Associations between fruit, vegetable and legume intakes and prostate cancer risk: results from the prospective Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI.MAX) cohort

Abou Diallo[1,2]*, Mélanie Deschasaux[1], Pilar Galan[1], Serge Hercberg[1,2], Laurent Zelek[1,3], Paule Latino-Martel[1] and Mathilde Touvier[1]

[1]*Sorbonne Paris Cité Epidemiology and Biostatistics Research Center, Inserm U1153, Inra U1125, Cnam, Paris 13, 5 and 7 Universities, Nutritional Epidemiology Research Team (EREN), 13 avenue de Paris, 93000 Bobigny, France*
[2]*Public Health Department, Avicenne Hospital, 125 rue de Stalingrad, 93000 Bobigny, France*
[3]*Oncology Department, Avicenne Hospital, 125 rue de Stalingrad, 93000 Bobigny, France*

Abstract

Although experimental studies suggest that fruits, vegetables and legumes may exert protective effects against prostate carcinogenesis through various bioactive compounds such as dietary fibre and antioxidants, epidemiological evidence is lacking. Notably, very few prospective studies have investigated the relationship between legume intake and prostate cancer risk. Our objective was to prospectively investigate the association between fruit, vegetable, tomato products, potatoes and legume intakes and prostate cancer risk. This study included 3313 male participants to the SUpplémentation en VItamines et Minéraux AntioXydants cohort (follow-up: 1994–2007) who completed at least three 24-h dietary records during the first 2 years of follow-up. Associations between tertiles of intake and prostate cancer risk were assessed by multivariate Cox proportional hazards models. After a median follow-up of 12·6 years, 139 incident prostate cancers were diagnosed. An inverse association was observed between prostate cancer risk and tertiles of legume intake (hazard ratio $(HR)_{T3v.T1} = 0.53$; 95 % CI 0·34, 0·85; $P_{trend} = 0.009$). This association was maintained after excluding soya and soya products from the legume group ($HR_{T3\ v.T1} = 0.56$; 95 % CI 0·35, 0·89; $P_{trend} = 0.02$). No association was observed between prostate cancer risk and tertiles of intakes of fruits ($P_{trend} = 0.25$), vegetables ($P_{trend} = 0.91$), potatoes ($P_{trend} = 0.77$) and tomato products ($P_{trend} = 0.09$). This prospective study confirms the null association between fruit and non-starchy vegetable intakes and prostate cancer risk observed in most previous cohorts. In contrast, although very few prospective studies have been published on the topic, our results suggest an inverse association between legume intake and prostate cancer risk, supported by mechanistic plausibility. These results should be confirmed by large-scale observational and intervention studies.

Key words: **Legumes: Fruits: Vegetables: Prospective studies: Prostate cancer**

Prostate cancer is the most common cancer among males in France, representing >28 % of new cancer cases[1]. It is the second most common cancer worldwide, and the fifth most common cause of cancer death among men: around 1·1 million new cases were recorded worldwide in 2012, accounting for 15 % of all new cases of cancer in men[2]. Prostate cancer is a multifactorial pathology involving lifestyle, anthropometrics, genetics and environmental factors. Among all these determinants, nutrition represents a modifiable factor, and thus a potentially key lever for prevention[2,3].

Fruits, vegetables and legumes represent broadly consumed food sources of bioactive compounds for which anti-carcinogenic roles have been suggested by experimental studies, either directly or after being metabolised by gut microbiota. Indeed, they contain vitamins and minerals, but also dietary fibre and polyphenols, for which anti-inflammatory, anti-insulin resistance and antioxidant properties have been demonstrated in animal or cell models, as well as a decreasing effect on circulating oestrogen and androgen levels (for dietary fibres), which could be beneficial against prostate carcinogenesis[4–8].

