Dairy consumption and risk of frailty in older adults: a prospective cohort study

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ABSTRACT

Background/Objectives. A high quality diet is associated with lower risk of frailty. However, there is little evidence on the effect of individual food consumption. This study examined the association between consumption of dairy products and the risk of frailty in community-dwelling older adults.

Design. Prospective cohort study.

Setting. General population from the Seniors-ENRICA cohort (Spain).

Participants. Community-dwelling adults aged ≥60 years who were free of frailty at baseline (N=1,871).

Measurements. In 2008-2010, food consumption was assessed with a validated diet history. Participants were again examined in 2012 to assess incident frailty, defined as at least three of the five Fried criteria (exhaustion, weakness, low physical activity, slow walking speed, unintentional weight loss). Analyses were performed with logistic regression and adjusted for the main confounders.

Results. During follow-up, 134 new cases of frailty were identified. Compared to consumers of <1 serving/week of low-fat milk/yogurt, the odds ratio (95% confidence interval) of frailty among those consuming ≥7 servings/week was 0.52 (0.29-0.90), *p trend*=.03. The corresponding values for the risk of slow walking speed were 0.64 (0.44-0.92), *p trend*=.01, and for the risk of weight loss were 0.54 (0.33-0.87), *p trend*=.02. No statistically significant association was found between consumption of whole dairy and frailty; the odds ratio (95% confidence interval) was 1.53 (0.90-2.60; *p trend*=.10) for ≥7 servings/week of whole milk/yogurt, and 0.91 (0.52-1.61; *p trend*=.61) for ≥7 servings/week of cheese.

Conclusions. Higher consumption of low-fat milk/yogurt was associated with a reduced risk of frailty and, specifically, of slow walking speed and weight loss. Current recommendations to prevent frailty include protein supplementation; thus, although experimental research is needed, increasing the consumption of low-fat yogurt/milk might prevent frailty among older adults.

KEYWORDS

Frailty; Older Adults; Diet; Dairy Products; Milk.

INTRODUCTION

Frailty is a frequent geriatric syndrome, which results from a cumulative decline in many physiological systems during a lifetime, and is characterized by a state of vulnerability to poor resolution of homoeostasis after even small stressor events (1). Frailty is of clinical and public health relevance because it increases the risk of falls, disability and death (2,3).

There is emerging evidence that links diet to frailty. Age-related anorexia and low-calorie diets might predict frailty (4). In addition, adherence to an index of diet quality (5) or to a Mediterranean diet has been related to lower risk of frailty (6,7). However, there is not much evidence of the effect of individual food consumption or selected nutrients on the risk of frailty. This information is needed to identify the specific components of diet which may explain its effects on frailty and also to help in developing food recommendations to prevent frailty and its adverse consequences. Specifically, it is known that high intake of antioxidant vitamins or proteins could diminish the risk of frailty (8). Moreover, it is biologically plausible that bioavailable calcium and phosphorus could delay sarcopenia and osteoporosis, which are closely related to some frailty criteria (9).

Dairy products are substantial sources of proteins, vitamins and minerals, especially for the elderly population (10,11). Thus, theoretically dairy products could reduce frailty incidence. However, high milk consumption could also have deleterious effects. It has been postulated that a high exposure to D-galactose, a product of the lactose hydrolysis, increases the oxidative stress and therefore may promote aging. In fact, in a large cohort study Michaëlsson el al (12) found that high milk intake was associated with higher mortality and fracture incidence. In addition, whole dairy products add saturated fatty acids to the diet. Despite this controversy, the main dietary guidelines in Spain and other countries recommend the daily consumption of dairy products as part of a healthy diet for the general population (13,14).

Some studies have found positive effects of dairy consumption among elderly people; but the evidence base for this recommendation remains scarce. Kim and Lee found that daily consumption of milk and milk products was inversely associated with functional disability in older men (15). Also, Radavelli-Bagatini et al. found that women consumers of dairy products had greater whole body lean mass and better physical performance than non-consumers (16). However, both studies had a cross-sectional design and did not assess frailty.

Therefore, this study aimed to examine the prospective association between habitual consumption of dairy products and the risk of frailty in older adults living in the community.

METHODS

Study design and participants

Data were taken from the Senior-ENRICA cohort, whose methods have been reported elsewhere (7,17). In brief, the Seniors-ENRICA cohort was derived from the ENRICA study, a cross-sectional survey conducted in 2008-2010 among 12,948 individuals representative of the non-institutionalized adult population of Spain. The primary aim of the ENRICA study was to assess the frequency and distribution of the main components of the natural history of cardiovascular disease, including food consumption and other behavioral risk factors, biological risk factors, early damage of target organs, and diagnosed morbidity (17). The study participants aged 60 years or older (n=2,614), the so-called Seniosr-ENRICA cohort, were again examined in 2012. At baseline, information on socio-demographic variables, lifestyle, health status and morbidity was collected through a phone interview. In two subsequent home visits, the research staff obtained dietary information, conducted a physical exam and obtained blood and urine samples. When the second wave of data collection was performed, we were able to conduct the analyses with 1,871 individuals. A diagram describing the flow of participants across the study is shown in **Figure 1**.

