Cross-sectional association between non-soy legume consumption, serum uric acid and hyperuricemia: The PREDIMED-Plus study

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Abstract

Purpose: To assess the association between the consumption of non-soy legumes and different subtypes of non-soy legumes and SUA or hyperuricemia in elderly individuals with overweight or obesity and metabolic syndrome.

Methods: A cross-sectional analysis was conducted in the framework of the PREDIMED-Plus study. We included 6,329 participants with information on non-soy legume consumption and SUA levels. Non-soy legume consumption was estimated using a semi-quantitative food frequency questionnaire. Linear regression models and Cox regression models were used to assess the associations between tertiles of non-soy legume consumption, different subtypes of non-soy legume consumption and SUA levels or hyperuricemia prevalence, respectively.

Results: Individuals in the highest tertile (T3) of total non-soy legume, lentil and pea consumption, had 0.14 mg/dL, 0.19 mg/dL and 0.12 mg/dL lower SUA levels, respectively, compared to those in the lowest tertile (T1), which was considered the reference one. Chickpea and dry bean consumption showed no association. In multivariable models, participants located in the top tertile of total non-soy legumes (Prevalence Ratio (PR): 0.89; 95%CI: 0.82 to 0.97; p-trend = 0.01, lentils (PR: 0.89; 95%CI: 0.82 to 0.97; p-trend = 0.01), dry beans (PR: 0.91; 95%CI: 0.84 to 0.99; p-trend = 0.03) and peas (PR: 0.89; 95%CI: 0.82 to 0.97; p-trend = 0.01) presented a lower prevalence of hyperuricemia (vs. the bottom tertile). Chickpea consumption was not associated with hyperuricemia prevalence.

Conclusions: In this study of elderly subjects with metabolic syndrome, we observed that despite being a purine-rich food, non-soy legumes were inversely associated with SUA levels and hyperuricemia prevalence.

Trial registration: ISRCTN89898870. Registration date: 24 July 2014

Keywords: serum uric acid, hyperuricemia, non-soy legumes, PREDIMED-Plus

Introduction

Hyperuricemia is not always a metabolic disorder, it results from urate overproduction (10%), underexcretion (90%), or often a combination of the two. It has been suggested that hyperuricemia increases not only the risk of gout[1], but also metabolic syndrome[2], type 2 diabetes[3], hypertension and cardiovascular disease (CVD)[4]. Therefore, strategies focused on decreasing the levels of serum uric acid (SUA) could be important to reduce the global burden of these cardiometabolic diseases.

SUA is the end-product of the endogenous purine metabolism and the exogenous pool (diet)[5]. A diet low in purines has been recommended as standard clinical practice to reduce the levels of SUA and the risk of gout for many years. The general advice to avoid purine-rich foods is based on data from studies conducted in animals and humans, which showed a reduction in SUA levels with the acute administration of oral purines[6, 7]. However, studies linking food consumption with SUA or hyperuricemia are limited and latest evidence suggested that not all purine-rich foods affect SUA levels in the same manner. For instance, meat and seafood consumption seems to be associated with increased levels[8, 9], whereas purine-rich vegetables are inversely[10] or not associated[10–12]. Therefore, the total purine content of food seems not to be the only factor associated with SUA levels. As far as we know, despite the fact that legumes are a purine-rich food, its association with SUA levels has not been well-studied thus far. This is reflected in the lack of consensus concerning their avoidance in the 2012 American College of Rheumatology Guidelines for the Management of Gout[13]. Legume consumption, which is a key component of the Mediterranean diet, has been prospectively associated in previous studies with a lower risk of type 2 diabetes[14] and cardiovascular disease[15]. Despite its high purine content, legumes also contain other healthy nutrients, such as polyphenols and antioxidants, which could help prevent increases in SUA levels and hyperuricemia risk[16]. In fact, previous studies have associated the consumption of soy and non-soy legumes with a lower risk of gout[17].

