8		43·8		
$\geq 30·0$	6·00		4·3		
Family history of prostate cancer (%)	10·1		4·8		0·05
Energy intake (kJ/d)‡	9472	2525	9560	2362	NS
Alcohol intake (g/d)	30·6	24·0	28·8	24·6	NS
Energy-adjusted total Ca (mg/d)	984	269	925	296	NS
Energy-adjusted dairy Ca (mg/d)	608	255	546	288	0·05
Energy-adjusted non-dairy Ca (mg/d)	376	109	379	125	NS
Energy-adjusted P (mg/d)	1369	206	1312	217	0·03
Dairy products (g/d)	327	171	296	178	NS

* χ^2 test for qualitative variables and Student *t* test for continuous variables.
† At the beginning of the follow-up period.
‡ Energy from diet.

The relationship between Ca intake (total or dairy) and the risk of prostate cancer was not changed substantially after adjustment for P intake (data not shown).

We also considered the dietary Ca:P ratio. An increase in the risk of prostate cancer was observed in the second (RR (95 % CI): 2·07 (0·96, 4·44)) and third (RR (95 % CI): 2·33 (1·09, 4·97)) quartile, but this increase was not observed in the fourth. A significant interaction was observed between P intake and Ca intake (*P* for interaction=0·02). The association between Ca intake and prostate cancer according to the level of P is presented in Table 3. Although neither the test for trend nor the RR reached statistical significance, a high Ca intake appeared to be associated with a slightly higher risk of prostate cancer among subjects with a low P intake.

Dairy products and prostate cancer

The crude and multivariate RR (95 % CI) of prostate cancer according to total dairy product consumption and specific dairy products (for categories of consumption and increment) are shown in Table 4. We also present multivariate risks after adjustment for Ca intake. We tested further adjustments (saturated fatty acids, vitamin D and other food groups) in order to better characterize the effect of Ca but findings were not changed substantially (results not tabulated).

A linear trend towards an increase in the risk of prostate cancer among subjects with increasing consumption of total dairy products was suspected (*P*=0·04), with RR (95 % CI) equal to 1·35 (1·02, 1·78) for an increase in dairy food consumption of 200 g. This relationship was no longer significant after adjustment for Ca. No association was observed between milk and cheese consumption and the risk of prostate cancer. In contrast, an increase in the risk of prostate cancer was seen among subjects with a high consumption of fresh cheese (*P*=0·02) even after adjustment for Ca. The multivariate RR (95 % CI) adjusted for Ca for subjects in the upper tertile of consumption compared with non-consumers was 2·13 (1·09, 4·15). Likewise, when tertiles of yoghurt consumption *v*. non-consumption were considered, we observed an increase in the risk of prostate cancer in men consuming yoghurt (*P*=0·05), but this association did not remain significant after adjustment for Ca. RR for a daily increment of 100 g fresh cheese were greater than unity but were not significant. RR for an increment of yoghurt consumption were statistically significant: the multivariate RR (95 % CI) adjusted for Ca of prostate cancer for an increase of 125 g in daily yoghurt consumption was 1·61 (1·07, 2·43).

Table 2. Crude and multivariate* relative risk (RR; 95 % CI) of prostate cancer by quartile of dietary energy-adjusted total, dairy and non-dairy calcium, and phosphorus intakes

	Quartile				
	1	2	3	4	*P* for trend
Total Ca					
Intake (mg/d)	<725	725–891	891–1081	>1081	
Cases (*n*)	8	18	24	19	
Crude RR (95 % CI)	1·00 (–)	2·38 (1·03, 5·50)	3·09 (1·38, 6·91)	2·39 (1·04, 5·46)	0·04
Multivariate RR (95 % CI)	1·00 (–)	2·43 (1·05, 5·66)	3·19 (1·41, 7·20)	2·43 (1·05, 5·62)	0·04
Dairy Ca					
Intake (mg/d)	<354	354–518	518–696	>696	
Cases (*n*)	6	19	26	18	
Crude RR (95 % CI)	1·00 (–)	3·05 (1·21, 7·68)	4·28 (1·75, 10·43)	2·90 (1·15, 7·31)	0·03
Multivariate RR (95 % CI)	1·00 (–)	3·11 (1·23, 7·89)	4·35 (1·77, 10·67)	2·94 (1·16, 7·51)	0·03
Non-dairy Ca					
Intake (mg/d)	<294	294–359	359–440	>440	
Cases (*n*)	19	14	15	21	
Crude RR (95 % CI)	1·00 (–)	0·79 (0·40, 1·59)	0·76 (0·39, 1·51)	1·12 (0·60, 2·09)	0·75
Multivariate RR (95 % CI)	1·00 (–)	0·78 (0·39, 1·57)	0·72 (0·36, 1·45)	1·12 (0·60, 2·11)	0·76
P					
Intake (mg/d)	<1167	1167–1291	1291–1434	>1434	
Cases (*n*)	12	12	22	23	
Crude RR (95 % CI)	1·00 (–)	1·04 (0·46, 2·32)	1·88 (0·92, 3·86)	1·83 (0·91, 3·69)	0·04
Multivariate RR (95 % CI)	1·00 (–)	1·03 (0·45, 2·32)	1·94 (0·94, 4·03)	1·83 (0·89, 3·73)	0·04
Ca:P ratio					
Intake	<0·60	0·60–0·70	0·70–0·79	>0·79	
Cases (*n*)	10	20	23	16	
Crude RR (95 % CI)	1·00 (–)	1·98 (0·93, 4·24)	2·42 (1·15, 5·09)	1·60 (0·72-3·53)	0·24
Multivariate RR (95 % CI)	1·00 (–)	2·07 (0·96, 4·44)	2·33 (1·09, 4·97)	1·68 (0·74-3·79)	0·23