The study protocol was approved by the Clinical Research Ethics Committee of "La Paz" University Hospital in Madrid. All study participants gave written informed consent.

Study variables

Consumption of dairy products

A validated diet history, developed from that used in the EPIC-cohort study in Spain, was used to assess the consumption of up to 880 foods during the last year (15). Specifically, the diet history collected consumption of dairy products, including whole cow milk, low-fat cow milk (2% reduced-fat milk, 1% low-fat milk and fat-free milk), whole and low-fat yogurt, and

cheese. For dairy products, the Pearson correlation coefficient of the diet history against the mean of seven 24-h recalls was 0.68 (18). This computerized diet history included sets of photographs to help participants in estimating the serving size. One standard serving of milk, yogurt and cheese was deemed to contain 250 ml, 125 ml and 40 g, respectively. Nutrient intake was estimated with standard food composition tables (19).

Frailty

We used a slight modification of the operational definition of frailty developed by Fried et al. in the Cardiovascular Health Study (CHS) (20). A participant was considered frail when presenting at least three of these five criteria: exhaustion, weakness, low physical activity, slow walking speed, and weight loss. These criteria were defined as follows: a) *Exhaustion*, as an affirmative answer to any of the following two questions taken from the Center for Epidemiologic Studies Depression Scale (21): "I felt that anything I did was a big effort" and "I felt that I could not get going", with a frequency higher than 3-4 days/week; b) *Weakness*, as the lowest quintile in the CHS of maximum strength on the dominant hand adjusted for sex and body mass index (BMI). Results were based on the highest value of two strength measures using a Jamar dynamometer (22); c) *Low physical activity*, as walking ≤2.5 h/week in men and ≤2 h/week in women; d) *Slow walking speed*, as the lowest quintile in our study sample for the three-meter walking speed test, adjusted for sex and height (22); and e) *Weight loss*, as self-reported involuntary loss ≥4.5 kg of body weight in the last year. Our modification of Fried criteria consisted of using cohort-specific quintiles rather than CHS-based quintiles to define low physical activity and slow walking speed.

Potential confounders

Besides the above variables, we also collected data on factors which could be associated with both dairy consumption and frailty at baseline. Specifically, we asked about socio-

demographic characteristics (sex, age, education, cohabitation) and lifestyle behaviors, including duration of nighttime sleep, smoking, alcohol consumption and physical activity at leisure time (23). Adherence to the Mediterranean diet was estimated with the Trichopoulou index (24), with the alcohol item excluded because alcohol consumption was considered separately. Total energy intake and the amount of proteins, saturated fat and calcium consumed from sources other than dairy products were also calculated.

Data were also obtained on several health-related conditions. First, weight and height were measured twice in each person, in both 2008 and 2012, by trained staff under standardized conditions, using electronic scales and portable extendable stadiometers. BMI was calculated as weight in kg divided by the square of the height in m. Second, diabetes mellitus was identified as fasting serum glucose >126 mg/dl or treatment with oral anti-diabetic drugs or insulin. Third, participants were asked if they were following a diet prescribed by a physician to control hypercholesterolemia, hypertension or hyperglycemia. Fourth, study subjects reported if they had been diagnosed with any of the following diseases: diabetes, cardiovascular disease, chronic obstructive lung disease, cancer at any site, musculoskeletal disorder (osteoarthritis, arthritis or hip fracture) and depression requiring treatment. Fifth, the Lawton-Brody scale of instrumental activities of daily living (IADL) was used to assess participants' functional status (25). An individual is independent if he/she does not report limitation in performing any of the eight instrumental activities considered. And sixth, self-rated health was ascertained with the question: "In general, would you say that your state of health is excellent, very good, good, fair or poor?" Optimal health was defined as excellent, very good or good health.

Statistical analysis

The magnitude of association between consumption of dairy products and the risk of frailty was estimated with odds ratios (OR), and their 95% confidence intervals (CI), obtained from logistic regression. Dairy consumption was classified into three categories, which were modeled with dummy terms: <1 serving/week, 1-6 servings/week, and ≥7serving per week. Two logistic models were built: the first one was adjusted for sex and age, and the second one was additionally adjusted for all the potential confounders described above. The fully-adjusted model was also used to assess the association between dairy consumption and the occurrence of each frailty criterion in robust individuals at baseline, that is, free of all frailty criteria. To test a dose-response relationship we calculated a P for linear trend, by modeling the categories of dairy consumption as a continuous variable.