However, epidemiological evidence is lacking regarding a potentially protective effect of fruit, vegetable and legume intakes on prostate cancer risk. In 2014, the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) performed a systematic review and meta-analyses of available studies and attributed the level of proof 'limited-no conclusion' to the associations between fruit, non-starchy vegetable, and legume intakes and prostate

cancer risk[9]. Although a substantial number of prospective studies was available regarding fruits and vegetables, it was not the case for legumes. Among the three available prospective studies on legume intake[10–12], two showed inverse associations with prostate cancer risk[10,11]. In addition, in a previous prospective investigation on the SUpplémentation en VItamines et Minéraux AntioXydants (SU.VI.MAX) cohort, we observed that dietary fibre intake from legumes was inversely associated with prostate cancer risk[13].

Our objective was to prospectively investigate the associations between fruit, vegetable, tomato products, potatoes and legume intakes and prostate cancer risk in the SU.VI.MAX cohort. Our hypothesis was that one or several of these food groups are inversely associated with prostate cancer risk.

Methods

Participants

The SU.VI.MAX study was at first designed as a randomised, double-blind, placebo-controlled primary prevention trial (registered at clinicaltrials.gov as NCT00272428) aiming to assess the effect of a daily supplementation with nutritional doses of antioxidants on the incidence of CVD and cancers[14]. In 1994–1995, 13 017 individuals (7876 women and 5141 men) were enrolled for an 8-year intervention study. Follow-up of health events lasted until September 2007. The SU.VI.MAX study was conducted according to the Declaration of Helsinki guidelines and was approved by the Paris–Cochin Hospital Ethics Committee for Studies with Human Subjects (CCPPRB nos 706 and 2364, respectively) and the French National Commission for Computed Data and Individual Freedom (CNIL nos 334641 and 907094, respectively). Written informed consent was obtained from all the participants.

Baseline data collection

Dietary data. Every 2 months during the trial phase (1994–2002), participants were invited to complete a 24-h dietary record via the Minitel Telematic Network, a French telephone-based terminal equivalent to an Internet prototype used widely at the beginning of the study. These records were randomly distributed between weeks and weekends and over seasons to take into account intra-individual variability. Participants assessed portion sizes using a validated picture booklet[15], and the amounts consumed from composite dishes were estimated using French recipes validated by food and nutrition professionals. The mean daily energy, alcohol, macronutrient and micronutrient intakes were estimated using a published French Food Composition Table[16]. During the trial phase, participants were advised against taking any self-prescribed supplementation.

Other covariates. Information regarding socio-demographics, smoking status, physical activity and family history of prostate cancer was collected by self-administered questionnaires from all participants at enrolment. Anthropometric measures (height and weight) were obtained during a medical examination by the study nurses and physicians.

A 35-ml fasting venous blood sample was collected into vacutainer tubes at baseline. Plasma samples were used to determine the concentrations of Se by flame atomic absorption spectrometry, α-tocopherol by HPLC and total prostate-specific antigen (PSA) by immunoassay (Roche Diagnostics)[17,18]. PSA tests were performed only once, on baseline samples that were analysed later, at the end of the trial phase in 2002–2003, as part of a *post hoc* research protocol. Following these PSA tests (in 2002–2003), participants and their treating physicians were contacted by the SU.VI.MAX investigators if they had a PSA $\geq 4.0\,\mu g/l$. Medical examinations following this PSA test were left to the discretion of the treating physician. There was no PSA follow-up during the study.

Case ascertainment

During the follow-up period, participants were invited to self-report health events (through a monthly questionnaire). All cases were verified with biopsies by histopathological examination in the hospital where they were diagnosed. An expert committee of physicians from the SU.VI.MAX study collected the corresponding pathological reports and validated all cancer cases[14]. Cases were classified using the International Chronic Diseases Classification, 10th revision, Clinical Modification[19]. All first-incident primary prostate cancers were considered as cases in this study.

Statistical analyses

From the 5141 male participants in the SU.VI.MAX study, we excluded forty-one men who reported a cancer diagnosis before the start of the follow-up. Among the remaining participants, 3313 provided at least three valid 24-h dietary records within the first 2 years of follow-up, and thus remained available for analysis. Only the 24-h dietary records collected at the beginning of the study (first 2 years) were taken into account in the analyses and considered as baseline data. Mean dietary intakes were calculated across these repeated 24-h records. As the proportion of missing values for each covariate was low (<5 %), they were replaced by the sex-specific mode value. This classical method is used very often in large-scale epidemiological studies in order to limit the loss of subjects with at least one missing value in multivariate models[20,21].