* Adjusted for: occupation (retired, white collar, inactive, self-employed, worker/farmer, employee), group of treatment (supplementation/placebo), smoking status (smoker, ex-smoker, never-smoker), overall physical activity (low, moderate, high), energy from fat (quartile), energy from other sources (quartile), ethanol intake (0, 0–16, 16–32, >32 g), BMI (<18·5, 18·5–25·0, 25·0–30·0, ≥30·0 kg/m^2), family history of prostate cancer in first-degree relative (yes/no).

Table 3. Multivariate* relative risk (RR; 95 % CI) of prostate cancer by quartile of energy-adjusted calcium intake to energy-adjusted phosphorus intake

	Ca intake quartile				
	1 (<725 mg/d)	2 (725–891 mg/d)	3 (891–1081 mg/d)	4 (>1081 mg/d)	*P* for trend
Low P intake, <1291 mg/d					
Cases (*n*)	5	7	10	2	
Multivariate RR (95 % CI)	1·00 (–)	1·71 (0·53, 5·60)	2·93 (0·95, 9·08)	2·11 (0·38, 11·77)	0·09
High P intake, ≥1291 mg/d					
Cases (*n*)	3	11	14	17	
Multivariate RR (95 % CI)	1·00 (–)	1·95 (0·52, 7·36)	1·46 (0·39, 5·40)	1·32 (0·37, 4·69)	0·81

* Adjusted for: occupation (retired, white collar, inactive, self-employed, worker/farmer, employee), group of treatment (supplementation/placebo), smoking status (smoker, ex-smoker, never-smoker), overall physical activity (low, moderate, high), energy from fat (quartile), energy from other sources (quartile), ethanol intake (0, 0–16, 16–32, >32 g), BMI (<18·5, 18·5–25·0, 25·0–30·0, ≥30·0 kg/m^2), family history of prostate cancer in first-degree relative (yes/no).

Discussion

Our findings support the hypothesis that high dairy product consumption is positively associated with the risk of prostate cancer while this relationship did not persist after adjustment for Ca intake. Ca and possibly P content may explain this relationship, as we found a positive association between Ca intake, particularly of dairy Ca, and the risk of prostate cancer. Some specific dairy foods may act on the risk of prostate cancer but as relationships were not obvious in our population, findings have to be interpreted cautiously.

One limitation in our study might have been a potential lack of statistical power due to the size of the studied sample. However, the fact that the small number of prostate cancer cases led us to find a significant association between the risk of prostate cancer and Ca intake strengthened the reality of that association. None the less, these results should be interpreted with caution, as Ca and P intakes were strongly correlated in our population. Indeed, it is difficult to assess the effect of each single nutrient, i.e. Ca and P, independently. The observed positive association of P might be at least partially confounded by that of Ca. We did not present the association between vitamin D intake and risk of prostate cancer as dietary intakes were low; most dairy products available in France during the dietary assessment period were not vitamin-enriched. Non-dairy Ca intake was not associated with the risk of prostate cancer in the present study. This result may be due to a lack of statistical power induced by the relatively low range of non-dairy Ca intake and/or number

Table 4. Crude and multivariate relative risk (RR; 95 % CI) of prostate cancer according to categories of total and specific dairy product consumption