Socio-demographic and clinical characteristics of study participants, which influence frailty risk, may lead to preferential consumption of whole versus low-fat varieties of dairy products and to the selection of nutrient-rich foods (e.g., cheese). Thus, we tested whether the study association varied with saturated fat, by using interaction terms defined as the product of the categories of dairy products consumption by quartiles of saturated fat intake. The models with and without interaction terms were compared using the likelihood ratio test. Given that we found a significant interaction (p=.02), the analyses have been broken down according to the fat content in dairy products. Stratified analyses by fat content can also be supported by the potential harmful effect of saturated fat from diary. To explore this hypothesis, we performed further analyses to examine whether saturated fat intake from dairy products (in tertiles) was associated with frailty incidence.

Several sensitivity analyses were run to assess the robustness of the main results. First, we replicated the analyses using the lowest quintile of grip strength in our sample to define weakness. Second, to rule out the influence of subclinical frailty status on the study

associations, we repeated the analyses after excluding the following subsets of participants defined at baseline: a) those with suboptimal self-rated health; b) those with diagnosed disease (cardiovascular disease, diabetes, cancer, chronic lung disease, or depression requiring treatment); c) those with limitations in IADL; and d) those who were following a diet (against hypercholesterolemia, hypertension or hyperglycemia) prescribed by a physician. And third, we ran a regression model with additional adjustment for changes in smoking status and physical activity as well as incident diseases between baseline and the end of follow-up 2010.

Statistical significance was set at 2-sided $p<.05$. The analyses were performed with the STATA software (version 13.0; Stata Corp., College Station).

RESULTS

Description of the study sample

The socio-demographic, lifestyle and clinical characteristics at baseline were similar in those who provided updated information at 2012 and in those who did not, although the latter were slightly older (70.0 years old vs. 68.8; p<.001), had lower educational level (15.5% with university studies vs 21.8%; p<.001) and a somewhat higher frequency of diabetes (18.9% vs. 15.4%; p=.05), cardiovascular disease (7.9% vs. 5.4%; p=.02) and other chronic diseases (62.0% vs. 55.2%; p=.005).

In this cohort, the mean (standard deviation) daily intake of total dairy products was 306.3 g (177.5). Specifically, participants consumed an average of 44.7 g (99.4) of whole milk, 158.9 g (157.9) of low-fat milk, 75.7 g (83.2) of yogurt and 27.0 g (35.3) of cheese. Among the 1,871 participants, 94 (5%) consumed ≥7 servings/week of whole milk and 249 (13.3%) of whole yogurt. Taking the two items together, we found that 381 (20.4%) individuals consumed ≥7 servings/week of whole milk/yogurt. The corresponding figures for low-fat milk, low-fat yogurt and low-fat milk/yogurt were 444 (23.7%), 342 (18.5%) and 811 (43.3%), respectively. Lastly, 431 (23.0%) individuals reported consumption of ≥7 servings of cheese per week.

Table 1 shows the characteristics of the study participants according to categories of dairy consumption. Compared to individuals who consumed <1 serving/week of whole milk/yogurt, those who consumed ≥7 servings/week were more frequently male and did less physical activity. They also had lower adherence to the Mediterranean diet, higher energy intake and a slightly greater intake of protein, saturated fat and calcium from sources other than dairy. Moreover, they had a lower prevalence of diabetes and less frequently followed a diet prescribed by a physician. In regard to low-fat milk/yogurt, those consuming ≥7

servings/week were less frequently males, had lower education, were less likely to be smokers, and drank less alcohol. Moreover, they had lower intake of total energy and of saturated fat from sources other than dairy, had a higher prevalence of diabetes and other chronic diseases, and were more likely to be on a diet prescribed by a physician. The characteristics of consumers of higher amounts of cheese were similar to those with a higher consumption of whole milk/yogurt. Lastly, compared with individuals consuming ≥7 servings/week of whole milk/yogurt, those who consumed the same amount of low-fat mil/yogurt were more frequently females, with healthier lifestyles (less smokers, lower alcohol intake and more physically active) but worse health status (more prevalence of diseases and worse self-reported health).

Dairy consumption and risk of frailty

During a mean follow-up of 3.5 years, the cumulative incidence of frailty was 7.2% (134 cases). After adjustment for sex and age, consumption of whole milk/yogurt was associated with an increased risk of frailty (*P trend*=.003). However, in the fully-adjusted analyses the association lost statistical significance (**table 2**). The results were similar when the consumption of whole milk and of whole yogurt was analyzed separately. Conversely, a higher consumption low-fat milk/yogurt was associated with a reduced risk of frailty. Compared to consumers of <1 serving/week of low-fat milk/yogurt, the fully-adjusted OR (95% CI) of frailty among those consuming 1-6 servings/week and ≥7 servings/week was, respectively, 0.55 (0.32-0.97) and 0.52 (0.29-0.90), *P trend*=.03 (**table 2**). Low-fat milk seemed to account for most of the association seen; the corresponding OR (95% CI) of frailty was 0.39 (0.24-0.68) and 0.57 (0.32-0.99), *P trend*=.02. Cheese consumption did not show an association with frailty (**table 2**). Lastly, we found no statistically significant association between saturated fat intake from dairy and frailty incidence. Compared to those in the first

tertile of saturated fat intake, the adjusted ORs (95% CI) for those in the second and third tertiles were, respectively, 0.84 (0.48-1.85) and 0.80 (0.46-1.41).