Therefore, to address this gap in knowledge regarding legume consumption and its association with SUA levels, we performed a cross-sectional analysis in the framework of the PREvención con DIeta MEDiterránea (PREDIMED) Plus trial to analyze the associations between total non-soy legume, different types of non-soy legume consumption, and SUA levels and hyperuricemia risk in an elderly Mediterranean population with overweight/obesity and metabolic syndrome.

Material and Methods

Study population

We conducted a cross-sectional evaluation of baseline data within the framework of the PREDIMED-Plus trial, whose design has been extensively described elsewhere[18] and the study protocol can be found on the PREDIMED-Plus website (https://www.predimedplus.com/). Briefly, PREDIMED-Plus study is an ongoing, 6-year, multicenter, parallel group, randomized clinical trial conducted in Spain to assess the effectiveness of an intensive weight-loss intervention program (based on an energy restricted Mediterranean diet, physical activity promotion and behavioral support) on hard cardiovascular events in comparison with a control group receiving usual care. The study was registered at the International Standard Randomized Controlled Trial registry (http://www.isrctn.com/) with the registration number 89898870. The results of the pilot study regarding changes in body weight and cardiovascular risk factors have recently been published[19].

Eligible participants were community-dwelling men (aged 55-75 years) and women (aged 60-75 years) with overweight or obesity (BMI $\geq$27kg/m^2 and <40kg/m^2), meeting at least 3 criteria for the metabolic syndrome definition[20], and free from CVD. We recruited 6,874 participants from October 2013 to December 2016 who were randomly allocated in a 1:1 ratio to the intensive diet and lifestyle intervention group or to the usual care group. All participants provided written informed consent and institutional review boards of each participating center approved the final protocol and procedures.

For the present analysis, we excluded 53 participants with missing information on baseline food frequency questionnaires, 188 participants with extreme total energy intake (women <500 and >3,500kcal/day, and men <800 and >4,000kcal/day[21]), and 304 participants with missing information on SUA levels at baseline. Finally, 6,329 participants were included for evaluation in the current study. The data were analyzed using the available complete PREDIMED-Plus database, dated 17 September 2018.

Dietary assessment

At baseline, a trained dietitian administered a 143-item semi-quantitative food frequency questionnaire in a face-to-face visit. Participants were asked about their frequency consumption of each specific item during the preceding year. There were nine possible answers ranging from never to more than 6 times per day, which were transformed to grams per day taking into account the standard portion size of each item. Four items from the food frequency questionnaire were specifically related to non-soy legume consumption: lentils, chickpeas, dry beans and peas. For the present analysis we considered total non-soy legumes as the sum of the aforementioned foods. Two Spanish food composition tables were used to calculate total energy and nutrient intake[22, 23].

Other covariates assessment

Socio demographic (age, sex, marital status, educational level) and lifestyle (physical activity, smoking habit, Mediterranean diet adherence) related variables, as well as information regarding medication use and personal and family history of illness, were collected at baseline.

Anthropometric variables and blood pressure were measured by PREDIMED-Plus trained staff following the study protocol. Weight and height were measured with participants with light clothes and no shoes using calibrated scales and wall-mounted stadiometers, respectively. BMI was calculated as the weight in kg divided by the square of the height in meters. Waist circumference was measured using an anthropometric tape at the midway between the lowest rib and the iliac crest. Blood pressure was measured in triplicate using a validated semiautomatic oscillometer (Omron HEM-705CP, Netherlands), with the participant in seated position after 5 minutes of rest and the mean of these values was recorded.

Leisure time physical activity was estimated using a validated short version of the Minnesota Leisure Time Physical Activity Questionnaire[24, 25].

Adherence to an energy-reduced Mediterranean diet was assessed using a 17-item questionnaire that was adapted from a validated 14-item questionnaire[26]. The total score ranged from 0 to 17. One question was related to non-soy legume consumption, therefore, in order to control the analysis for the overall dietary pattern, we used this Mediterranean diet questionnaire score after removing the variable about non-soy legume consumption.