Hazard ratios (HR) and 95 % CI obtained from Cox proportional hazards models, with age as the primary time variable, were used to characterise the association between tertiles of fruit and vegetable intakes and incidence of prostate cancer. Dietary intakes of interest were as follows: total fruits and non-starchy vegetables, fruits (including 100 % fruit juices), non-starchy vegetables, tomato products, potatoes and legumes (beans, lentils and peas as well as soya + maize and chestnuts that were grouped with legumes due to their high complex carbohydrate content). Participants contributed person-time until the date of diagnosis of prostate cancer, the date of last completed questionnaire, the date of death or 30 September 2007, whichever occurred first. Participants who reported a cancer other than prostate cancer during the study period (*n* 163) were included and censored at the date of diagnosis

(except those with basal cell skin carcinoma, which was not considered to be cancer). Participants who were lost to follow-up were included in the analysis and censored at the date of last completed questionnaire. We confirmed that the assumptions of proportionality were satisfied through examination of the log–log (survival) *v.* log–time plots for all studied food groups. Tests for linear *trend* were performed using the ordinal score on tertiles of dietary intake. Multivariate models were adjusted for factors constitutive to the study design (initial SU.VI.MAX trial intervention group (yes/no), number of dietary records (continuous)), socio-demographic variables (age (timescale) and educational level (primary, secondary or university)), lifestyle factors (smoking status (never, former or current), physical activity (irregular <1 h/d or ≥1 h/d walking or equivalent) and alcohol intake (continuous)), anthropometric factors (height (continuous) and BMI (continuous)), factors indicating higher individual susceptibility to prostate cancer (family history of prostate cancer (yes/no) and baseline PSA concentrations (continuous)) and dietary factors (dietary intakes of energy without alcohol, Ca, dairy products (continuous) and plasma α-tocopherol and Se concentrations (continuous)).

These dietary factors were those for which the association with prostate cancer risk was established or suggested according to the 2014 WCRF report[9].

Analyses were performed overall and separately for low-grade (Gleason < 7) and high-grade (Gleason ≥ 7) prostate cancer. Interactions with the SU.VI.MAX antioxidant supplementation/placebo group were tested. All tests were two-sided, and $P < 0.05$ was considered to be statistically significant. SAS version 9.3 (SAS Institute Inc.) was used for analyses.

Results

During a median follow-up of 12·6 years (37 877 person-years), 139 men developed a first, primary prostate cancer with a mean age at diagnosis of 63 years. A total of 5·2 % of the participants were lost to follow-up. The mean number of dietary records per subject was 9·7 (SD 3·3). Table 1 presents the characteristics of the participants according to tertiles of total fruit and non-starchy vegetable intakes. The mean total fruit and non-starchy vegetable intake was 444·9 (SD 197) g/d. In all, 55·5 % of the study population

Table 1. Baseline characteristics of the participants (*n* 3313) according to tertiles of total fruit and non-starchy vegetable intakes, SUpplémentation en VItamines et Minéraux AntioXydants cohort, France, 1994–2007
(Mean values and standard deviations; numbers of participants and percentages)