Supplemental Table 1 shows the results of the sensitivity analyses only for low fat milk/yogurt, as whole milk/yogurt and cheese were not associated with frailty. Results were similar when we repeated the analyses using the sample-specific cut-offs for grip strength (n=1,981) and after excluding individuals with suboptimal subjective health (n=604), severe diagnosed diseases (n=1,207), limitations in IADL (n=207) or who followed a diet prescribed by the physician to control hypercholesterolemia, hypertension or hyperglycemia at baseline (n=1,016). Results were also similar with additional adjustment for changes in lifestyle and for incident diseases between baseline and the end of follow-up.

Table 3 presents the association between consumption of dairy products and each frailty criterion. Higher consumption of whole milk/yogurt showed a non-statistically significant tendency towards increased risk of slow walking speed and weight loss. However, a higher consumption of low-fat milk/yogurt was associated with a reduced risk of these same frailty criteria. Specifically the OR (95% CI) of slow walking speed for those consuming ≥7 versus <1 serving/week was 0.64 (0.44-0.92) and the corresponding value for weight loss was 0.54 (0.33-0.87).

DISCUSSION

Among older adults, a higher consumption of low-fat dairy products, and low-fat milk in particular, was associated with a decreased risk of frailty over a 3.5 year follow-up. This association was mostly due to a reduction in the risk of slow walking speed and weight loss. By contrast, consumption of whole dairy or cheese did not seem to have an effect on frailty after adjustment for several sociodemographic, lifestyle, dietetic and health related characteristics.

In Spain, the Ministry of Health recommends consuming dairy products on a daily basis, but does not support any specific intake. As in the vast majority of Western countries, Spanish food guidelines have encouraged the consumption of skimmed and low-fat dairy because it is a nutrient-rich food providing less energy than whole-fat alternatives (26). For this reason, low-fat milk is largely the choice for fluid milk consumers in Europe and the USA (27,28). Moreover, another advantage of low-fat milk is that it provides less saturated fat than whole milk. Fatty acids, in particular those with a medium or long chain (e.g. lauric, myristic and palmitic), increase LDL-cholesterol and promote atherosclerosis (29). Recent meta-analyses have shown that low-fat milk consumption decreases the risk of cardiometabolic disorders, including excess weight, hypertension, diabetes and cardiovascular disease (30-32). Our results showed that older adults in Spain -- particularly those with diagnosed diseases -- also prefer low-fat dairy, probably because they are already following physician advice to prevent complications.

Consumption of low-fat milk/yogurt may reduce the risk of frailty through several mechanisms. Calcium and protein intake from milk could delay sarcopenia and bone loss (33), which are health disorders associated with frailty. Moreover, dairy products are a main source of proteins, vitamins and minerals among the elderly (34). Consumption of dairy

products could also lower the risk of frailty by reducing the frequency of some cardiometabolic conditions (35,36). A meta-analysis of cohort studies found a modest inverse association between dairy consumption and cardiovascular disease, probably due to the positive effects of dairy on blood pressure (37). Several well-designed prospective studies reported a reduction in the incidence of hypertension among high consumers of low-fat but not whole-fat dairy products (38,39). Milk minerals (e.g. calcium, potassium, magnesium and phosphorus) might be responsible for the antihypertensive effect (37). Furthermore, bioactive peptides from milk casein and whey proteins haven been recently shown to have a beneficial impact on blood pressure. Among their properties, they seem to facilitate mineral absorption, to inhibit angiotensin-converting enzyme and to have opioid-like activities that can modulate blood pressure (26). Dairy products also seem to reduce inflammatory markers, to augment insulin sensitivity and to lower plasma insulin (40), which are well known core risk factors for frailty (36). Nevertheless, milk minerals, bioactive peptides and other of the components mentioned above are present both in low-fat and in whole-fat dairy, and we found a different association of dairy products with frailty according to their fat content. These results suggest that the saturated fat content in dairy products could influence the risk of frailty. In fact, low-fat dairy products combine some beneficial effects of dairy without the detrimental effects of saturated fats (40). However, given that we did not find a higher risk of frailty among consumers of higher amounts of saturated fat, another possible explanation for the divergent finding on the role of whole versus low-fat dairy on frailty is that individuals choosing low-fat dairy products have clinical characteristics which are different from those who choose the whole-fat varieties, and which have not been adequately addressed in our analyses. In any case, our results on a different effect of low-fat and whole-fat products did not derive from a hypothesis formulated *a priori*, and should be confirmed in future research.