After an overnight fast, baseline blood samples were collected and laboratory technicians, who were blinded to the intervention group, performed biochemical analyses on fasting plasma glucose, triglycerides, cholesterol and SUA using standard enzymatic procedures. Hyperuricemia was defined as SUA levels >7mg/dL in men and >6mg/dL in women, as has been defined previously[27].

Statistical analyses

Participants were categorized into tertiles according to total non-soy legume and different types of non-soy legume consumption, adjusted for total energy intake using the residual method[28]. Baseline characteristics of study participants were presented as percentages and numbers (categorical variables) and means ± standard deviations or median [P25-P7] (continuous variables). The chi-square test and the one-way ANOVA or Kruskal Wallis test were used to compare baseline characteristics among tertiles of energy-adjusted total non-soy legume consumption.

Multivariable linear regression models were fitted to evaluate associations between tertiles of total non-soy legume, different types of non-soy legume consumption and SUA levels. For that purpose, two dummy variables (k - 1), which represent tertiles of total non-soy legume consumption, were introduced in the linear regression model, with the first category serving as the reference. The prevalence of hyperuricemia in the present sample size was high (34%). Therefore, to assess prevalence ratios (PR) and 95% confidence intervals of hyperuricemia according to tertiles of energy-adjusted total non-soy legume and different types of non-soy legume consumption, we performed Cox regression models with constant follow-up time (t=1) and robust variance. This has been suggested as a better method than logistic regression in cross-sectional studies when the outcome is common (prevalence >10%) as odds ratios could overestimate or underestimate the risk in logistic regression[29, 30]. Linear and Cox regression models were adjusted for several potential confounders. Model 1 was adjusted for age (years), sex, diabetes (yes/no), hypertension (yes/no), glomerular filtration rate (ml/min/1.73 m^2), use of uricosuric agents [including allopurinol and flebuxostat (yes/no)] and center (in quartiles by number of participants). In Cox regression models, center was used as strata variable. Model 2 was additionally adjusted for leisure time physical activity (METs.min/week), BMI (kg/m2), smoking habit (never, former or current), educational level (primary, secondary or university/graduate), alcohol consumption in g/day (and adding the quadratic term) and 16-point screener (excluding legumes) of energy-reduced Mediterranean diet adherence (continuous).

In all regression models, the robust variance estimators to account for intra-cluster correlations, considering as clusters the members of the same household (n=372 couples) were used.

To assess the linear trend, exposure variables (total non-soy legume and different types of non-soy legume consumption) were modeled as continuous in linear regression models.. In Cox regression models, the median value of each tertile of total non-soy legume and different types of non-soy legume consumption was assigned to each participant, and this new variable was modeled as continuous.

Stratified analyses were conducted to evaluate whether the association observed between energy-adjusted total non-soy legume consumption and the risk of hyperuricemia could be modified by sex (men/women), diabetes (yes/no), body mass index ($<30kg/m^2/\geq30kg/m^2$) and chronic kidney disease (yes/no). Statistical interactions were tested by means of likelihood ratio tests, comparing the fully adjusted model of the Cox regression with and without cross-product terms between the aforementioned variables and tertiles of total non-soy legume consumption.

Data were analyzed using software program Stata 14 (StataCorp) and statistical significance was set at a 2-tailed *P*-value <0.05.

Results

Table 1 displays baseline characteristics of the study population according to tertiles of energy-adjusted total non-soy legume consumption. Participants located in the highest tertile of total non-soy legume consumption were more likely to be women, physically active and to have diabetes than those in the lowest tertile. Moreover, they were also less likely to smoke, had lower educational level, BMI, hypertension and took less uricosuric drugs. In general, participants with high consumption of total non-soy legumes had a better dietary pattern characterized by consuming more fruit, vegetables, nuts, fish and dairy products and eating less olive oil, cereals, meat, biscuits and alcohol than those individuals with low consumption of total non-soy legumes.

In multivariable linear regression analyses (**Table 2**), those individuals located in the top tertile of total non-soy legume, lentil, and pea consumption had 0.14 mg/dL, 0.19 mg/dL and 0.12 mg/dL lower SUA levels, respectively, than those located in the bottom tertile after adjusting for multiple potential confounders. No association was observed between chickpea and dry bean consumption and SUA levels.