	Consumption category				*P* for trend	Increment	*P* for trend
Dairy products							
Intake (g/d)	<160	160–272	272–396	>396		200	
Cases (*n*)	10	23	17	19			
Crude RR (95 % CI)	1·00 (–)	2·14 (1·01, 4·53)	1·78 (0·81, 3·93)	2·20 (0·99, 4·90)	0·12	1·31 (1·00, 1·72)	0·05
Multivariate RR1* (95 % CI)	1·00 (–)	2·02 (0·95, 4·29)	1·75 (0·79, 3·87)	2·16 (0·96, 4·85)	0·12	1·35 (1·02, 1·78)	0·04
Multivariate RR2† (95 % CI)	1·00 (–)	1·50 (0·68, 3·30)	1·18 (0·50, 2·80)	1·33 (0·52, 3·45)	0·81	1·20 (0·83, 1·75)	0·34
Milk							
Intake (g/d)	<25	25–128	128–253	>253		100	
Cases (n)	16	16	21	16			
Crude RR (95 % CI)	1·00 (–)	1·02 (0·51, 2·05)	1·29 (0·67, 2·49)	1·13 (0·55, 2·31)	0·59	1·05 (0·89, 1·23)	0·59
Multivariate RR1* (95 % CI)	1·00 (–)	1·04 (0·52, 2·11)	1·31 (0·68, 2·55)	1·13 (0·54, 2·34)	0·59	1·04 (0·89, 1·23)	0·61
Multivariate RR2† (95 % CI)	1·00 (–)	1·02 (0·50, 2·07)	1·08 (0·55, 2·12)	0·83 (0·39, 1·77)	0·71	0·96 (0·80, 1·15)	0·68
Cheese							
Intake (g/d)	<25	25–46	46–71	>71		30	
Cases (n)	18	13	20	18			
Crude RR (95 % CI)	1·00 (–)	0·71 (0·34, 1·46)	1·17 (0·59, 2·29)	0·92 (0·44, 1·94)	0·84	1·06 (0·87, 1·30)	0·55
Multivariate RR1* (95 % CI)	1·00 (–)	0·69 (0·33, 1·43)	1·12 (0·56, 2·21)	0·90 (0·42, 1·91)	0·92	1·06 (0·87, 1·31)	0·56
Multivariate RR2† (95 % CI)	1·00 (–)	0·59 (0·28, 1·23)	0·89 (0·44, 1·82)	0·65 (0·29, 1·44)	0·49	0·98 (0·78, 1·24)	0·87
Fresh cheese							
Intake (g/d)	Non-consumer	<20	20–50	>50		100	
Cases (n)	34	13	9	13			
Crude RR (95 % CI)	1·00 (–)	1·91 (1·00, 3·62)	1·28 (0·61, 2·67)	2·26 (1·19, 4·28)	0·02	1·29 (0·82, 2·02)	0·27
Multivariate RR1* (95 % CI)	1·00 (–)	2·07 (1·08, 3·97)	1·29 (0·61, 2·72)	2·38 (1·23, 4·62)	0·02	1·34 (0·83, 2·15)	0·23
Multivariate RR2† (95 % CI)	1·00 (–)	2·06 (1·07, 3·96)	1·24 (0·59, 2·62)	2·13 (1·09, 4·15)	0·04	1·26 (0·77, 2·06)	0·36
Yoghurt							
Intake (g/d)	Non-consumer	<50	50–100	>100		125	
Cases (n)	15	18	19	17			
Crude RR (95 % CI)	1·00 (–)	1·34 (0·67, 2·68)	2·07 (1·04, 4·10)	1·69 (0·83, 3·44)	0·07	1·61 (1·13, 2·30)	0·01
Multivariate RR1* (95 % CI)	1·00 (–)	1·37 (0·68, 2·74)	2·28 (1·13, 4·58)	1·81 (0·87, 3·76)	0·05	1·67 (1·16, 2·40)	0·01
Multivariate RR2† (95 % CI)	1·00 (–)	1·21 (0·60, 2·44)	1·98 (0·98, 4·03)	1·46 (0·68, 3·14)	0·18	1·61 (1·07, 2·43)	0·02

* RR1 was adjusted for: occupation (retired, white collar, inactive, self-employed, worker/farmer, employee), group of treatment (supplementation/placebo), smoking status (smoker, ex- smoker, never-smoker), overall physical activity (low, moderate, high), energy from fat (quartile), energy from others sources (quartile), ethanol intake (0, 0–16, 16–32, >32 g), BMI (<18·5, 18·5–25·0, 25·0–30·0, ≥30·0 kg/m^2), family history of prostate cancer in first-degree relative (yes/no).
† RR2 was adjusted for all covariates in the RR1 model plus dietary energy-adjusted Ca intake.

of cases, as adjustment for other dairy nutrients (saturated fatty acids and P) did not modify our results substantially. Nevertheless we cannot decline an effect of another dairy-related compound which may be correlated to dairy Ca and thus not correlated to non-dairy Ca.