No previous studies have explored the association between dairy consumption and frailty. Nevertheless, a recent examination of the effect of dairy on endpoints related to frailty showed results concordant with ours. Kim and Lee carried out a cross-sectional analysis among 747 community-dwelling individuals aged ≥65 from the Korea National Health and Nutrition Examination Survey; in this analysis, consumption of dairy products in men was inversely associated with IADL limitations, a frequent consequence of frailty (15). In another cross-sectional study with 1,456 Australian women aged 70-85 years, Radavelli-Bagatini et al. found that those in the highest tertile of dairy consumption had greater lean body mass and grip strength as well as lower odds for a poor timed-up-and-go test (a measure of walking speed) (16).

We also observed that a higher intake of low-fat dairy was associated with a lower risk of slow walking speed and weight loss. This is particularly important because slowness is usually considered the most important frailty criterion (41). Birnie et al. found that consumption of milk and calcium during childhood was associated with faster walking time from the timed-up-and-go test among individuals aged 63-86 years (42). Also, as commented above, Radavelli-Bagatini et al. (16) obtained results consistent with ours on gait speed. Nevertheless, the lower risk of weight loss associated with low-fat dairy could be explained by reverse causality. Participants who tend to lose weight may have been advised to avoid low-fat dairy products, unlike individuals with appropriate weight management.

Our study has several strengths and limitations. Among the strengths is the relatively large size of the study cohort, and the use of a validated instrument for estimating usual intake of foods and nutrients and with sufficient detail on the main varieties of dairy products (18). Moreover, a good number of sensitivity analyses produced similar results, which suggest that they are robust.

Among the limitations is that, despite using a validated diet history, there could still be some recall bias in diet assessment; although this type of bias usually tends to underestimate study associations, it did not preclude the observation of an inverse relationship between low-fat milk/yogurt and frailty. Second, the competitive risk with mortality may have led to underestimation of frailty incidence, because the more robust individuals are more likely to survive until the end of follow-up. Nevertheless, the mortality rate was low, so this bias is probably small. Third, weight-loss was self-reported, which might have led to a certain classification error in the observed associations. Fourth, some residual confounding cannot be ruled out. One study found that individuals who complied with dietary guidelines consumed low-fat dairy products more frequently than non-compliers (43). However, this was not the case in our study because older individuals with higher consumption of low fat milk/yogurt showed quite similar adherence to the Mediterranean diet and comparable intakes of protein, saturated fat and calcium from sources other than dairy. Moreover, the prevalence of obesity and other chronic diseases was similar, or even slightly higher, in those in the highest versus the lowest tertile of low-fat dairy intake; this would not affect or would simply tend to increase the risk of frailty in the consumers of higher amounts of low-fat dairy. Lastly, the analyses were adjusted for a large number of confounders, including education, cohabitation, lifestyle and clinical characteristics. Therefore, we believe that uncontrolled confounding cannot entirely explain the protective association between low-fat dairy and frailty.

In conclusion, in this prospective cohort study of older adults, consumption of at least 7 servings/week of low-fat milk and yogurt was associated with a lower risk of frailty and, specifically, of slow walking speed and weight loss. Current recommendations to prevent or treat frailty include protein supplementation (2). Our results suggest that, among individuals with a low consumption of low-fat yogurt/milk, an increase in the consumption of these products may be a useful and easy-to-implement intervention to prevent frailty by providing

these nutrients; nevertheless, the efficacy of this intervention should be assessed in experimental studies.

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Conflict of interest

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Elements of Financial/Personal Conflicts	***Author 1: Alberto Lana**		**Author 2: Fernando Rodríguez-Artalejo**		**Author 3: Esther López-Garcia**	
	Yes	**No**	**Yes**	**No**	**Yes**	**No**
Employment or Affiliation		**x**		**x**		**x**
Grants/Funds		**x**		**x**		**x**
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Speaker Forum		**x**		**x**		**x**
Consultant		**x**		**x**		**x**
Stocks		**x**		**x**		**x**
Royalties		**x**		**x**		**x**
Expert Testimony		**x**		**x**		**x**
Board Member		**x**		**x**		**x**
Patents		**x**		**x**		**x**
Personal Relationship		**x**		**x**		**x**

Author Contributions

EL-G and FR-A conceived and designed the study. AL and EL-G conducted the statistical analyses. AL drafted the manuscript. All authors made substantial contributions to the analysis and interpretation of the data, revised the manuscript for important intellectual content, and approved the final version. FR-A is guarantor.

Sponsor's Role

The study funders had no role in study design or in the collection, analysis, and interpretation of data. The authors have sole responsibility for the manuscript content. Fernando Rodríguez-Artalejo has full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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GRAPHICS