The prevalence ratios and 95% CI for hyperuricemia across tertiles of total non-soy legume and different types of non-soy legume consumption are presented in **Table 3**. Total non-soy legume consumption was inversely associated with hyperuricemia prevalence (PR: 0.89; 95%CI: 0.82 to 0.97; p-trend= 0.01, for 3^{rd} *vs* 1^{st} tertile). Similarly, individuals in the highest tertile of lentils were 11% less likely to have hyperuricemia than those in the lowest tertile (PR: 0.89; 95%CI: 0.82 to 0.97; p-trend= 0.01). Likewise, participants located in the highest tertile of dry bean and pea consumption were 9% and 11% less likely to have hyperuricemia than those in the lowest tertile (PR: 0.91; 95%CI: 0.84 to 0.99; p-trend = 0.03 and PR: 0.89; 95%CI: 0.82 to 0.97; p-trend= 0.01, respectively). Chickpea consumption was not associated with hyperuricemia prevalence.

When we repeated all the analyses (linear regression models and Cox regression models) adjusting model 3 for tertiles of fruit, vegetable, meat, fish and dairy product consumption instead of using the MedDiet adherence score, since they have been considered as SUA influencing foods, results remained essentially unchanged (data not shown).

No statistically significant interactions were detected between total non-soy legume consumption and sex, diabetes status, BMI and chronic kidney disease (**Figure 1**). Nonetheless, stratification showed that total non-soy legume consumption was only associated with hyperuricemia in women (PR: 0.84; 95%CI: 0.74 to 0.95), in individuals without type 2 diabetes (PR: 0.86; 95%CI: 0.78 to 0.95), in those with BMI <30kg/m^2 (PR: 0.76; 95%CI: 0.64 to 0.91) and those without chronic kidney disease (PR: 0.90; 95%CI: 0.82 to 0.99).

Discussion

The main findings of the present cross-sectional study conducted in elderly individuals with metabolic syndrome suggest that high consumption of total non-soy legumes and some subtypes of non-soy legumes, such as lentils and peas, were associated with lower levels of SUA. However, chickpea and dry bean consumption were not associated with SUA levels. Regarding hyperuricemia prevalence, there was an inverse association with total non-soy legume, lentil, dry bean and pea consumption. Nonetheless, chickpea consumption was not associated with SUA levels. The present results provide new evidence for the potential benefit of non-soy legume consumption on SUA levels and hyperuricemia, despite their high purine content.

Little is known about the association between non-soy legume consumption and SUA levels or hyperuricemia. To the best of our knowledge, only one previous study has assessed, in an indirect way, the relation between legume consumption and the risk of hyperuricemia[31]. The analysis was conducted in the framework of the PREDIMED study, where authors evaluated the prevalence of hyperuricemia according to the accomplishment of each 14-items of the Mediterranean diet adherence questionnaire. The results showed that those individuals that fulfilled the item of consuming 3 or more servings per week of legumes were 26% less likely to have hyperuricemia than those that did not consume 3 or more servings per week[31]. These results are in line with our findings where those individuals located in the third tertile (whose legume consumption, 28.68 g/day, was approximately 3 servings/week) presented a lower risk of hyperuricemia. Our results are also in line with another previous study, the Singapore Chinese Health Study[17], which prospectively evaluated the association between non-soy legume consumption and the risk of gout (uric acid associated disease). In this study, participants located in the fourth quartile of non-soy legume consumption had a significant 17% lower risk of gout incidence than those in the first quartile. All the aforementioned results support previous holistic recommendations, driven by a review conducted by Choi et al., regarding the advice of consuming legumes, since they do not increase the risk of gout and could have other healthy implications on comorbidities associated with gout and hyperuricemia[32].