	Tertile 1 (*n* 1104)		Tertile 2 (*n* 1105)		Tertile 3 (*n* 1104)	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	51·2	4·5	52·0	4·7	52·3	4·8
BMI (kg/m²)	25·5	3·1	25·3	2·9	25·2	3·2
≥25 kg/m²*	613	55·5	581	52·6	558	50·5
Height (cm)	173·2	6·2	173·5	6·5	174·2	6·2
Intervention group of the initial trial (yes)*	570	51·6	563	51·0	557	50·5
Smoking status*						
Never	315	28·5	382	34·6	418	37·9
Former	569	51·5	589	53·3	588	53·3
Current	220	19·9	134	12·1	98	8·9
Physical activity*						
Irregular	289	26·2	244	22·1	250	22·6
<1 h/d walking or equivalent	250	22·6	278	25·2	254	23·0
≥1 h/d walking or equivalent	565	51·2	583	52·8	600	54·3
Educational level*						
Primary	278	25·2	255	23·1	231	20·9
Secondary	422	38·2	372	33·7	381	34·5
University	404	36·6	478	43·3	492	44·6
Family history of prostate cancer (yes)*†	59	5·3	63	5·7	49	4·4
Plasma PSA level (µg/l)	1·2	1·4	1·3	1·4	1·3	1·8
Energy intake (kJ/d)	8483·0	2079·4	9453·3	1975·7	10 453·3	2266·9
Energy intake (kcal/d)	2027·5	497·0	2259·4	472·2	2498·4	541·8
Alcohol intake (g/d)	33·4	27·4	29·7	23·6	24·3	21·6
Total fruit and non-starchy vegetable intakes (g/d)	243·6	71·0	427·2	47·3	663·9	144·3
Fruit intake (g/d)‡	102·6	60·4	220·0	71·7	390·8	144·8
Non-starchy vegetable intake (g/d)	140·5	53·3	206·4	65·7	272·3	95·2
Tomato products intake (g/d)	23·8	21·7	34·4	26·8	44·8	38·3
Legume intake (g/d)§	20·2	24·3	23·3	24·3	24·7	24·8
Potato intake (g/d)	85·9	62·6	89	61·2	93·6	69·0
Dairy product intake (g/d)	266·5	155·1	298·8	163·5	328·4	174·2
Ca intake (mg/d)	889·8	312·5	1008·3	308·9	1143·7	340·6
Plasma α-tocopherol level (µmol/l)	31·9	7·8	32·3	7·5	31·9	7·4
Plasma Se level (µmol/l)	1·1	0·2	1·1	0·2	1·1	0·2

PSA, prostate-specific antigen.
* *n* and %.
† Among first-degree relatives.
‡ Including 100 % fruit juices.
§ Legumes (beans, lentils, peas, soya) + maize and chestnuts.

Table 2. Associations between tertiles of fruit, non-starchy vegetable, tomato products, potatoes and legume intakes and prostate cancer risk from multivariate Cox proportional hazards models, SUpplémentation en VItamines et Minéraux AntioXydants (SU.VI.MAX) cohort, France, 1994–2007 (139 cases out of 3313 men)*
(Hazard ratios (HR) and 95% confidence intervals)

	Tertile 1	Tertile 2		Tertile 3		
	HR	HR	95% CI	HR	95% CI	P_{trend}
Total fruits and non-starchy vegetables						
Number of cases/person-years	48/12 475	40/12 741		51/12 663		
Multivariate	1	0·71	0·46, 1·09	0·73	0·46, 1·16	0·25
Fruits						
Number of cases/person-years	51/12 431	38/12 652		50/12 784		
Multivariate	1	0·55	0·35, 0·89	0·76	0·49, 1·18	0·25
Non-starchy vegetables						
Number of cases/person-years	41/12 530	46/12 730		52/12 608		
Multivariate	1	1·03	0·67, 1·58	0·98	0·62, 1·53	0·91
Tomato products						
Number of cases/person-years	40/12 541	42/12 708		57/12 630		
Multivariate	1	1·12	0·72, 1·74	1·44	0·94, 2·21	0·09
Potatoes						
Number of cases/person-years	47/12 431	45/12 785		47/12 652		
Multivariate	1	0·85	0·55, 1·30	0·93	0·56, 1·45	0·77
Legumes						
Number of cases/person-years	49/12 409	54/12 730		36/12 740		
Multivariate	1	0·99	0·66, 1·48	0·53	0·34, 0·85	0·009

* Cut-off points for tertiles of intake were 345·3 and 511·7 g/d for total fruits and non-starchy vegetables; 284·4 and 401·5 g/d for fruits; 336·7 and 447·9 g/d for vegetables; 172·5 and 193·8 g/d for tomato products; 506·3 and 544·2 g/d for potatoes; 6·2 and 26·5 g/d for legumes. Multivariate models were adjusted for age (timescale), energy intake without alcohol, intervention group of the initial SU.VI.MAX trial, number of 24-h dietary records, smoking status, educational level, physical activity, height, BMI, alcohol intake, family history of prostate cancer, baseline plasma prostate-specific antigen concentration, Ca intake, dairy product intake and plasma α-tocopherol and Se concentrations.

reached the 400 g/d minimal French recommendation[22]. The mean legume intake was 22·0 (SD 24·3) g/d.