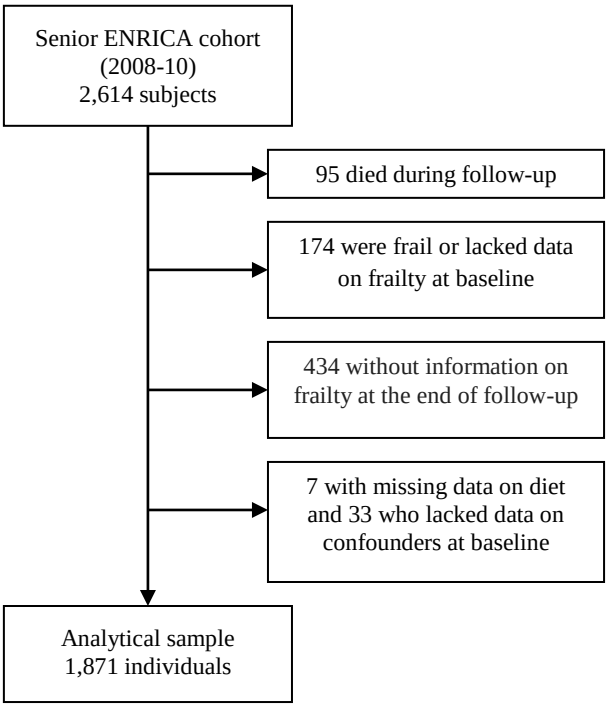

Figure 1. Flow diagram

Table 1. Baseline characteristics of the study participants, according to categories of dairy products consumption (N=1,871)

	Whole milk/yogurt			Low fat milk/yogurt			Cheese		
	<1 serving/week	**1-6 serving/week**	**≥7 servings/week**	**<1 serving/week**	**1-6 serving/week**	**≥7 servings/week**	**<1 serving/week**	**1-6 serving/week**	**≥7 servings/week**
Participants, n (%)	1,007 (50.8)	483 (25.8)	381 (20.4)	417 (22.3)	643 (34.4)	811 (43.3)	546 (29.2)	894 (47.8)	431 (23.0)
Dairy intake, g/d	3.8 (7.6)	93.1 (50.3)	255.8 (150.5)	0.6 (3.8)	144.7 (55.0)	348.9 (154.8)	0.9 (1.5)	19.8 (9.6)	74.9 (44.1)
Pre-frail, %	20.7	18.6	21.8	19.2	21.6	19.9	22.1	19.6	19.7
Gender, male	46.1	52.0	50.7	59.0	48.5	43.2***	44.9	47.7	55.0**
Age, y	68.8 (6.3)	68.3 (6.3)	68.7 (6.6)	68.0 (6.0)	68.9 (6.7)	68.8 (6.4)	68.8 (6.4)	68.5 (6.3)	68.8 (6.6)
Living alone, %	17.4	12.2	16.3*	15.6	14.6	16.9	18.7	13.9	16.2
Education, primary or less, %	54.3	47.8	55.6	50.4	51.0	55.7*	55.5	53.1	49.2
Night sleep, h/d	6.8 (1.4)	6.9 (1.3)	6.9 (1.4)	6.9 (1.4)	6.8 (1.3)	6.9 (1.4)	6.8 (1.4)	6.9 (1.3)	6.8 (1.4)
Current smoker, %	10.5	15.3	10.2	16.3	12.8	8.5***	12.6	10.5	13.0*
Alcohol intake, g/d	10.3 (17.9)	10.6 (17.6)	11.2 (18.1)	15.5 (23.9)	10.1 (15.7)	8.3 (25.2)***	9.6 (17.1)	10.7 (17.5)	11.5 (18.4)
Physical activity, METs h/wk	22.2 (15.7)	21.8 (15.0)	20.8 (14.9)	21.7 (16.4)	21.4 (15.1)	22.2 (15.1)	21.2 (15.8)	22.1 (15.0)	21.8 (15.6)
Mediterranean diet score[a]	4.7 (1.5)	4.6 (1.4)	3.9 (1.5)***	4.6 (1.7)	4.8 (1.6)	4.3 (1.4)**	4.8 (1.5)	4.7 (1.5)	3.9 (1.6)***
Energy intake, kcal/d[b]	1,777 (541)	1,936 (527)	1,917 (543)***	1,927 (544)	1,886 (563)	1,775 (517)***	1,752 (538)	1,894 (544)	1,869 (534)**
Protein intake, g/d[b]	78.5 (20.3)	80.4 (26.6)	80.1 (22.6)	79.5 (23.5)	79.4 (23.1)	79.1 (25.7)	77.3 (27.7)	80.4 (22.6)	79.5 (24.2)
Saturated fat, g/d[b]	17.1(8.3)	19.5 (8.4)	20.0 (8.2)***	19.4 (8.5)	19.0 (8.6)	17.2 (8.1)**	17.1 (7.9)	19.0 (8.7)	18.3 (8.3)
Calcium, mg/d[b]	473 (159)	483 (141)	535 (160)***	460 (157)	462 (147)	523 (157)***	477 (164)	494 (147)	490 (165)
Body mass index, kg/m^2	28.4 (4.3)	28.2 (3.8)	28.6 (4.5)	28.1 (4.2)	28.5 (4.2)	28.5 (4.3)	28.0 (4.1)	28.5 (4.2)	28.7 (4.5)*
Diabetes, %	15.1	16.2	12.9	12.0	15.7	15.8	16.9	14.9	12.5
Cardiovascular disease, %	5.9	4.6	4.2	5.5	4.4	5.7	5.0	4.6	6.7
Chronic obstructive lung disease, %	8.2	7.0	6.6	7.9	6.4	8.4	7.7	7.5	7.7
Cancer, %	1.9	1.9	1.6	0.2	1.9	2.6*	2.2	0.9	3.3*
Musculoskeletal disorder , %	49.7	43.9	45.4	41.0	46.0	51.5**	46.9	48.4	45.5
Depression requiring treatment, %	6.9	8.5	6.8	6.0	6.5	8.6	8.1	6.2	8.8
On a diet prescribed by a physician, %	57.8	49.9	50.7**	43.9	54.3	59.7***	50.6	56.3	55.0
Independent in IADL, %	89.5	87.6	89.2	88.5	88.0	89.9	89.4	89.3	87.4
Self-rated health, good to excellent,%	65.9	71.8	67.2	72.7	67.7	65.2*	65.8	67.3	72.2*