In the stratified analysis of the present study, the association between total non-soy legume consumption and hyperuricemia remained significant in women, in individuals without diabetes, in those with a body mass index less than 30 kg/m^2 and in those without chronic kidney disease. One previous study also showed in its stratified analysis, that non-soy legume consumption was associated with a lower risk of gout development in women, but not in men[17]. However, there is no plausible explanation for the observed differences between men and women in the hyperuricemia risk associated with non-soy legume consumption. Similarly, we cannot offer a biological explanation for the observed differences in hyperuricemia risk by diabetes status. Therefore, the results could be by chance and further studies are warranted in the future to confirm these possible differences by sex and diabetes status. Regarding the other stratification variables, obesity and chronic kidney disease are conditions that have been associated with higher SUA levels[33–35]. As a consequence, the potential beneficial effect of legumes on hyperuricemia risk could be limited by the high levels of SUA observed in individuals that have these conditions.

The association between non-soy legumes and SUA levels or hyperuricemia observed in the present study is not as expected considering their high purine content. However, it has been suggested that the estimation of the actual content of purines of foods is difficult, particularly for cooked or processed foods[36]. Moreover, the purine bioavailability could vary substantially from one food to another, and it has been reported that for the same amount of food, RNA has a greater bioavailability than DNA[37], and adenine greater than guanine[7]. These findings could explain the observed differences in the association between purine-rich foods, SUA levels and hyperuricemia. In addition, despite being considered a purine-rich food, legumes contain other nutrients that could exert a beneficial effect on SUA levels. Legumes are rich in polyphenols, mainly phenolic acids and flavonoids. Previous studies have suggested that dietary polyphenols could act as anti-hyperuricemic agents[16]. In fact, it has been shown that flavonoid glycosides isolated from two legume plants (*Vicia faba and lotus edulis*) are potent inhibitors of xanthine oxidase activity, the enzyme involved in the catalysis of xanthine to uric acid[38].

The present study has several limitations that need to be mentioned. First, its cross-sectional design does not allow us to establish a cause-effect relationship, and the possiblility of reverse causation should be acknowledged. Second, we cannot extrapolate the findings to other study populations since the participants from the PREDIMED-Plus study are elderly individuals with metabolic syndrome. Third, the use of a food frequency questionnaire to estimate food consumption is subject to possible measurement error, especially if single foods instead of food groups are assessed. The lack of detail and specificity that other dietary assessment methods have, such as the recalls or dietary records, makes difficult the accurate estimation of absolute single foods consumption. Nevertheless, a carefully developed food frequency questionnaire offers an advantage, the assessment of the usual diet, which is one of the main interest in epidemiologic studies. The current study also has some strengths, which include the relatively large sample size, the analysis of different types of legumes as exposure, and we were able to control for a large number of potential confounding factors.

Conclusions

In conclusion, in individuals with metabolic syndrome, total non-soy legume, lentil, and pea consumption were inversely associated with SUA levels. Moreover, non-soy legumes and their different subtypes, with the exception of chickpeas, were associated with a lower prevalence of hyperuricemia. Our findings add new insights about the potential beneficial role of non-soy legumes on SUA levels and hyperuricemia risk and could inform future evidence-based dietary guidelines for hyperuricemia prevention.

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Ethical standards

All participants provided written informed consent, and the study protocol and procedures were approved according to the ethical standards of the Declaration of Helsinki by all the participating institutions

Conflict of interest

The authors declare that they have no conflict of interest related to this article

Figure Legend:

Figure 1. Prevalence ratios (95% CIs) for hyperuricemia according tertiles (3rd *vs* 1st) of total non-soy legumes consumption stratified by sex, BMI, type 2 diabetes and chronic kidney disease status. All prevalence ratios were adjusted for age (years), sex (in the case of sex stratification, adjustment for sex was excluded), diabetes (yes/no) (in the case of diabetes stratification, adjustment for diabetes prevalence was excluded), hypertension (yes/no), glomerular filtration rate (ml/min/1.73 m^2) (in the case of chronic kidney disease stratification, adjustment for glomerular filtration was excluded), use of hypouricemic agents (yes/no), center (in quartiles by number of participants), leisure time physical activity (METs.min/week), body mass index (kg/m^2) (in the case of BMI stratification, adjustment for BMI was excluded), smoking habit (never, former or current), educational level (primary, secondary or university/graduate), alcohol consumption in g/day (and adding the quadratic term) and 16-point screener (excluding legumes) of Mediterranean diet adherence (continuous).