Table 2 summarises the associations between fruit, vegetable, tomato products, potato and legume intakes and prostate cancer risk. An inverse association was observed between prostate cancer risk and tertiles of legume intake ($HR_{T3v.T1} = 0.53$; 95% CI 0·34, 0·85; $P_{trend} = 0.009$). The survival plot corresponding to legume intake is provided Fig. 1. No association was observed between prostate cancer risk and tertiles of intakes of fruits ($P_{trend} = 0.25$), vegetables ($P_{trend} = 0.91$), potatoes ($P_{trend} = 0.77$) and tomato products ($P_{trend} = 0.09$) (Table 2). No interaction was detected with the SU.VI.MAX intervention group ($P > 0.29$) for all dietary exposures.

Table 3 summarises the associations between legume intake and prostate cancer risk separately for low- and high-grade cancers. An inverse association was observed between low-grade prostate cancer risk and tertiles of legume intake ($P_{trend} = 0.03$), whereas no association was observed for high-grade prostate cancer ($P_{trend} = 0.35$). No difference was observed between low- and high-grade prostate cancer for other studied food groups (data not shown).

In sensitivity analyses, results remained unchanged when cancer cases diagnosed during the first 2 years of follow-up were excluded (five cases in 3313 men, $HR_{T3v.T1} = 0.60$; 95% CI 0·37, 0·95; $P_{trend} = 0.03$ for legumes) or when considering only men who completed at least six 24-h dietary records during the first 2 years of follow-up (123 cases in 2771 men). Likewise, there was no modification in the results when soya and soya products were excluded from the legume group ($HR_{T3v.T1} = 0.56$; 95% CI 0·35, 0·89; $P_{trend} = 0.02$). Results were unchanged when chestnuts and maize were not included with
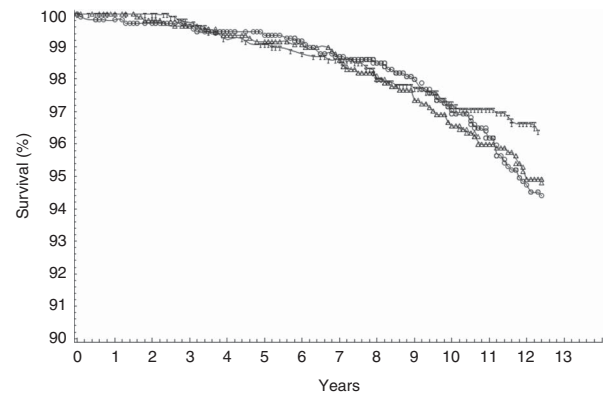

Fig. 1. Survival plots for associations between tertiles of legume intake and prostate cancer risk by multivariable Cox model, SUpplémentation en VItamines et Minéraux AntioXydants (SU.VI.MAX) cohort, France, 1994–2007; 139 cases out of 3313 men. Models were adjusted for age (timescale), energy intake without alcohol, intervention group of the initial SU.VI.MAX trial, number of 24-h dietary records, smoking status, educational level, physical activity, height, BMI, alcohol intake, family history of prostate cancer, baseline plasma prostate-specific antigen (PSA) concentration, calcium intake, dairy product intake and plasma α-tocopherol and selenium concentrations. △△△, Tertile 1; ⊖⊖⊖, tertile 2; ┬┬┬, tertile 3.

legumes ($HR_{T3v.T1} = 0.52$; 95% CI 0·32, 0·86; $P_{trend} = 0.02$). The proportion of subjects with at least one missing value was similar between cases and controls (20 and 19%, respectively, $P = 0.8$). When analyses were carried out after excluding subjects with at least one missing value for covariates (n 635), the results were similar, although borderline significant owing to loss of statistical power (for legumes: $HR_{T3v.T1} = 0.65$; 95% CI 0·39, 1·08; $P_{trend} = 0.10$).