One serving of milk = 250 ml / One serving of yogurt = 125 ml / One serving of cheese = 40 g. IADL: Instrumental activities of daily living.
For continuous variables mean and standard deviation (SD) are reported.
*p<.05; **p<.01; ***p<.001: differences between extreme categories of consumption.
[a]Trichopoulou index (excluding alcohol consumption).
[b]From sources other than dairy products.

Table 2. Odds ratios (95% confidence interval) for the association between consumption of dairy products and risk of frailty during a 3.5 year follow-up of older adults. (N=1,871)

	<1 serving/week	1-6 servings/week	≥7 servings/week	P-value for trend
Whole milk/yogurt				
Frail events, n	62	32	40	
Model 1	1.00	1.25 (0.79-1.98)	1.95 (1.26-3.03)	.003
Model 2	1.00	1.26 (0.75-2.13)	1.53 (0.90-2.60)	.10
Whole milk				
Frail events, n	92	31	11	
Model 1	1.00	1.46 (0.93-2.28)	2.10 (1.04-4.24)	.001
Model 2	1.00	1.49 (0.89-2.49)	1.50 (0.65-3.44)	.12
Whole yogurt				
Frail events, n	84	19	31	
Model 1	1.00	0.96 (0.56-1.63)	2.11 (1.33-3.35)	.006
Model 2	1.00	0.87 (0.47-1.61)	1.76 (1.01-3.14)	.12
Low-fat milk/yogurt				
Frail events, n	34	45	55	
Model 1	1.00	0.63 (0.39-1.04)	0.62 (0.39-0.99)	.07
Model 2	1.00	0.55 (0.32-0.97)	0.52 (0.29-0.90)	.03
Low-fat milk				
Frail events, n	53	51	30	
Model 1	1.00	0.48 (0.31-0.73)	0.58 (0.36-0.95)	.02
Model 2	1.00	0.39 (0.24-0.68)	0.57 (0.32-0.99)	.02
Low-fat yogurt				
Frail events, n	83	24	27	
Model 1	1.00	0.81 (0.50-1.33)	1.03 (0.64-1.66)	.92
Model 2	1.00	0.80 (0.45-1.40)	0.87 (0.47-1.60)	.53
Cheese				
Frail events, n	48	53	33	
Model 1	1.00	0.69 (0.45-1.05)	0.93 (0.57-1.50)	.61
Model 2	1.00	0.66 (0.41-1.07)	0.91 (0.52-1.61)	.61

One serving of milk = 250 ml; one serving of yogurt = 125 ml: one serving of cheese = 40 g.
Model 1: logistic regression model adjusted for sex and age (<65, 65-69, 70-74, 75-79, ≥80 years).
Model 2: logistic regression model additionally adjusted for living alone (yes, no), educational level (primary or less, secondary, university), night sleep (quartiles of hours/d), smoking (never smoker, past, current), alcohol intake (quartiles of g/d), physical activity at leisure time (quartiles of METs h/week), Trichopoulou index (tertiles), energy (quartiles of kcal/d), protein (quartiles of g/d), calcium (quartiles of mg/d) and saturated fat intake (quartiles of g/d) from sources other than dairy products. body mass index (<25, 25-<30, ≥30 kg/m^2), diabetes, cardiovascular disease, chronic obstructive lung disease, cancer, musculoskeletal disorder, depression, following a diet prescribed by a physician, independent in IADL, and self-rated health (optimal, suboptimal).