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Table 1. Baseline characteristics of the study population by tertiles of energy-adjusted total legume consumption*

	Tertiles of total non-soy legume consumption			
	T1 (lowest)	T2	T3 (Highest)	*P*-value[†]
	n=2,110	n=2,110	n=2,109	
Total non-soy legume consumption, g/day	11 ± 4	19 ± 2	32 ± 11	
Lentils, g/day	3.9 [3.4-4.4]	5.0 [4.2-8.5]	8.6 [8.2-9.0]	
Chickpeas, g/day	3.7 [2.9-4.2]	4.3 [4.0-5.4]	8.4 [7.9-8.9]	
Dry beans, g/day	3.5 [0.4-4.0]	4.1 [3.8-4.5]	8.3 [4.3-8.7]	
Peas, g/day	0.5 [0-3.4]	3.9 [0.5-4.4]	4.20 [3.5-8.2]	
Age, years	65 ± 5	65 ± 5	65 ± 5	<0.01
Women, % (n)	45.26 (955)	48.86 (1,031)	50.88 (1,073)	<0.01
BMI, kg/m^2	32.67 ± 3.44	32.42 ± 3.35	32.61 ± 3.54	0.04
Leisure time physical activity, METs.min/week	1734 [839-3170]	1989 [923-3497]	1881 [839-3469]	<0.01
Smoking habit, % (n)				<0.01
Never	41.28 (871)	45.12 (952)	46.94 (990)	
Former	46.21 (975)	42.65 (900)	40.87 (862)	
Current	12.51 (264)	12.23 (258)	12.19 (257)	
Education, % (n)				<0.01
Primary	44.17 (932)	48.96 (1,033)	55.10 (1,162)	
Secondary	30.14 (636)	29.10 (614)	27.12 (572)	
University/graduate	25.69 (542)	21.94 (463)	17.78 (375)	
Hypertension, % (n)	84.08 (1,774)	83.32 (1,758)	82.46 (1,739)	0.37
Diabetes, % (n)	24.88 (525)	28.20 (595)	29.87 (630)	<0.01
Use of uricosuric agents, % (n)	9.62 (203)	7.16 (151)	8.49 (179)	0.02

Serum uric acid, mg/dL	6.12 ± 1.46	5.98 ± 1.42	5.88 ± 1.46	<0.01
Food consumption, g/day‡				
Fruit	329 ± 196	354 ± 187	381 ± 195	<0.01
Vegetables	294 ± 127	324 ± 127	360 ± 147	<0.01
Nuts	13 ± 17	14 ± 15	17 ± 18	<0.01
Olive oil	41 ± 16	42 ± 16	38 ± 17	<0.01
Cereals	157 ± 70	154 ± 64	141 ± 62	<0.01
Meat	151 ± 55	148 ± 51	145 ± 53	<0.01
Fish	95 ± 46	102 ± 43	108 ± 48	<0.01
Dairy products	342 ± 199	340 ± 188	356 ± 202	0.01
Biscuits	29 ± 31	27 ± 26	24 ± 26	<0.01
Alcohol	7 [3-18]	7 [3-15]	6 [1-13]	<0.01
MedDiet score (17-points)	8 ± 3	8 ± 3	9 ± 3	<0.01

*Data are expressed as means ± SD or median [P25-P75] and percentage (number) for continuous and categorical variables, respectively

†P-value for differences between tertiles of total legume consumption was calculated by chi-square and ANOVA or Kruskal-Wallis as appropriate

‡Dietary variables were adjusted for total energy intake using the residual method

Abbreviations: T, tertile; BMI, body mass index; METs, metabolic equivalent; MedDiet, Mediterranean diet