Table 3. Associations between tertiles of legume intake and low-grade/high-grade prostate cancer risk from multivariate Cox proportional hazards models, Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI.MAX) cohort, France, 1994–2007*
(Hazard ratios (HR) and 95 % confidence intervals)

	Tertile 1	Tertile 2		Tertile 3		
	HR	HR	95 % CI	HR	95 % CI	P_{trend}
Low-grade prostate cancer (Gleason < 7)						
Number of cases/person-years	25/12 215	27/12 473		16/12 585		
Multivariate	1	0·99	0·56, 1·75	0·46	0·23, 0·91	0·03
High-grade prostate cancer (Gleason ≥ 7)						
Number of cases/person-years	21/12 180	24/12 481		19/12 631		
Multivariate	1	1·07	0·59, 1·97	0·73	0·38, 1·43	0·35

* Cut-off points for tertiles of legume intake were 6·2 and 26·5 g/d. Multivariate models were adjusted for age (timescale), energy intake without alcohol, intervention group of the initial SU.VI.MAX trial, number of 24-h dietary records, smoking status, educational level, physical activity, height, BMI, alcohol intake, family history of prostate cancer, baseline plasma prostate-specific antigen concentration, Ca intake, dairy product intake and plasma α-tocopherol and Se concentrations.

Discussion

In this prospective study, legume intake was associated with reduced prostate cancer risk, whereas no association was observed for fruit, non-starchy vegetable, tomato products and potatoes intakes.

Our null results are consistent with results of the 2014 WCRF/AICR[9] meta-analyses of prospective studies, in which no association was observed between prostate cancer risk and vegetable intake (summary HR for a 100 g/d increment = 0·99; 95 % CI 0·98, 1·00; thirteen prospective studies included), tomato product intake (summary HR for a 100 g/d increment = 0·93; 95 % CI 0·79, 1·09; seven studies) and fruit intake (summary HR for a 100 g/d increment = 1·00; 95 % CI 0·99, 1·01; sixteen studies).

In contrast, only three prospective studies have been published on legume intake and prostate cancer risk[10–12], among which two observed inverse associations[10,11] in line with our results. In the Multiethnic Cohort Study, Park et al.[10] reported a significant inverse trend for total prostate cancer risk (HR = 0·90; 95 % CI 0·81, 1·01; P_{trend} = 0·01). In our study, the association between legume intake and prostate cancer risk tended to be stronger in low-grade prostate cancer; however, the number of cases was low in the analyses stratified by the Gleason grade, and thus should be considered with caution. Park et al.[10] reported a significant inverse association for non-localised prostate cancer (defined as cancer that was regional or distant) grouped with high-grade prostate cancer (defined as Gleason score ≥ 7), but results for low-grade prostate cancer were not presented. In the Netherlands Cohort Study, Schuurman et al.[11] reported an inverse association between legume intake and prostate cancer risk (HR = 0·71; 95 % CI 0·51, 0·98; P = 0·01). In contrast, Smit et al.[12] reported no association with intake of legumes in a study in Porto Rico; however, the outcome was cancer mortality and not cancer incidence.

Furthermore, two prospective studies observed no association with prostate cancer risk or mortality but they focused only on boiled beans[23] and dried beans[24]. Two other prospective studies investigated the association between beans, lentils and peas and prostate cancer risk: one showed an inverse association[25], whereas the other study reported no association[26].

The inverse association between legume intake and prostate cancer risk is supported by mechanistic data from experimental studies. Several bioactive compounds are contained in legumes, and among them antioxidants. However, they do not seem to play an important role in prostate cancer prevention as fruits and vegetables are also abundant sources of antioxidants, but were not associated with prostate cancer risk (in this study as in most of the existing literature)[9]. Besides, antioxidant supplementation in the SU.VI.MAX trial was not associated with prostate cancer risk[27].