Table 3. Odds ratios (95% confidence interval)[a] for the association between consumption of dairy products and each frailty criterion during a 3.5-year follow-up of older adults. (N=1,871)

	<1 serving/week	1-6 servings/week	≥7 servings/week	P-value for trend
Exhaustion				
Whole milk/yogurt	1.00	0.84 (0.57-1.22)	1.13 (0.76-1.67)	.78
Low-fat milk/yogurt	1.00	0.83 (0.55-1.25)	0.80 (0.53-1.21)	.33
Cheese	1.00	0.71 (0.51-1.01)	0.78 (0.51-1.18)	.16
Low physical activity				
Whole milk/yogurt	1.00	1.24 (0.90-1.71)	1.20 (0.83-1.73)	.24
Low-fat milk/yogurt	1.00	0.83 (0.58-1.19)	0.86 (0.67-1.31)	.94
Cheese	1.00	1.20 (0.87-1.66)	0.98 (0.66-1.46)	.97
Slow walking speed				
Whole milk/yogurt	1.00	1.73 (1.26-2.37)	1.22 (0.84-1.77)	.07
Low-fat milk/yogurt	1.00	0.84 (0.59-1.18)	0.64 (0.44-0.92)	.01
Cheese	1.00	1.02 (0.74-1.41)	1.15 (0.79-1.69)	.51
Weight loss				
Whole milk/yogurt	1.00	1.16 (0.75-1.79)	1.52 (0.96-2.41)	.08
Low-fat milk/yogurt	1.00	0.66 (0.42-1.06)	0.54 (0.33-0.87)	.01
Cheese	1.00	0.98 (0.64-1.48)	0.91 (0.54-1.53)	.74
Muscle weakness				
Whole milk/yogurt	1.00	1.29 (1.00-1.69)	1.17 (0.77-1.41)	.50
Low-fat milk/yogurt	1.00	0.82 (0.61-1.11)	0.89 (0.67-1.23)	.65
Cheese	1.00	0.92 (0.71-1.19)	1.04 (0.76-1.42)	.87

One serving of milk=250 ml; one serving of yogurt=125 ml; one serving of cheese=40 g.

[a]Obtained from logistic regression models adjusted sex, age (<65, 65-69, 70-74, 75-79, ≥80 years), living alone (yes, no), educational level (primary or less, secondary, university), night sleep (quartiles of hours/d), smoking (never smoker, past, current), alcohol intake (quartiles of g/d), physical activity at leisure time (quartiles of METs h/week), Trichopoulou index (tertiles), energy (quartiles of kcal/d), protein (quartiles of g/d), calcium (quartiles of mg/d) and saturated fat intake (quartiles of g/d) from sources other than dairy products. body mass index (<25, 25-<30, ≥30 kg/m2), diabetes, cardiovascular disease, chronic obstructive lung disease, cancer, musculoskeletal disorder, depression, following a diet prescribed by a physician, independent in IADL, and self-rated health (optimal, suboptimal).

Supplemental Table 1. Sensitivity analyses for the association between consumption of low-fat milk/yogurt and risk of frailty during a 3.5 year follow-up of older adults. (N=1,871)

	<1 serving/week	1-6 servings/week	≥7 servings/week	P-value for trend
Defining weakness as lowest quintile of grip strength in our sample				
Frail events, n	25	35	47	
OR (95% CI)[a]	1.00	0.45 (0.23-0.90)	0.60 (0.32-1.16)	.07
Excluding people with suboptimal self-rated health				
Frail events, n	23	32	38	
OR (95% CI)[a]	1.00	0.32 (0.14-0.74)	0.37 (0.17-0.83)	.03
Excluding people with diagnosed disease				
Frail events, n	31	40	51	
OR (95% CI)[a]	1.00	0.41 (0.21-0.79)	0.49 (0.26-0.91)	.009
Excluding people with limitations in IADL				
Frail events, n	11	21	14	
OR (95% CI)[a]	1.00	0.19 (0.02-1.62)	0.08 (0.01-1.00)	.04
Excluding people who were following physician diet advice				
Frail events, n	17	27	34	
OR (95% CI)[a]	1.00	0.25 (0.09-0.68)	0.25 (0.11-0.63)	.02
Additionally adjusted for changes during follow-up				
Frail events, n	34	45	55	
OR (95% CI)[b]	1.00	0.45 (0.25-0.83)	0.51 (0.29-0.91)	.01

One serving of milk = 250 ml; one serving of yogurt = 125 ml: one serving of cheese = 40 g.

[a]Obtained from logistic regression models adjusted for sex, age (<65, 65-69, 70-74, 75-79, ≥80 years), living alone (yes, no), educational level (primary or less, secondary, university), night sleep (quartiles of hours/d), smoking (never smoker, past, current), alcohol intake (quartiles of g/d), physical activity at leisure time (quartiles of METs h/week), Trichopoulou index (tertiles), energy (quartiles of kcal/d), protein (quartiles of g/d), calcium (quartiles of mg/d) and saturated fat intake (quartiles of g/d) from sources other than dairy products. body mass index (<25, 25-<30, ≥30 kg/m^2), diabetes, cardiovascular disease, chronic obstructive lung disease, cancer, musculoskeletal disorder, depression, following a diet prescribed by a physician, independent in IADL, and self-rated health (optimal, suboptimal).

[b]Additionally adjusted for change in smoking status (maintenance or quitted smoking), change in physical activity (maintenance, less or more physical activity) and incident diseases between baseline and the end of follow-up 2010