The mechanism underlying the association between the dairy component and the risk of prostate cancer may involve the modulation of vitamin D metabolism by Ca and P. In experimental studies, 1,25-hydroxyvitamin D was consistently found to reduce prostate cancer promotion and stimulate differentiation of prostate epithelial cells which expressed the VDR receptor (Chan & Giovannucci, 2001; Chen & Holick, 2003). High dietary Ca and P intakes reduce the production of 1,25-hydroxyvitamin D by modulation of parathyroid hormone. Furthermore, P may prevent Ca from decreasing the production of 1,25-hydroxyvitamin by binding Ca in the gut. This mechanism could explain the observed interaction of Ca and P with the risk of prostate cancer, since subjects with high levels of Ca intake and low levels of P were at higher risk of prostate cancer.

Some previously published studies have reported a significant increase in the risk of prostate cancer with a high intake of dietary Ca (Giovannucci *et al.* 1998; Chan *et al.* 2001; Rodriguez *et al.* 2003; Tseng *et al.* 2005). In contrast, two European prospective studies (Schuurman *et al.* 1999; Chan *et al.* 2000) and three large case–control studies (Tavani *et al.* 2001, 2005; Kristal *et al.* 2002) did not confirm this relationship. Concerning the prospective studies, their findings may be related to a lower range between opposite categories of Ca intake or to a lack of subjects with sufficiently low Ca intakes. Indeed, the studies were carried out among subjects whose Ca intake of the lower class was approximately 800 mg/d. A recent study (Tseng *et al.* 2005) found an increase in the risk of prostate cancer with increasing P intake, but this relationship did not remain after adjustment for Ca intake. Another study (Chan *et al.* 2000) investigated the effect of both Ca and P in data from a large Finnish prospective study (Alpha-Tocopherol Beta-Carotene Cancer Prevention Study). Like our findings, they observed an interaction between P and Ca intake and the risk of prostate cancer, with a lower risk for subjects with a high intake of P and a low intake of Ca, as we interpreted above. Nevertheless, it was difficult in our study to distinguish a specific effect of Ca independently from that of P, since intakes of these nutrients were strongly correlated. High consumption of dairy products and/or milk was also frequently associated with a higher risk of prostate cancer (Giovannucci *et al.* 1998; Schuurman *et al.* 1999; Chan *et al.* 2001; Michaud *et al.* 2001; Tseng *et al.* 2005). In contrast, in the Finnish prospective study (Alpha-Tocopherol Beta-Carotene study), no association was found between dairy product consumption and the risk of prostate cancer, perhaps because of a very high mean level of consumption, as suggested by the authors. Data from a randomized clinical trial initially designed to test the effect of Ca supplementation on the chemoprevention incidence of adenoma were analysed to estimate the impact of Ca supplementation on the risk of prostate cancer (Baron *et al.* 2005). No effect of supplementation upon the risk of prostate cancer was observed, and findings even suggested a decrease in the level of prostate-specific antigen among supplemented subjects.

Few studies have investigated the effect of specific dairy products other than milk. Two American prospective studies investigated the effect of cottage cheese (Michaud *et al.* 2001; Tseng *et al.* 2005), a fresh dairy product similar to the fresh cheese consumed in France. In the first of those studies (Michaud *et al.* 2001), no association between cottage cheese consumption or total dairy products on the risk of prostate cancer was found. In the second (Tseng *et al.* 2005), an effect of total dairy product consumption was observed, but not for cottage cheese.

Comparing tertiles of consumption with a no-consumer class, a weak effect of yoghurt (relative risks not significant) and fresh cheese was found on the risk of prostate cancer. Our results suggested a specific effect of yoghurt on the risk of prostate cancer ($P=0{\cdot}02$) when considering a daily increase of 125 g (one portion), even after adjustment for Ca intake. This relationship has to be considered carefully as the range of consumption was limited, as was the number of cases, and non-consumers were frequent in our population. We could only suspect a possible threshold effect, but further analyses on large studies are required.

In conclusion, the main finding of the present study consisted of a relationship between Ca intake and the risk of prostate cancer, which may be modulated by P intake. This relationship may be considered partly responsible for the association between the risk of prostate cancer and dairy product consumption, but some other compounds, specific to yoghurt and fresh cheese, may also play a role and further investigations are required. Since dairy products consumed in Europe are somewhat different from those consumed in the USA, further investigations involving large-scale studies in Europe would be helpful to understand the effect of specific dairy foods on the risk of prostate cancer.

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