Table 2. Multivariate-adjusted β-coefficients and 95% confidence interval for serum uric acid levels according to tertiles of energy-adjusted total legume and different subtypes of legume consumption

	Tertiles of non-soy legume consumption in g/day			
	T1 (lowest)	T2	T3 (highest)	*P*-trend
Total non-soy legumes, median (P25-P75)	11.95 (9.37 to 13.66)	18.42 (16.84 to 20.68)	28.68 (25.75 to 33.05)	
Crude model	0 (Ref.)	-0.14 (-0.23 to -0.05)	-0.24 (-0.33 to -0.16)	<0.01
Multivariable model 1	0 (Ref.)	-0.11 (-0.19 to 0.03)	-0.19 (-0.27 to -0.11)	<0.01
Multivariable model 2	0 (Ref.)	-0.08 (-0.16 to -0.01)	-0.14 (-0.22 to -0.06)	<0.01
Lentils, median (P25-P75)	3.72 (3.24 to 3.99)	7.22 (4.45 to 8.10)	8.81 (8.59 to 9.08)	
Crude model	0 (Ref.)	-0.23 (-0.31 to -0.14)	-0.39 (-0.47 to -0.30)	<0.01
Multivariable model 1	0 (Ref.)	-0.15 (-0.23 to -0.07)	-0.22 (-0.31 to -0.14)	<0.01
Multivariable model 2	0 (Ref.)	-0.13 (-0.21 to -0.05)	-0.19 (-0.28 to -0.11)	<0.01
Chickpeas, median (P25-P75)	3.42 (0.79 to 3.75)	4.38 (4.17 to 4.65)	8.61 (8.30 to 8.96)	
Crude model	0 (Ref.)	-0.20 (-0.29 to -0.11)	-0.24 (-0.33 to -0.16)	<0.01
Multivariable model 1	0 (Ref.)	-0.05 (-0.13 to 0.03)	-0.11 (-0.20 to -0.03)	<0.01
Multivariable model 2	0 (Ref.)	-0.04 (-0.12 to 0.04)	-0.07 (-0.15 to 0.01)	0.04
Dry beans, median (P25-P75)	0.78 (0.11 to 3.45)	4.13 (3.96 to 4.31)	8.40 (7.86 to 8.80)	
Crude model	0 (Ref.)	-0.10 (-0.19 to -0.02)	-0.16 (-0.25 to -0.07)	0.19
Multivariable model 1	0 (Ref.)	-0.04 (-0.12 to 0.04)	-0.09 (-0.18 to -0.01)	0.04
Multivariable model 2	0 (Ref.)	-0.02 (-0.10 to 0.06)	-0.06 (-0.14 to 0.02)	0.31
Peas, median (P25-P75)	0.04 (0 to 0.34)	3.65 (3.21 to 3.90)	4.76 (4.37 to 8.46)	
Crude model	0 (Ref.)	0 (-0.08 to 0.09)	-0.19 (-0.28 to -0.11)	0.18
Multivariable model 1	0 (Ref.)	-0.04 (-0.12 to 0.04)	-0.13 (-0.21 to -0.05)	0.06
Multivariable model 2	0 (Ref.)	-0.03 (-0.10 to 0.05)	-0.12 (-0.20 to -0.04)	0.11

Abbreviations: T, tertile.

Multivariable model 1 adjusted for age (years), sex, diabetes (yes/no), hypertension (yes/no), glomerular filtration rate (ml / min/ 1.73 m^2), use of hypouricemic agents (yes/no) and center (in quartiles by number of participants). Multivariable model 2 additionally adjusted for leisure time physical activity (METs.min/week), body mass index (kg/m^2), smoking habit (never, former or current), educational level (primary, secondary or university/graduate), alcohol consumption in g/day (and adding the quadratic term) and 16-point screener (excluding legumes) of Mediterranean diet adherence (continuous).