Dietary fibre is another major component of legumes and probably plays a key role in the observed association. Indeed, in the SU.VI.MAX cohort, we previously observed[13] an inverse association between prostate cancer risk and total dietary fibre intake, and more specifically with dietary fibre intake from legumes and insoluble dietary fibre intake (legume fibre being mainly insoluble)[28,29]. Besides, dietary fibre content is higher in legumes than in fruits and non-starchy vegetables, which may contribute to explain the null result observed for the latter food groups. First, experimental studies showed that dietary fibre exerts a down-regulation role on inflammation[30], probably through the production of SCFA when fibres are fermented in the colon by gut microbiota. Fermentation products, particularly butyrate[31] and propionate[32], have shown anti-inflammatory properties. Experimental data suggest that inflammation has a pro-carcinogenic role in prostate cancer development[26,33–35]. Consistently, in a prospective case–control study nested in the SU.VI.MAX cohort, we observed that the baseline plasma concentration of highly sensitive C-reactive protein (hs-CRP) was directly associated with increased prostate cancer risk[36]. In the subsample of the present study with available data (n 832), the level of hs-CRP was lower in subjects of the third v. first tertile of legume intake (1·9 (sd 3·0) v. 3·0 (sd 6·7) mg/l; P = 0·03, data not tabulated). Second, increased concentrations of circulating sex hormones could be associated with a greater risk of prostate cancer[5]. Dietary fibre may reduce concentrations of circulating oestrogens and androgens, notably through increased sex hormone-binding globulin concentration[37], modified enterohepatic circulation of steroid hormones[38,39] and increased faecal excretion of these hormones, resulting from binding to insoluble fibres[40]. Finally, experimental studies suggested that insulin resistance and hyperinsulinaemia, by

increasing insulin-like growth factor (IGF) concentrations, may stimulate prostate carcinogenesis[4]. Several studies have suggested that dietary fibre may reduce insulin resistance[41,42], notably through a decrease in carbohydrate absorption rate[28,43,44], and an increase in IGF binding protein 3 concentrations[45], leading to decreased IGF bioactivity[4,33].

In the legume food group, a role of soya phyto-oestrogens has also been postulated to explain the inverse association with prostate cancer risk[9]. However, in our study and in another prospective study[10], significant inverse associations between legume intake and prostate cancer risk were observed even after exclusion of soya and soya products, suggesting that phyto-oestrogens might not entirely explain the observed association. Other legumes also contain phyto-oestrogens but the concentrations are very small compared with the ones observed in soya-based foods (e.g. <70 *v.* >6400 µg/100 g in soya)[46].

Strengths of this study include its prospective design, long follow-up and detailed evaluation of dietary intake by repeated 24-h records. However, some limitations should be acknowledged. First, the relatively small number of cases may have limited our ability to detect some of the hypothesised associations. However, this is unlikely to explain the observed relationships that were statistically significant despite this potential power limitation. Next, participants became aware of their baseline PSA values (if >4·0 µg/l) only at the end of the trial phase (after 2003). Therefore, it could not have influenced their baseline dietary and other lifestyle behaviours, and thus this is unlikely to explain the significant observed associations. However, PSA testing in our cohort must be taken into account when extrapolating our results to the whole middle-aged male French population, as it may have influenced the number of cases diagnosed at the end of follow-up and probably led to an over-representation of early-stage prostate cancers. Finally, the observed relationships could be partly affected by unmeasured or residual confounding. However, main potential confounding factors for prostate cancer risk have been accounted for in this study, notably lifestyle factors indicating 'healthy behaviours', anthropometric factors and established or suspected dietary factors according to the 2014 WCRF/AICR report[9]. Thus, it is unlikely that residual confounding entirely explains the observed associations.

In conclusion, this prospective study brings new insights into the role of fruit, vegetable and legume intakes in prostate carcinogenesis. It confirms the null association between fruit and non-starchy vegetable intakes and prostate cancer risk observed in most previous studies[9]. In contrast, our results suggest an inverse association between legume intake and prostate cancer risk, supported by mechanistic plausibility. As very few prospective studies have been published on the topic, these results should be confirmed by large-scale observational and intervention studies.

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