Table 3. Multivariate-adjusted prevalence ratios and 95% confidence interval for hyperuricemia according to tertiles of energy-adjusted total legume and different subtypes of legume consumption

	Tertiles of non-soy legume consumption in g/day			
	T1 (lowest) n=2,110	T2 n=2,110	T3 (highest) n=2,109	*P*-trend
Total non-soy legumes, median (P25-P75)	11.95 (9.37 to 13.66)	18.42 (16.84 to 20.68)	28.68 (25.75 to 33.05)	
Hyperuricemia, % (n)	36.64 (773)	33.70 (711)	31.67 (668)	
Crude model	1 (Ref.)	0.2 (0.85 to 0.99)	0.86 (0.79 to 0.94)	<0.01
Multivariable model 1	1 (Ref.)	0.92 (0.85 to 0.99)	0.85 (0.78 to 0.93)	<0.01
Multivariable model 2	1 (Ref.)	0.94 (0.86 to 1.01)	0.89 (0.82 to 0.97)	0.01
Lentils, median (P25-P75)	3.72 (3.24 to 3.99)	7.22 (4.45 to 8.10)	8.81 (8.59 to 9.08)	
Hyperuricemia, % (n)	36.64 (773)	33.27 (702)	32.10 (677)	
Crude model	1 (Ref.)	0.91 (0.84 to 0.99)	0.88 (0.81 to 0.95)	<0.01
Multivariable model 1	1 (Ref.)	0.91 (0.84 to 0.99)	0.87 (0.80 to 0.95)	<0.01
Multivariable model 2	1 (Ref.)	0.92 (0.85 to 1.00)	0.89 (0.82 to 0.97)	0.01
Chickpeas, median (P25-P75)	3.42 (0.79 to 3.75)	4.38 (4.17 to 4.65)	8.61 (8.30 to 8.96)	
Hyperuricemia, % (n)	36.02 (760)	33.55 (708)	32.43 (684)	
Crude model	1 (Ref.)	0.93 (0.86 to 1.01)	0.90 (0.83 to 0.98)	0.04
Multivariable model 1	1 (Ref.)	0.94 (0.87 to 1.02)	0.90 (0.83 to 0.98)	0.03
Multivariable model 2	1 (Ref.)	0.95 (0.87 to 1.03)	0.93 (0.86 to 1.01)	0.17
Dry beans, median (P25-P75)	0.78 (0.11 to 3.45)	4.13 (3.96 to 4.31)	8.40 (7.86 to)	
Hyperuricemia, % (n)	35.64 (752)	34.60 (730)	31.77 (670)	
Crude model	1 (Ref.)	0.97 (0.89 to 1.05)	0.89 (0.82 to 0.97)	0.01
Multivariable model 1	1 (Ref.)	0.97 (0.89 to 1.05)	0.89 (0.82 to 0.97)	0.01
Multivariable model 2	1 (Ref.)	0.97 (0.90 to 1.05)	0.91 (0.84 to 0.99)	0.03
Peas, median (P25-P75)	0.04 (0 to 0.34)	3.65 (3.21 to 3.90)	4.76 (4.37 to 8.46)	
Hyperuricemia, % (n)	35.69 (753)	34.12 (720)	32.20 (679)	
Crude model	1 (Ref.)	0.96 (0.88 to 1.04)	0.90 (0.83 to 0.98)	0.02
Multivariable model 1	1 (Ref.)	0.95 (0.87 to 1.03)	0.89 (0.82 to 0.97)	0.01

Multivariable model 2	1 (Ref.)	0.96 (0.88 to 1.04)	0.89 (0.82 to 0.97)	0.01

Abbreviations: T, tertile.

Multivariable model 1 adjusted for age (years), sex, diabetes (yes/no), hypertension (yes/no), glomerular filtration rate (ml / min/ 1.73 m^2), use of hypouricemic agents (yes/no) and center (in quartiles by number of participants). Multivariable model 2 additionally adjusted for leisure time physical activity (METs.min/week), body mass index (kg/m^2), smoking habit (never, former or current), educational level (primary, secondary or university/graduate), alcohol consumption in g/day (and adding the quadratic term) and 16-point screener (excluding legumes) of Mediterranean diet adherence (continuous). All the models were stratified by center (in quartiles by number of participants).